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# Electrophilic Intramolecular Cyclization of Functional Derivatives of Unsaturated Compounds: IV.* Cyclosulfenylation of 5-Hexenoic Acid Amides and Nucleophilic Cleavage of Reaction Products

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**Abstract**—Anilides of 5-hexenoic acid react with arylsulfenyl chlorides in nitromethane in the presence of lithium perchlorate affording products of electrophilic cyclization, *N*-{6-[(arylsulfanyl)methyl]tetrahydro-2*H*-pyran-2-ylidene}anilinium perchlorates. The treatment of the latter with sodium acetate or secondary cycloalkylamines in the presence of water results in the opening of the tetrahydropyran ring and provides anilides or cycloalkylamides of 6-arylsulfanyl-5-hydroxyhexanoic acid.

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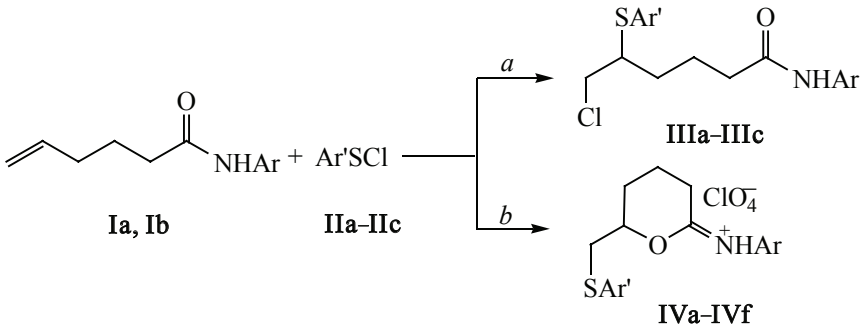
Electrophilic intramolecular cyclizations of amides of unsaturated carboxylic acids is an efficient synthetic tool for designing lactones and lactams containing in the side chain halogen atoms and selenyl moieties [2, 3].

Yet the cyclosulfenylation of unsaturated acid is described in the literature far less often [4, 5], and this promoted us to carry out a systematic research in order to establish the effect of the structural parameters of reagents and of the external conditions on the cyclization process. In particular, we formerly investigated the reaction of arylsulfenyl chlorides with *N*-substituted amides of cinnamyl- [6], styryl- [1], allylacetic acids [7]. In the latter case stable intermediates of iminium type were isolated and the conditions were developed for their selective conversion into 5-[(arylsulfanyl)methyl]furan-2-ones. It looked reasonable to carry out this type reaction with 5-hexenoic acid amides, homologs of allylacetamides. It was expected that the introducing of an additional methylene unit between the nucleophilic sites, alkenyl and carbamoyl groups, would somehow affect both the

**Scheme 1.**




**Ia, Ib** **IIa–IIc** **IIIa–IIIc** **IVa–IVf**

**I**, Ar = Ph (**a**), 4-$MeOC_6H_4$ (**b**); **II**, Ar′ = Ph (**a**), 4-$MeC_6H_4$ (**b**), 4-$NO_2C_6H_4$ (**c**); **III**, Ar = 4-$MeOC_6H_4$, Ar′ = 4-$MeC_6H_4$ (**a**), 4-$NO_2C_6H_4$ (**b**); Ar = Ph, Ar′ = 4-$MeC_6H_4$ (**c**); **IV**, Ar = Ph, Ar′ = 4-$NO_2C_6H_4$ (**a**), Ph (**c**), 4-$MeC_6H_4$ (**d**); Ar = 4-$MeOC_6H_4$, Ar′ = 4-$NO_2C_6H_4$ (**b**), Ph (**e**), 4-$MeC_6H_4$ (**f**).

* For Communication III, see [1]

stage of the formation of the primary cyclic structure and the stages of further transformations. Formerly the 5-hexenoic acid [8] and its nitrile [9, 10] were used as initial compounds in the synthesis of 6-functionalized δ-lactones.

Here we report on the study of the reaction between *N*-arylhex-5-enamides **Ia, Ib** with arylsulfenyl chlorides **IIa–IIc** in chloroform, acetic acid, and nitromethane. It was found by an example of anilide **Ib** and sulfenyl chlorides **IIb, IIc** that in the weakly polar chloroform the sulfenyl chlorides added to the multiple bond C=C of the unsaturated acid amide with the formation of 5-arylsulfanyl-6-chlorohexanoic acid amides **IIIa, IIIb** in 54–64% yields (Scheme 1, *a*).

