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SHORT COMMUNICATIONS

First Selenium-containing Mucochloric Acid Derivatives

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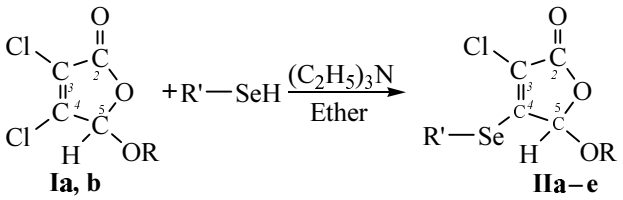
Mucochloric acid [3,4-dichloro-5-hydroxy-2-(5*H*)-furanone (**Ia**)] is an available polyfunctional heterocycle of high reactivity [1]. Thanks to the presence of several active sites this compound possesses great synthetic opportunities, permits incorporation into the lactone ring of various functional groups to obtain new compounds with useful characteristics. Among them compounds were found with antitumor activity, fungicidal, bactericidal, herbicidal properties etc. [2–5]. We report here on preparation and characterization of the first selenium-containing derivatives of mucochloric acid that presumably also could show biological activity and versatile reactivity [6].

Reactions of mucochloric acid with selenophenols were performed in ethyl ether in the presence of triethylamine at equimolar ratio of reagents and base (1:1:1).

Isolated compounds **IIa–d** are stable solids; their purity and homogeneity was checked by TLC, and the composition was confirmed by elemental analysis.



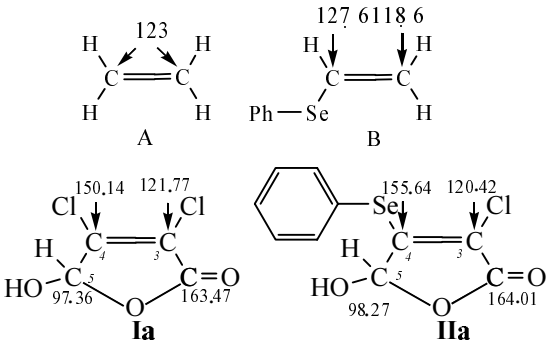
Ia, b **IIa–e**

I, R = H (**a**), C_2H_5 (**b**); II, R = H, R' = Ph (**a**), 3-$CH_3C_6H_4$ (**b**), 3-$CH_3OC_6H_4$ (**c**), 4-BrC_6H_4 (**d**); R = C_2H_5, R' = Ph (**e**).

The compounds synthesized were identified with the use of IR and NMR spectroscopy. The IR spectra of compounds **IIa–d** contain a broad absorption band of medium intensity in the region 3250–3300 cm^{-1} (stretching vibrations of hydroxy group), a strong band in the region 1760–1772 cm^{-1} (stretching vibrations of C=O bond in γ-lactone [7]) often accompanied by a weak band in the region 1742–1744 cm^{-1}, and a narrow strong band at 1580–1600 cm^{-1} characteristic of the stretching vibrations of C=C bonds in the aromatic system. The comparison of IR spectra of mucochloric acid and compounds **IIa–d** suggests that the reaction occurs with the retention of the lactone ring and replacement of one chlorine atom.

In the ^1H NMR spectra of compounds **IIa–d** three principal types of signals are observed: a singlet in the region 5.4–6.0 ppm belonging to the methine proton at atom C^5, a multiplet at 7.0–8.0. ppm characteristic of aromatic protons, and a signal of hydroxy group proton (a wide diffuse peak in the region 2.5–4.5 ppm in $CDCl_3$ solutions, and in the spectrum of compound **IIa** registered in DMSO-d_6 the peak at 8.2 ppm).

The chlorine atom in **Ia** can be replaced both in position *3* and *4* of the lactone ring. Interestingly, phenol as nucleophile substitutes the chlorine in position *3* [8], whereas thiophenol gives rise to a 4-substituted product [9, 10]. The location of PhSe group was established by comparison of ^{13}C NMR spectra in DMSO-d_6 solutions of furanones **Ia** and **IIa**, and model compounds A and B [11]:



Ia **IIa**

General trends in the chemical shifts variation of ethylene carbon atoms under the influence of the phenylselenium group (strong downfield shift of C^{α} resonance and upfield shift of C^{β} peak) unambiguously indicate that the replacement of chlorine occurred at C^4 atom. Similar structure have also selenoethers **IIb–d** and compound **IIe** obtained in reaction of selenophenol with 3,4-dichloro-5-ethoxy-2(5*H*)-furanone (**Ib**). In the ^{1}H NMR spectrum of compound **IIe** appear signals of benzene ring protons at 7.3–7.8 ppm, of ethoxy group as a triplet of methyl protons and two multiplets of diastereotopic methylene protons characterized by strong nonequivalence (Δδ 0.52 ppm), and also a singlet (δ 5.47 ppm) from the proton attached to atom C^5 of γ-lactone. Comparison of ^{13}C NMR spectra belonging to compounds **Ib** and **IIe** and also with those of compounds **IIa–d** proved that the lactone ring is retained in compound **IIe**, and chlorine substitution occurred in the β-position with respect to the carbonyl group.

The results obtained suggest a conclusion that in the presence of bases arylselenoles behave similar to arylthiols [9, 10].

