ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 8, pp. 1146–1152. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © A.I. Vas'kevich, N.M. Tsizorik, E.B. Rusanov, V.I. Stanitets, M.V. Vovk, 2011, published in Zhurnal Organicheskoi Khimii, 2011, Vol. 47, No. 8, pp. 1130–1135.

Intramolecular Electrophilic Cyclization of Functional Derivatives of Unsaturated Compounds: I. Synthesis of 5-Arylsulfanyl-6-phenylpiperidin-2-ones from Cinnamylacetamides and Arylsulfenyl Chlorides

A. I. Vas'kevich, N. M. Tsizorik, E. B. Rusanov, V. I. Stanitets, and M. V. Vovk

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev, 02094 Ukraine
e-mail: vaskevich@ioch.kiev.ua

Received January 10, 2010

Abstract—Sterically nonhindered N-alkyl(aryl)amides of cinnamylacetic acid in the reaction with phenyl(4-tolyl)sulfenyl chlorides in acetic acid in the presence of lithium perchlorate undergo a selective cyclization into 5-arylsulfanyl-6-phenylpiperidin-2-ones. Under similar conditions the reaction with arylsulfenyl chlorides of amides containing bulky substituents at the nitrogen atom resulted in 5-arylsulfanyl-6-phenyltetrahydropyran-2-iminium perchlorates, which by treatment with aqueous ethanol were converted into the corresponding derivatives of pyran-2-ones.

DOI: 10.1134/S1070428011080057

Piperidin-2-ones are compounds with unique biological characteristics [1–3]. They underlie the preparation of piperidine systems included into the composition of many alkaloids and physiologically active substances [4–6]. Therefore nowadays new substituted piperidones are synthesized [7–11].

The introduction of sulfanyl groups in the piperidone ring can essentially modify the chemical and biological characteristics. In particular, among the sulfanyl derivatives of piperidin-2-oneов (δ-lactams) compounds were found capable to inhibit the activation of p38MAP-kinase [12], a very important quality both for prophylactic and treatment of inflammation and autoimmune diseases, rheumatoid arthritis, infectious diseases, atherosclerosis, and pancreatitis.

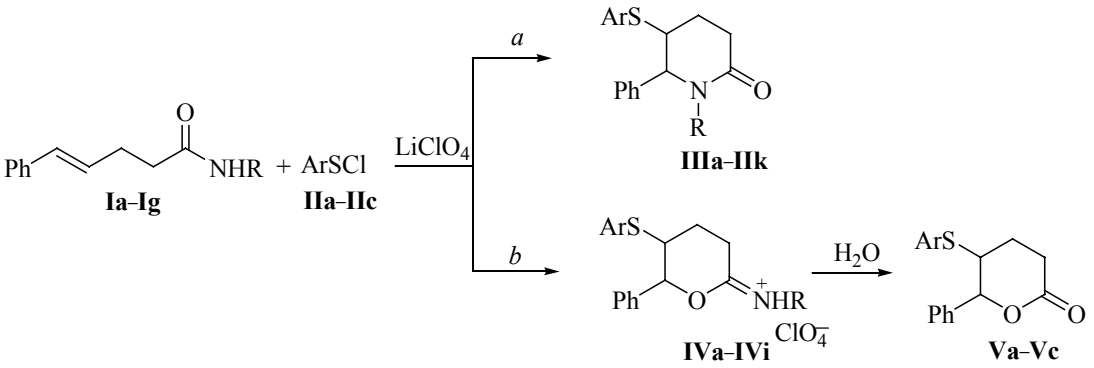
Although there are well developed approaches to nonfunctional piperidones, the methods of the synthesis of 5-alkyl(aryl)sulfanyl-substituted piperidones [12–14] are multistage and apply difficultly accessible and toxic reagents.