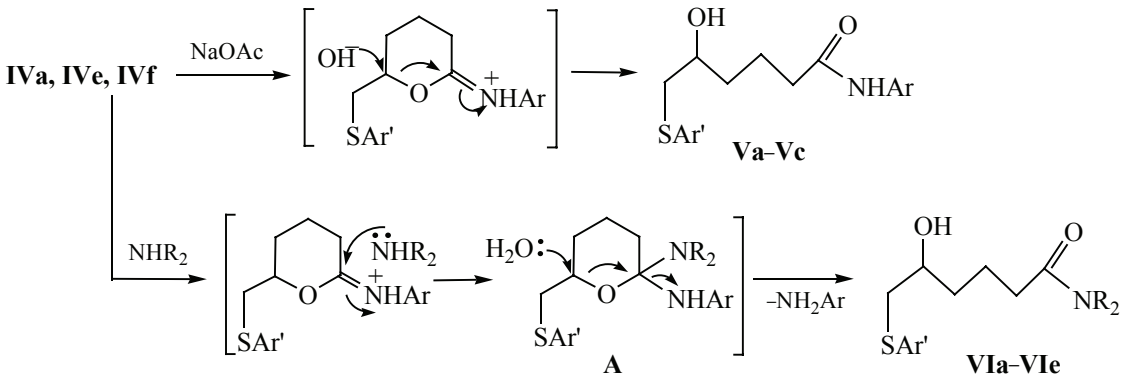
The increase in the ionizing ability of the environment at the use of acetic acid and equimolar addition of lithium perchlorate was successfully used to obtain the products of electrophilic intramolecular cyclization [11, 12]. We found that these conditions were hardly suitable for the reactions of hexenamides **Ia, Ib** with sulfenyl chlorides **IIa, IIb** since in most events mixtures of addition products **III** and cyclization products **IV** formed in the ratio 1 : 1. Due to instability of these products in the conditions of chromatography we failed to separate these mixtures. Only solid noncyclic compound **IIIc** was isolated individually from the reaction mixture in a 38% yield. In the case of the more electrophilic 4-nitrophenylsulfenyl chloride (**IIc**) the reaction occurred with a high selectivity and led to the formation in 74 and 85% yields of sparingly soluble in the acetic acid cyclic perchlorates **IVa, IVb** (Scheme 1, *b*).

The most effectively the reaction was directed to the formation of cyclic compounds **IV** at the application as solvent of nitromethane with equimolar addition of $LiClO_4$. Under these conditions the reaction of amides **Ia, Ib** with arylsulfenyl chlorides **IIa, IIb** gave rise to *N*-aryl-*N*-{6-[(arylsulfanyl)methyl]tetrahydropyran-2*H*-ylidene}aminium perchlorates **IVc–IVf** in 58–91% yields. Salt-like compounds **IVa–IVf** are stable in the absence of air moisture and gradually decompose at prolonged storage. They belong to the rare type of iminium salts, only two of which have been isolated before in the individual state [13, 14].

The structure of all compounds synthesized is consistent with their spectral parameters. In the $^1$H NMR spectra of addition products **IIIa–IIIc** the informative signals are the multiplets of the protons $H^5$ at 3.80–4.02 ppm, and in the $^{13}$C NMR spectra, the signals of atoms $C^5$ at 42–47 ppm. In their turn in the $^1$H NMR spectra of iminium salts **IVa–IVf** multiplets are observed from the protons $H^6$ of the tetrahydropyran ring in the range 4.79–5.05 ppm, and also multiplets of an exocyclic methylene group in the region 3.22–3.61 ppm. The most characteristic signals in the $^{13}$C NMR spectra are the signals of atoms $C^6$ at 85–86 ppm.

*N*-{5-[(Arylsulfanyl)methyl]dihydrofuran-2(3*H*)-ylidene}-*N*-alkyl(aryl)aminium perchlorates under the action of sodium acetate converted into the corresponding 5-[(arylsulfanyl)methyl]lactones, and under the treatment with secondary cycloalkylamines in the presence of water suffered a transamidation with the opening of the tetrahydrofuran ring and the formation of 5-arylsulfanyl-4-hydroxypentanoic acid amides [7]. It seemed reasonable to estimate the behavior of their closest structural analogs,

**Scheme 2.**




**V**, Ar = Ph, Ar′ = 4-$NO_2C_6H_4$ (**a**); Ar = 4-$MeOC_6H_4$, Ar′ = Ph (**b**), 4-$MeC_6H_4$ (**c**); **VI**, $R_2 = (CH_2)_5$, Ar′ = Ph (**a**), 4-$MeC_6H_4$ (**b**), 4-$NO_2C_6H_4$ (**c**); $R_2 = (CH_2)_4$, Ar′ = 4-$NO_2C_6H_4$ (**d**); $R_2 = (CH_2)_2O(CH_2)_2$, Ar′ = 4-$NO_2C_6H_4$ (**e**).

*N*-aryl-*N*-{6-[(arylsulfanyl)methyl]tetrahydropyran-2*H*-ylidene}aminium perchlorates **IV**, in the reactions with the mentioned nucleophilic reagents.

Salts **IVa, IVe, IVf** are less stable against sodium acetate than the furanylideneaminium analogs and in such reactions under mild conditions undergo the opening of the tetrahydropyran ring with the formation of 6-arylsulfanyl-5-hydroxyhexanoic acid amides **Va–Vc** (Scheme 2). We believe that the most probable scheme should assume the primary attack of the hydroxyl anion on the atom $C^6$ of the tetrahydropyran followed by the opening of the iminolactone ring.

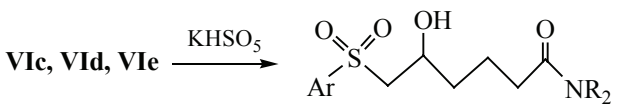
In the reaction with the secondary cyclic amines in the presence of water salts **IVa, IVe, IVf** behave similarly to furanylideneaminium analogs; consequently, the pyran ring undergoes the opening forming the transamidation products **VIa–VIe**. This reaction apparently proceeds through a cyclic intermediate **A** that easily opens at the subsequent water attack on the atom $C^6$. The results obtained to a certain extent are in agreement with the HSAB principle which requires that the attack of hard nucleophiles, hydroxyl anion and water, should be directed at the hard electrophilic site $C^6$, and the attack of softer amines should be directed at a softer electrophilic site $C^2$ of iminium salts **IV**.