IR spectra were recorded on spectrometer Specord M80 from mulls in mineral oil, cell thickness *d* 0.10–0.12 mm. NMR spectra were registered on spectrometers Varian Unity-300 with operating frequencies 299.94 (^{1}H) and 75.13 (^{13}C) MHz and Varian Gemini-200 with operating frequencies 200 (^{1}H) and 50.46 (^{13}C) MHz at 25°C from solutions in $CDCl_3$ and DMSO-d_6. Chemical shifts were measured from signals of residual protons of solvents. TLC analyses were carried out on Silufol UV-254 plates, eluent acetone–benzene, 1:8 by volume. Commercial mucochloric acid (**Ia**) was recrystallized from water.

General preparation procedure for 3-chloro-4-arylseleno-5-hydroxy-2(5*H*)-furanones (IIa–d). To a solution of 1 g (6 mmol) of mucochloric acid in ether was slowly added dropwise at vigorous stirring 6 mmol of solution of selenophenol in ether, and then 6 mmol of triethylamine. Therewith the reaction mixture slightly self-heated, and precipitated white salt $(C_2H_5)_3N{\cdot}HCl$. The precipitate was filtered off, washed with ether. The filtrate was evaporated to dryness in a vacuum of a water-jet pump. The residue was recrystallized from a mixture petroleum ether–benzene, 1:1.

3-Chloro-4-phenylseleno-5-hydroxy-2(5*H*)-furanone (IIa). Yield 57%, mp 148°C, R_f 0.58. IR spectrum, ν, cm^{-1}: 3272 br (OH), 1772, 1744 (C=O), 1596 (C=C arom). ^{1}H NMR spectrum (200 MHz, DMSO-d_6), δ, ppm: 6.03 s (1H, C^5H), 7.2–8.0 m (5H, Ph), 8.19 s (1H, OH). ^{13}C NMR spectrum (50 MHz, DMSO-d_6), δ, ppm: 98.27 (C^5), 120.42 (C^3), 122.83, 128.22, 129.53, 135.74 (C, Ar), 155.64 (C^4), 164.01 (C^2). Found, %: C 42.30; H 2.14; Cl 12.48. $C_{10}H_7ClO_3Se$. Calculated, %: C 41.48; H 2.44; Cl 12.24.

3-Chloro-4-(3-methylphenyl)seleno-5-hydroxy-2-(5*H*)-furanone (IIb). Yield 60%, mp 93°C, R_f 0.60. IR spectrum, ν, cm^{-1}: 3250 br (OH), 1772, 1744 (CO), 1592 (C=C arom). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 1.38 s (3H, Me), 2.5–3.5 br.s (1H, OH), 5.46 s (1H, C^5H), 7.2–7.8 m (4H, C_6H_4). Found, %: C 45.66; H 2.48; Cl 11.73. $C_{11}H_9ClO_3Se$. Calculated, %: C 43.81; H 2.00; Cl 11.55.

3-Chloro-4-(3-methoxyphenyl)seleno-5-hydroxy-2(5*H*)-furanone (IIc). Yield 69%, mp 117°C, R_f 0.50. IR spectrum, ν, cm^{-1}: 3260 br (OH), 1760 (CO), 1586 (C=C arom). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 3.79 s (3H, Me), 4.0–4.6 br.s (1H, OH), 5.77 s (1H, C^5H), 6.9–7.4 m (4H, C_6H_4). Found, %: C 41.86; H 2.63; Cl 10.89. $C_{11}H_9ClO_4Se$. Calculated, %: C 41.34; H 2.84; Cl 11.09.

3-Chloro-4-(4-bromophenyl)seleno-5-hydroxy-2-(5*H*)-furanone (IId). Yield 56%, mp 146°C, R_f 0.61. IR spectrum, ν, cm^{-1}: 3300 br (OH), 1768, 1742 (C=O), 1592 (C=C arom). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 3.2–4.2 br.s (1H, OH), 5.76 s (1H, C^5H), 7.3–7.7 m (4H, C_6H_4). Found, %: C 33.89; H 1.63; Br 22.09; Cl 9.80. $C_{10}H_6BrClO_3Se$. Calculated, %: C 32.60; H 1.64; Br 21.70; Cl 9.60.

3,4-Dichloro-5-ethoxy-2(5*H*)-furanone (Ib) was prepared by known procedure [12].

3-Chloro-4-phenylseleno-5-ethoxy-2(5*H*furanone (IIe) was obtained in the same way as compounds **IIa–d** from reagent **Ib** and PhSeH. Yield 66%, mp 65°C (petroleum ether–ethyl ether), R_f 0.65. IR spectrum, ν, cm^{-1}: 1776, 1760 (C=O), 1592 (C=C arom). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ, ppm: 1.01 t (3H, Me), 3.09 d.q (1H, ^3J 7.1, ^2J 9.1 Hz), 3.61 d. q (1H, ^3J 7.1, ^2J 9.1 Hz), 5.47 s (1H, C^5H), 7.3–7.8 m (5H, Ph). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ, ppm: 14.48 (Me), 65.89 (CH_2), 101.71 (C^5), 121.27 (C^3), 121.98, 129.55, 130.19, 136.90 (C, Ph), 153.25 (C^4), 164.04 (C^2). Found, %: C 43.28; H 1.97; Cl 11.18. $C_{12}H_{11}ClO_3Se$. Calculated, %: C 43.35; H 3.40; Cl 11.18.

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