Considering the synthetic potential of the reaction of electrophilic cyclization of unsaturated amides [15] and aiming at the development of the synthesis of 5-arylsulfanylpiperidin-2-ones we examined in detail the arylsulfenylation of cinnamylacetamides **Ia–Ig**. These compounds react with arylsulfenyl chlorides **IIa–IIc** at room temperature in acetic acid in the presence of an equimolar amount of $LiClO_4$ as "dopping-additive" [16, 17] forming cyclization products whose structure is controlled mainly by the steric parameters of the substituent at the nitrogen atom of the nucleophilic substrate and the electronic characteristics of the electrophilic reagent.

Amide with sterically nonhindered aliphatic (**Ib, Ic**) or aromatic (**If, Ig**) substituents react with phenyl- or 4-tolylsulfenyl chlorides (**IIa, IIb**) giving 5-arylsulfanyl-6-phenylpiperidones **IIIb–IIIg, IIIi, IIIj** (path *a*) in 81–95% yield (Scheme 1). In event of 4-nitrophenylsulfenyl chloride a decreased selectivity of reaction is observed due to the nucleophilic involvement of the oxygen atom of the iniial amides (path *b*), and as a result forms a mixture of compounds **III** and **IV** in the ratio 5 : 1 from amide **If** and 4 : 1 from amide **Ig**.

In the reaction of unsubstituted amide **Ia** with 4-tolylsulfenyl chloride (**IIb**) lactam **IIIa** was isolated.

Scheme 1.



I, R = H(**a**), Bu(**b**), $PhCH_2$(**c**), *i*-Pr(**d**), *t*-Bu(**e**), Ph(**f**), 4-$MeOC_6H_4$(**g**); **II**, **V**, Ar = Ph(**a**), 4-MeC_6H_4(**b**), 4-$NO_2C_6H_4$(**c**); **III**, R = H, Ar = 4-MeC_6H_4(**a**); R=Bu, Ar = Ph(**b**), 4-MeC_6H_4(**c**); R=$PhCH_2$, Ar = Ph(**d**), 4-MeC_6H_4(**e**); R = A r= Ph(f); R = Ph, Ar = 4-MeC_6H_4(**g**), 4-$NO_2C_6H_4$(**h**); R = 4-$MeOC_6H_4$, Ar = Ph(**i**), 4-MeC_6H_4(**j**), 4-$NO_2C_6H_4$(**k**); **IV**, R = H, Ar = Ph(**a**); R = *i*-Pr, Ar = Ph(**b**), 4-MeC_6H_4(**c**), 4-$NO_2C_6H_4$(**d**); R = *t*-Bu, Ar = Ph(**e**), 4-MeC_6H_4(**f**), 4-$NO_2C_6H_4$(**g**); R = Ph, Ar = 4-$NO_2C_6H_4$(**h**); R = 4-$MeOC_6H_4$, Ar = 4-$NO_2C_6H_4$(**i**).

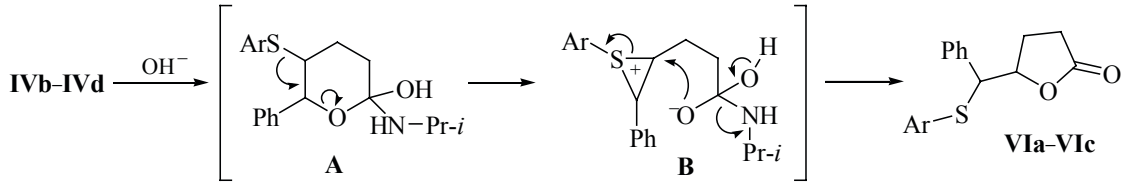
The application of phenyl- and 4-nitrophenylsulfenyl chloride resulted in the prevailing formation of pyran-2-iminium perchlorate (**IVa**).