Compounds **Va–Vc, VIa–VIe** are new specimen of 5-hydroxyhexanoic acid amides that lately attract the attention of researchers [15–17]. Their sulfanyl group is easy for modification as we have shown by the example of the oxidation of 6-sulfanyl-substituted amides **VIc, VId, VIe** into 6-sulfonyl derivatives **VIIa–VIIc** (Scheme 3).

## EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from pellets with KBr or solutions in $CH_2Cl_2$. $^1H$ and $^{13}C$ NMR spectra were registered on a spectrometer Bruker Advance DRX-500 (500.13, 125.75 MHz respectively), internal reference TMS. GC-MS measurements were carried out on an instrument Agilent110\DAD\HSD\VLG 119562.

**Scheme 3.**




**VIIa–VIIc**

**VII**, Ar′ = 4-$NO_2C_6H_4$, $R_2$ = $(CH_2)_5$ (**a**), $(CH_2)_4$ (**b**), $(CH_2)_2O(CH_2)_2$ (**c**).

**Compounds IIIa, IIIb.** To a solution of 2 mmol of amide **Ib** in 10 ml of chloroform at 15°C was added dropwise while stirring a solution of 2 mmol of arylsulfenyl chloride **IIb, IIc** in 5 ml of chloroform. The reaction mixture was stirred at room temperature for 12 h, the solvent was evaporated in a vacuum, to the residue 5 ml of ethyl ether was added, the formed precipitate was filtered off and dried in air.

**5-[(4-Methylphenyl)sulfanyl]-N-(4-methoxyphenyl)-6-chlorohexanamide (IIIa).** Yield 54%, mp 80–81°C. $^1H$ NMR spectrum (DMSO), δ, ppm: 1.41–1.93 m (4H, $2CH_2$), 2.23–2.41 m (5H, $CH_3$, $CH_2$), 3.58–3.80 m (6H, $OCH_3$, $CH_2$, CH), 6.87 d ($2H_{arom}$, *J* 8.7 Hz), 7.17 d ($2H_{arom}$, *J* 8.1 Hz), 7.37 d ($2H_{arom}$, *J* 7.8 Hz), 7.49 d ($2H_{arom}$, *J* 8.7 Hz), 9.78 s (1H, NH). $^{13}C$ NMR spectrum (DMSO), δ, ppm: 21.09 ($CH_3$), 22.92 ($C^3$), 30.87 ($C^4$), 37.11 ($C^2$), 47.44 ($C^6$), 50.65 ($C^5$), 55.47 ($OCH_3$), 114.13, 121.92, 129.40, 129.94, 131.05, 133.42, 138.18, 156.47 ($C_{arom}$), 170.65 ($C^1$). Found, %: C 63.51; H 6.45; N 3.67. $C_{20}H_{24}ClNO_2S$. Calculated, %: C 63.56; H 6.40; N 3.71.

***N*-(4-Methoxyphenyl)-5-[(4-nitrophenyl)sulfanyl]-6-chlorohexanamide (IIIb).** Yield 64%, mp 81–82°C. $^1H$ NMR spectrum (DMSO), δ, ppm: 1.58–2.00 m (4H, $2CH_2$), 2.26–2.38 m (2H, $CH_2$), 3.72 s (3H, $OCH_3$), 3.82–3.96 m (3H, $CH_2$, CH), 6.86 d ($2H_{arom}$, *J* 9 Hz), 7.49 d ($2H_{arom}$, *J* 8.5 Hz), 7.62 d ($2H_{arom}$, *J* 8.5 Hz), 8.14 d ($2H_{arom}$, *J* 8.5 Hz), 9.83 s (1H, NH). $^{13}C$ (NMR spectrum (DMSO), δ, ppm: 22.83 ($C^3$), 31.33 ($C^4$), 36.24 ($C^2$), 47.63 ($C^5$), 47.98 ($C^6$), 55.62 ($OCH_3$), 114.24, 121.09, 124.54, 128.82, 132.93, 145.63, 145.69, 155.53 ($C_{arom}$), 170.69 ($C^1$). Mass spectrum: *m/z* 409.2 $[M+1]^+$. Found, %: C 55.90; H 5.14; N 6.90. $C_{19}H_{21}ClN_2O_4S$. Calculated, %: C 55.81; H 5.18; N 6.85. m 408.9.

**Compounds IIIc, IVa, IVb**. To a solution of 2.2 mmol of amide **Ia, Ib** and 0.23 g (2.2 mmol) of lithium perchlorate in 10 ml of acetic acid at 15°C was added dropwise 2.2 mmol of arylsulfenyl chloride in 5 ml of acetic acid. The reaction mixture was stirred at room temperature for 4 h. The solvent was evaporated in a vacuum, the residue was extracted with chloroform (5 ml), the inorganic precipitate was filtered off, the filtrate was evaporated, the residue was treated with a mixture ether–hexane, 1:2 (5 ml), the formed precipitate (compound **IIIc**) was filtered off and washed with hexane. To isolate compounds **IVa, IVb** the precipitate from the reaction mixture was filtered off and washed with acetic

acid and hexane.

**5-[(4-Methylphenyl)sulfanyl]-*N*-phenyl-6-chlorohexanamide (IIIc).** Yield 38%, mp 62°C. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.67–2.03 m (3H, $CH_2$, CH), 2.07–2.55 m (6H, $CH_3$, $CH_2$, CH), 2.97–3.17 m (1H, CH), 3.22–3.42 m (1H, CH), 3.80–4.02 m (1H, CH), 6.83–7.61 m ($9H_{arom}$). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 21.00 ($CH_3$), 22.20 ($C^3$), 35.78 ($C^4$), 36.89 ($C^2$), 42.82 ($C^6$), 60.78 ($C^5$), 119.94, 124.34, 129.01, 130.02, 131.11, 131.18, 137.25, 137.83 ($C_{arom}$), 170.51 ($C^1$). Found, %: C 65.63; H 6.41; N 4.07. $C_{19}H_{22}ClNOS$. Calculated, %: C 65.59; H 6.37; N 4.03.

***N*-(6-{[(4-Nitrophenyl)sulfanyl]-methyl}tetrahydro-2H-pyran-2-ylidene)anilinium perchlorate (IVa)**. Yield 74%, mp 163–164°C. IR spectrum, ν, cm$^{-1}$: 1675 (C=N), 1505, 1350, 1110. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 1.85–2.09 m (3H, $CH_2$, CH), 2.19–2.28 m (1H, CH), 2.91–3.07 m (2H, $CH_2$), 3.42–3.49 m (1H, CH), 3.53–3.59 m (1H, CH), 4.93–5.04 m (1H, CH), 7.32–7.44 m ($7H_{arom}$), 7.99 d ($2H_{arom}$, *J* 9 Hz), 10.74 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.46 ($C^4$), 25.89 ($C^3$), 26.61 ($C^5$), 35.57 ($CH_2S$), 85.91 ($C^6$), 123.28, 123.89, 127.26, 128.93, 129.49, 132.77, 145.32, 145.71 ($C_{arom}$), 176.92 ($C^2$). Found, %: C 48.84; H 4.27; N 6.37. $C_{18}H_{19}ClN_2O_7S$. Calculated, %: C 48.81; H 4.32; N 6.33.

**4-Methoxy-*N*-(6-{[(4-nitrophenyl)-sulfanyl]methyl}tetrahydro-2H-pyran-2-ylidene)anilinium perchlorate (IVb)**. Yield 85%, mp 155–156°C. IR spectrum, ν, cm$^{-1}$: 1650 (C=N), 1515, 1335, 1115. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 2.02–2.12 m (3H, $CH_2$, CH), 2.23–2.30 m (1H, CH), 2.92–3.06 m (2H, $CH_2$), 3.43–3.50 m (1H, CH), 3.54–3.61 m (1H, CH), 3.80 s (3H, $CH_3$), 4.97–5.05 m (1H, CH), 6.89 d ($2H_{arom}$, *J* 9 Hz), 7.33 d ($2H_{arom}$, *J* 9 Hz), 7.41 d ($2H_{arom}$, *J* 9 Hz), 7.99 d ($2H_{arom}$, *J* 9 Hz), 10.60 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.54 ($C^4$), 25.98 ($C^3$), 26.44 ($C^5$), 35.49 ($CH_2S$), 55.34 ($OCH_3$), 85.67 ($C^6$), 114.46, 123.80, 124.73, 125.42, 127.06, 145.50, 145.55, 159.68 ($C_{arom}$), 175.90 ($C^2$). Found, %: C 48.36; H 4.45; N 5.87. $C_{19}H_{21}ClN_2O_8S$. Calculated, %: C 48.26; H 4.48; N 5.92.

**Compounds IVc–IVf**. To a solution of 2.2 mmol of amide **Ia, Ib** and 0.23 g (2.2 mmol) of lithium perchlorate in 10 ml of nitromethane at 15°C was added dropwise a solution of 2.2 mmol of arylsulfenyl chloride **IIa, IIb** in 5 ml of nitromethane, and the mixture was stirred at room temperature for 4 h. The solvent was evaporated in a vacuum, the residue was extracted with chloroform (10 ml), the inorganic precipitate was filtered off, the filtrate was evaporated. The residue was diluted with hexane (10 ml), the formed precipitate was filtered off and washed with hexane.

***N*-{6-[(Phenylsulfanyl)methyl]tetrahydro-2H-pyran-2-ylidene}anilinium perchlorate (IVc)**. Yield 58%, mp 63–64°C. IR spectrum, ν, cm$^{-1}$: 1660 (C=N), 1125. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 1.81–2.07 m (3H, $CH_2$, CH), 2.17–2.26 m (1H, CH), 2.90–3.08 m (2H, $CH_2$), 3.29–3.37 m (1H, CH), 3.38–3.45 m (1H, CH), 4.84–4.94 m (1H, CH), 7.24 d ($1H_{arom}$, *J* 7.2 Hz), 7.30 t ($2H_{arom}$, *J* 7.2 Hz), 7.38 d ($2H_{arom}$, *J* 7.6 Hz), 7.42–7.46 m ($1H_{arom}$), 7.47–7.58 m ($4H_{arom}$), 10.76 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.46 ($C^4$), 25.80 ($C^3$), 26.69 ($C^5$), 37.50 ($CH_2S$), 85.99 ($C^6$), 123.34, 126.93, 128.99, 129.34, 129.60, 129.86, 133.04, 134.73 ($C_{arom}$), 176.96 ($C^2$). Found, %: C 54.36; H 5.09; N 3.48. $C_{18}H_{20}ClNO_5S$. Calculated, %: C 54.33; H 5.07; N 3.52.