Path *b* prevails also in the reactions of sterically hindered amides **Id, Ie** with arylsulfenylchlorides **IIa–IIc**. As a result tetrahydropyrano-2-iminium perchlorates **IVb–IVg** formed in 66–86% yields. Their structure was reliably proved by spectral methods by an example of compounds **IVb, IVc** isolated from the reaction mixture in the analytically pure state. The salts **IVb–IVg** without additional purification were treated with aqueous ethanol to obtain 5-arylsulfanylpyran-2-ones **Va–Vc** in 48–64% yields.

At the treating of iminium salts **IVb–IVd** with a water solution of sodium acetate in acetone alongside with δ-lactones **Va–Vc** we detected in the reaction mixture by means of ^1H spectroscopy and GC-MS method also γ-lactones **VIa–VIc**. We succeeded to isolate compound **VIc** in 68% yield (Scheme 2). Most probably their formation is not caused by the primary amine elimination from the addition product **A**, but by its intramolecular structural rearrangement involving the cleavage of the C^6–O bond and leading to episulfonium intermediate **B**, followed by the cyclization of the latter into lactone **VI** [14].

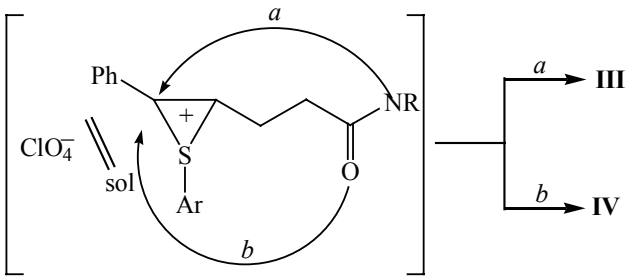
Proceeding from the concept of the increasing effective electrophilicity of sulfenyl chlorides in reactions Ad_E [16, 17] and basing on the previous experimental results of their application to the reactions of intramolecular cyclization [18–20], it is presumable that in the reaction of amides **I** with arylsulfenyl chlorides **II** in the medium of acetic acid in the presence of $LiClO_4$ episulfonium intermediates **C** are formed being a solvent-separated ion pair where the perchlorate prevents the formation of products of acyclic addition. In the course of the intramolecular electrophilic cyclization depending on substituent R the episulfonium ring of intermediate **C** is attacked either by the nitrogen atom (path *a*) or the oxygen atom (path *b*) leading to the formation of compounds **III** or

Scheme 2.



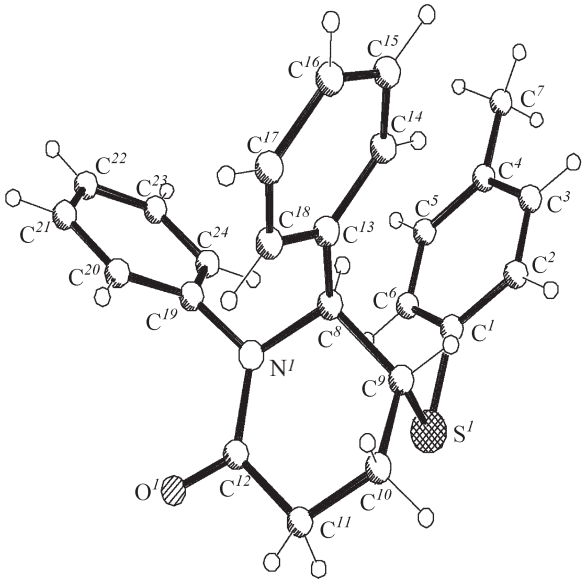
VI, Ar = Ph(**a**), 4-MeC_6H_4(**b**), 4-$NO_2C_6H_4$(**c**).

IV respectively (Scheme 3). The low selectivity of the reaction at the use of 4-$NO_2C_6H_4SCl$ (**IIc**) compared to sulfenyl chlorides **IIa, IIb** originates from the decreased stability and increased reactivity of intermediate **C** due to the electron-withdrawing character of the nitro group.