***N*-(6-{[(4-Methylphenyl)sulfanyl]-methyl}tetrahydro-2H-pyran-2-ylidene)anilinium perchlorate (IVd)**. Yield 70%, mp 66–67°C. IR spectrum, ν, cm$^{-1}$: 1655 (C=N), 1120. $^1$H ($CD_3CN$), δ, ppm: 1.84–2.06 m (3H, $CH_2$, CH), 2.15–2.24 m (1H, CH), 2.26 s (3H, $CH_3$), 2.88–3.06 m (2H, $CH_2$), 3.24–3.31 m (1H, CH), 3.33–3.40 m (1H, CH), 4.82–4.91 m (1H, CH), 7.11 d ($2H_{arom}$, *J* 8 Hz), 7.29 d ($2H_{arom}$, *J* 8.4 Hz), 7.39–7.59 m ($5H_{arom}$), 10.69 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.46 ($C^4$), 20.06 ($CH_3$), 25.74 ($C^3$), 26.70 ($C^5$), 38.18 ($CH_2S$), 86.19 ($C^6$), 123.24, 128.92, 129.58, 129.97, 130.69, 130.93, 133.03, 137.39 ($C_{arom}$), 176.90 ($C^2$). Found, %: C 55.37; H 5.41; N 3.36. $C_{19}H_{22}ClNO_5S$. Calculated, %: C 55.40; H 5.38; N 3.40.

**4-Methoxy-*N*-{6-[(phenylsulfanyl)-methyl]tetrahydro-2H-pyran-2-ylidene}anilinium perchlorate (IVe)**. Yield 58%, mp 114–115°C. IR spectrum, ν, cm$^{-1}$: 1660 (C=N), 1515, 1120. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 1.81–2.04 m (3H, $CH_2$, CH), 2.16–2.27 m (1H, CH), 2.86–3.04 m (2H, $CH_2$), 3.27–3.36 m (1H, CH), 3.37–3.44 m (1H, CH), 3.82 s (3H, $CH_3$), 4.82–4.90 m (1H, CH), 6.99 d ($2H_{arom}$, *J* 8.8 Hz), 7.24 d ($1H_{arom}$, *J* 6.4 Hz), 7.30 t ($2H_{arom}$, *J* 7.2 Hz), 7.38 d ($2H_{arom}$, *J* 7.6 Hz), 7.44 d ($2H_{arom}$, *J* 8.8 Hz), 10.60 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.52 ($C^4$), 25.87 ($C^3$), 26.53 ($C^5$), 37.49 ($CH_2S$), 55.42 ($OCH_3$), 85.64 ($C^6$), 114.65, 124.71, 125.85, 126.88, 129.29, 129.78, 134.81, 159.69 ($C_{arom}$), 175.81 ($C^2$). Found, %: C 53.46; H 5.06; N 3.34. $C_{19}H_{22}ClNO_6S$. Calculated, %:

C 53.33; H 5.18; N 3.27.

**4-Methoxy-*N*-(6-{[(4-methylphenyl)-sulfanyl] methyl}tetrahydro-2*H*-pyran-2-ylidene)anilinium perchlorate (IVf)**. Yield 91%, mp 125–126°C. IR spectrum, ν, cm$^{-1}$: 1660 (C=N), 1520, 1115. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 1.80–2.03 m (3H, $CH_2$, CH), 2.13–2.21 m (1H, CH), 2.27 s (3H, $CH_3$), 2.84–3.01 m (2H, $CH_2$), 3.22–3.29 m (1H, CH), 3.31–3.38 m (1H, CH), 3.81 s (3H, $CH_3$), 4.79–4.87 m (1H, CH), 6.98 d ($2H_{arom}$, *J* 8.8 Hz), 7.10 d ($2H_{arom}$, *J* 8 Hz), 7.27 d ($2H_{arom}$, *J* 8 Hz), 7.40 d ($2H_{arom}$, *J* 8.8 Hz), 10.53 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 15.51 ($C^4$), 20.04 ($CH_3$), 25.81 ($C^3$), 26.54 ($C^5$), 38.18 ($CH_2S$), 55.42 ($OCH_3$), 85.79 ($C^6$), 114.63, 124.65, 125.87, 129.97, 130.61, 131.03, 137.32, 159.69 ($C_{arom}$), 175.74 ($C^2$). Found, %: C 54.41; H 5.43; N 3.24. $C_{20}H_{24}ClNO_6S$. Calculated, %: C 54.36; H 5.47; N 3.17.

**Compounds Va–Vc**. To a solution of 1 mmol of iminium salt **IVa, IVe, IVf** in 3 ml of ethanol was added a solution of 1.5 mmol of sodium acetate in 2 ml of water, and the mixture was left standing for 24 h. Ethanol was evaporated, organic layer insoluble in water was extracted with chloroform (2 × 5 ml), the extract was dried with anhydrous magnesium sulfate, filtered, evaporated, the residue was crystallized from benzene.

**5-Hydroxy-6-[(4-nitrophenyl)sulfanyl]-*N*-phenylhexanamide (Va).** Yield 55%, mp 136–137°C. $^1$H NMR spectrum ($CD_3CN$), δ, ppm: 1.49–1.60 m (1H, CH), 1.62–1.78 m (2H, $CH_2$), 1.79–1.87 m (1H, CH), 2.34 t (2H, $CH_2$, *J* 6.8 Hz), 3.06–3.13 m (1H, CH), 3.16–3.23 m (1H, CH), 3.76–3.85 m (1H, CH), 7.06 t ($1H_{arom}$, *J* 7.2 Hz), 7.30 t ($2H_{arom}$, *J* 7.6 Hz), 7.44 d ($2H_{arom}$, *J* 8.8 Hz), 7.54 d ($2H_{arom}$, *J* 7.6 Hz), 8.08 d ($2H_{arom}$, *J* 8.8 Hz), 8.28 s (1H, NH). $^{13}$C NMR spectrum ($CD_3CN$), δ, ppm: 21.33 ($C^3$), 35.64 ($C^2$), 36.39 ($C^4$), 38.95 ($C^6$), 69.17 ($C^5$), 119.43, 123.51, 123.78, 126.44, 128.76, 139.10, 145.06, 148.07 ($C_{arom}$), 171.49 ($C^1$). Mass spectrum: *m/z* 361.0 [*M* + 1]$^+$. Found, %: C 60.10; H 5.54; N 7.81. $C_{18}H_{20}N_2O_4S$. Calculated, %: C 59.98; H 5.59; N 7.77. m 360.4.

**5-Hydroxy-*N*-(4-methoxyphenyl)-6-(phenylsulfanyl) hexanamide (Vb).** Yield 53%, mp 88–89°C. IR spectrum, ν, cm$^{-1}$: 1655 (C=O), 1520, 1235. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.50–1.71 m (2H, $CH_2$), 1.77–1.89 m (2H, $CH_2$), 2.29–2.41 m (2H, $CH_2$), 2.81–2.90 m (1H, CH), 3.07–3.17 m (1H, CH), 3.62–3.74 m (1H, CH), 3.78 s (3H, $CH_3$), 6.84 d ($2H_{arom}$, *J* 8.8 Hz), 7.17–7.31 m ($3H_{arom}$), 7.34–7.44 m ($4H_{arom}$). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 21.88 ($C^3$), 35.03 ($C^2$), 36.95 ($C^4$), 42.10 ($C^6$), 55.46 ($OCH_3$), 69.19 ($C^5$), 114.08, 121.75, 126.65, 129.07, 130.00, 131.04, 135.15, 156.39 ($C_{arom}$), 171.18 ($C^1$). Mass spectrum: *m/z* 346.2 [*M* + 1]$^+$. Found, %: C 66.11; H 6.65; N 4.01. $C_{19}H_{23}NO_3S$. Calculated, %: C 66.06; H 6.71; N 4.05. m 345.5.

**5-Hydroxy-*N*-(4-methoxyphenyl)-6-[(4-methylphenyl)sulfanyl]hexanamide (Vc).** Yield 56%, mp 110–111°C. IR spectrum, ν, cm$^{-1}$: 1655 (C=O), 1530, 1245. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.47–1.66 m (2H, $CH_2$), 1.76–1.87 m (2H, $CH_2$), 2.22–2.39 m (5H, $CH_3$, $CH_2$), 2.73–2.83 m (1H, CH), 3.01-3.09 m (1H, CH), 3.59–3.66 m (1H, CH), 3.76 s (3H, $CH_3$), 6.82 d ($2H_{arom}$, *J* 7.6 Hz), 7.08 d ($2H_{arom}$, *J* 7.2 Hz), 7.20–7.30 m ($2H_{arom}$), 7.37 d ($2H_{arom}$, *J* 8.8 Hz). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 21.01 ($CH_3$), 21.94 ($C^3$), 34.94 ($C^2$), 37.00 ($C^4$), 42.91 ($C^6$), 55.47 ($OCH_3$), 69.07 ($C^5$), 114.10, 121.73, 129.89, 130.91, 131.08, 131.15, 137.03, 156.37 ($C_{arom}$), 171.11 ($C^1$). Mass spectrum: *m/z* 360.2 [*M* + 1]$^+$. Found, %: C 66.74; H 7.10; N 3.87. $C_{20}H_{25}NO_3S$. Calculated, %: C 66.82; H 7.01; N 3.90. m 359.5.

**Compounds VIa–VIe**. To 1 ml of piperidine, pyrrolidine, or morpholine was added 1 mmol of iminium salt **IVa, IVe, IVf**, and the mixture was left standing for 12 h and then it was diluted with 5 ml of water. The oily reaction product was extracted with chloroform (2 × 5 ml), the extract was dried with anhydrous magnesium sulfate, the solvent was evaporated, the residue was chromatographed on silica gel (eluent ethyl acetate–chloroform, 3:1) (compounds **VIa, VIb**) or crystallized from an appropriate solvent (compounds **VIc—VIe**).

**5-Hydroxy-1-(piperidin-1-yl)-6-(phenylsulfanyl) hexan-1-one (VIa).** Yield 60%, oily substance. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.43–1.66 m (8H, $4CH_2$), 1.69–1.79 m (2H, $CH_2$), 2.23–2.38 m (2H, $CH_2$), 2.86–2.94 m (1H, CH), 3.02–3.10 m (1H, CH), 3.29–3.37 m (2H, $CH_2$), 3.45–3.53 m (2H, $CH_2$), 3.61–3.69 m (1H, CH), 7.16 t ($1H_{arom}$, *J* 7.4 Hz), 7.25 t ($2H_{arom}$, *J* 7.4 Hz), 7.34 d ($2H_{arom}$, *J* 6.8 Hz). $^{13}$C NMR spectrum ($CDCl_3$), δ, ppm: 21.03 ($C^3$), 24.55, 25.60, 26.53, 42.79, 46.64 ($C_{piperidine}$), 32.79 ($C^2$), 35.75 ($C^4$), 41.71 ($C^6$), 69.04 ($C^5$), 126.31, 128.98, 129.69, 135.68 ($C_{arom}$), 171.20 ($C^1$). Mass spectrum: *m/z* 308.2 [*M* + 1]$^+$. Found, %: C 66.50; H 8.18; N 4.53. $C_{17}H_{25}NO_2S$. Calculated, %: C 66.41; H 8.20; N 4.56. m 307.4.

**5-Hydroxy-6-[(4-methylphenyl)sulfanyl]-1-(piperidin-1-yl)hexan-1-one (VIb).** Yield 42%, oily substance. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.45–1.67 m (8H, $4CH_2$), 1.71–1.80 m (2H, $CH_2$), 2.23–2.41 m

(5H, $CH_3$, $CH_2$), 2.81–2.90 m (1H, CH), 3.01–3.09 m (1H, CH), 3.32–3.40 m (2H, $CH_2$), 3.48–3.57 m (2H, $CH_2$), 3.60–3.67 m (1H, CH), 7.10 d ($2H_{arom}$, *J* 8 Hz), 7.29 d ($2H_{arom}$, *J* 8 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 21.03 ($CH_3$), 21.09 ($C^3$), 24.57, 25.60, 26.53, 42.78, 46.65 ($C_{piperidine}$), 32.83 ($C^2$), 35.67 ($C^4$), 42.54 ($C^6$), 68.97 ($C^5$), 129.78, 130.69, 131.65, 136.70 ($C_{arom}$), 171.19 ($C^1$). Mass spectrum: *m/z* 322.2 $[M + 1]^+$. Found, %: C 67.28; H 8.43; N 4.39. $C_{18}H_{27}NO_2S$. Calculated, %: C 66.41; H 8.20; N 4.56. m 321.5.

**5-Hydroxy-6-[(4-nitrophenyl)sulfanyl]-1-(piperidin-1-yl)hexan-1-one (VIc).** Yield 75%, mp 103–104°C (ether). IR spectrum, ν, $cm^{-1}$: 1630 (C=O), 1585, 1510, 1340. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.48–1.57 m (4H, $2CH_2$), 1.58–1.66 m (3H, $CH_2$, CH), 1.67–1.74 m (1H, CH), 1.76–1.87 m (2H, $CH_2$), 2.32–2.44 m (2H, $CH_2$), 3.10–3.18 m (2H, $CH_2$), 3.35–3.41 m (2H, $CH_2$), 3.51–3.57 m (2H, $CH_2$), 3.79–3.85 m (1H, CH), 7.39 d ($2H_{arom}$, *J* 8.5 Hz), 8.10 d ($2H_{arom}$, *J* 9 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 20.61 ($C^3$), 24.49, 25.59, 26.50, 42.90, 46.62 ($C_{piperidine}$), 32.49 ($C^2$), 36.10 ($C^4$), 49.60 ($C^6$), 69.26 ($C^5$), 123.86, 126.63, 145.90, 147.39 ($C_{arom}$), 171.19 ($C^1$). Mass spectrum: *m/z* 353.1 $[M + 1]^+$. Found, %: C 57.86; H 6.94; N 7.91. $C_{17}H_{24}N_2O_4S$. Calculated, %: C 57.93; H 6.86; N 7.95. m 352.4.

**5-Hydroxy-6-[(4-nitrophenyl)sulfanyl]-1-(pyrrolidin-1-yl)hexan-1-one (VId).** Yield 74%, mp 90–91°C (hexane). IR spectrum, ν, $cm^{-1}$: 1625 (C=O), 1585, 1520, 1340. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.59–1.75 m (2H, $CH_2$), 1.80–2.00 m (6H, $3CH_2$), 2.25–2.42 m (2H, $CH_2$), 3.09–3.20 m (2H, $CH_2$), 3.34–3.50 m (4H, $2CH_2$), 3.78–3.89 m (1H, CH), 4.20 s (1H, OH), 7.40 d ($2H_{arom}$, *J* 8.5 Hz), 8.11 d ($2H_{arom}$, *J* 8 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 20.06 ($C^3$), 24.37, 26.07, 45.82, 46.63 ($C_{pyrrolidine}$), 33.93 ($C^2$), 36.18 ($C^4$), 39.53 ($C^6$), 69.18 ($C^5$), 123.84, 126.55, 145.13, 147.52 ($C_{arom}$), 171.65 ($C^1$). Found, %: C 56.81; H 6.52; N 8.31. $C_{16}H_{22}N_2O_4S$. Calculated, %: C 56.78; H 6.55; N 8.28.

**5-Hydroxy-1-(morpholin-4-yl)-6-[(4-nitrophenyl) sulfanyl]hexan-1-one (VIe).** Yield 70%, mp 100–101°C (benzene). IR spectrum, ν, $cm^{-1}$: 1640 (C=O), 1585, 1520, 1340. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.56–1.75 m (2H, $CH_2$), 1.78–1.88 m (2H, $CH_2$), 2.30–2.46 m (2H, $CH_2$), 3.05–3.13 m (1H, CH), 3.15–3.22 m (1H, CH), 3.41–3.50 m (2H, $CH_2$), 3.57–3.70 m (6H, $3CH_2$), 3.78–3.87 m (1H, CH), 7.39 d ($2H_{arom}$, *J* 8.8 Hz), 8.11 d ($2H_{arom}$, *J* 8.8 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 20.51 ($C^3$), 32.35 ($C^2$), 35.99 ($C^4$), 39.69 ($C^6$), 42.08, 45.92, 66.59, 66.90 ($Cm_{op\phi.}$), 69.35 ($C^5$), 123.98, 126.73, 145.26, 147.06 ($C_{arom}$), 171.59 ($C^1$). Mass spectrum: *m/z* 355.2 $[M + 1]^+$. Found, %: C 54.31; H 6.29; N 7.85. $C_{16}H_{22}N_2O_5S$. Calculated, %: C 54.22; H 6.26; N 7.90. m 354.4.

**Compounds VIIa–VIIc**. To a solution of 1 mmol of compound **VIc, VId, VIe** in 5 ml of methanol was added at stirring 1.2 g (2 mmol) of $KHSO_5$ dissolved in 5 ml of water. The reaction mixture was stirred for 5 h at 70°C, cooled, the inorganic precipitate was filtered off, the filtrate was evaporated, the residue was crystallized from water.

**5-Hydroxy-6-[(4-nitrophenyl)sulfonyl]-1-(piperidin-1-yl)hexan-1-one (VIIa).** Yield 96%, mp 104–105°C. IR spectrum, ν, $cm^{-1}$: 1620 (C=O), 1540, 1350. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.42–1.57 m (6H, $3CH_2$), 1.58–1.72 m (3H, $CH_2$, CH), 1.75–1.84 m (1H, CH), 2.25–2.42 m (2H, $CH_2$), 3.23 d (1H, CH, *J* 14.8 Hz), 3.31–3.41 m (3H, $CH_2$, CH), 3.46–3.56 m (2H, $CH_2$), 4.11–4.20 m (1H, CH), 8.14 d ($2H_{arom}$, *J* 8.4 Hz), 8.38 d ($2H_{arom}$, *J* 8.8 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 19.72 ($C^3$), 24.46, 25.56, 26.46, 42.98, 46.59 ($C_{piperidine}$), 32.05 ($C^2$), 36.53 ($C^4$), 62.70 ($C^6$), 65.43 ($C^5$), 124.18, 129.79, 145.77, 150.80 ($C_{arom}$), 171.09 ($C^1$). Mass spectrum: *m/z* 385.2 $[M + 1]^+$. Found, %: C 53.15; H 6.25; N 7.32. $C_{17}H_{24}N_2O_6S$. Calculated, %: C 53.11; H 6.29; N 7.29. m 384.4.

**5-Hydroxy-6-[(4-nitrophenyl)sulfonyl]-1-(pyrrolidin-1-yl)hexan-1-one (VIIb).** Yield 95%, mp 134–135°C. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.47–1.58 m (2H, $CH_2$), 1.62–1.72 m (1H, CH), 1.74–2.00 m (5H, $2CH_2$, CH), 2.17–2.27 m (1H, CH), 2.28–2.39 m (1H, CH), 3.17–3.25 m (1H, CH), 3.28–3.47 m (5H, $2CH_2$, CH), 4.09–4.20 m (1H, CH), 8.11 d ($2H_{arom}$, *J* 7.2 Hz), 8.35 d ($2H_{arom}$, *J* 8.4 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 19.07 ($C^3$), 24.34, 26.04, 45.89, 46.62 ($C_{pyrrolidine}$), 33.47 ($C^2$), 36.64 ($C^4$), 62.73 ($C^6$), 65.28 ($C^5$), 124.16, 129.74, 145.86, 150.78 ($C_{arom}$), 171.58 ($C^1$). Mass spectrum: *m/z* 371.2 $[M + 1]^+$. Found, %: C 51.92; H 5.96; N 7.61. $C_{16}H_{22}N_2O_6S$. Calculated, %: C 51.88; H 5.99; N 7.56. m 370.4.

**5-Hydroxy-1-(morpholin-4-yl)-6-[(4-nitro-phenyl) sulfonyl]hexan-1-one (VIIc).** Yield 98%, mp 70–71°C. IR spectrum, ν, $cm^{-1}$: 1635 (C=O), 1535–1540, 1350. $^1H$ NMR spectrum ($CDCl_3$), δ, ppm: 1.53–1.61 m (2H, $CH_2$), 1.70–1.83 m (2H, $CH_2$), 2.27–2.44 m (2H, $CH_2$), 3.21–3.28 m (1H, CH), 3.32–3.39 m (1H, CH), 3.42–

3.48 m (2H, $CH_2$), 3.57–3.62 m (2H, $CH_2$), 3.63–3.71 m (4H, $2CH_2$), 4.17–4.25 m (1H, CH), 8.14 d ($2H_{arom}$, *J* 8.8 Hz), 8.40 d ($2H_{arom}$, *J* 8.8 Hz). $^{13}C$ NMR spectrum ($CDCl_3$), δ, ppm: 19.69 ($C^3$), 31.94 ($C^2$), 36.34 ($C^4$), 42.13, 45.88, 66.52, 66.83 ($C_{morph.}$), 62.57 ($C^6$), 65.54 ($C^5$), 124.37, 129.62, 145.58, 150.88 ($C_{arom}$), 171.51 ($C^1$). Mass spectrum: *m/z* 387.0 $[M + 1]^+$. Found, %: C 49.81; H 5.73; N 7.27. $C_{16}H_{22}N_2O_7S$. Calculated, %: C 49.73; H 5.74; N 7.25. m 386.4.

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