C

The structure of compounds synthesized was confirmed by physicochemical investigations. ^{1}H NMR spectra of piperidinones **IIIa–IIIk** contain a single set of doublets of atom H^5 in the region 4.40–5.08 ppm with the coupling constant 3.0–3.6 Hz and a multiplet of atom H^4 in the region 3.55–4.33 ppm indicating their axial-equatorial location and proving the diastereoselective character of the arylsulfanyllactamization. In the ^{13}C NMR spectra the signals of the atoms C^5 and C^6 of the piperidine ring appear in the regions 46–49 and 63–69 ppm respectively. The unambiguous confirmation of the structure of the lactams synthesized was obtained by XRD analysis of a single crystal of compound **IIIg** the general arrangement of whose molecule is shown on the figure.



General view of the molecule of 1,6-diphenyl-5-[(4-methylphenyl)sulfanyl]piperidin-2-one (**IIIg**). Main bond lengths and bond angles: C^8–N^1 1.474(2), C^8–C^9 1.526(3), C^9–C^{10} 1.512(3), C^{10}–C11 1.521(3), C^{11}–C^{12} 1.501(3), C^{12}–N^1 1.361(2), C^{12}–O^1 1.222(2), C^9–S^1 1.826(2) C^1–S^1 1.773(2) E; $N^1C^8C^9$ 111.59(15), $C^8C^9C^{10}$ 110.67(16), $C^9C^{10}C^{11}$ 110.48(18), $C^{10}C^{11}C^{12}$ 116.56(17), $N^1C^{12}C^{11}$ 118.68(18), $C^{12}N^1C^8$ 125.41(16), $C^{10}C^9S^1$ 108.23(14), $C^8C^9S^1$ 113.27(14), $C^1S^1C^9$ 101.15(9)°.

The distribution of bond lengths and bond angles in the central six-membered hetrocycle $N^1C^8C^{12}$ is usual for such systems. The bond lengths C^8–C^9, C^9–C^{10}, and C^{10}–C^{11} fall in the range typical of the sp^3-hybridized carbon atoms whereas the bond C^{11}–C^{12} 1.501(3) Å is slightly shortened. Endocyclic C–N bonds are nonequivalent due to the conjugation of the lone electron pairs of atom N^1 with the π-system of the C=O bond as shows the flattening of the atom N^1 [sum of bond angles at this atom is 359.73(16)°]. The central heterocycle proper is not planar and exists in the *semichair* conformation. The group of atoms $N^1C^8C^{10}C^{11}C^{12}$ forms a plane, and the maximum deviation of atoms from this plane does not exceed 0.070(1) Å, and the plane $C^8C^9C^{10}$ forms with it an angle of 49.14(13)°. The lengths of the C–S bonds are not equal apparently due to different hybridization of C^1 and C^9 atoms, namely, because of the conjugation of the lone electron pairs of sulfur atom with the π-system of the tolyl substituent.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from pellets with KBr or from solutions in CH_2Cl_2. ^{1}H 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 performed on an instrument Agilent 110\DAD\HSD\VLG 119562.

XRD investigation of the single crystal of compound **IIIg** of the size 0.20 × 0.40 × 0.50 mm was carried out at room temperature on a diffractometer Bruker Smart Apex II (λMoK_α-radiation, graphite monochromator, θ_{max} 26.5°, spherical segment $-14 \le h \le 14$, $-22 \le k \le 18$, $-23 \le l \le 22$). Total collected reflections 19504, among them 4079 independent (*R*-factor of averaging 0.0368). The correction for extinction was performed by multiscanning using SADABS program (the ratio of minimal to maximal correction T_{min}/T_{max} 0.681997). The structure was solved by the direct method and refined by the least-squares method in the anisotropic approximation for all nonhydrogen atoms applying SHELXS97

and SHELXL97 software [21, 22]. The positions and thermal parameters of all hydrogen atoms were refined together with the positions and thermal parameters of the corresponding carbon atoms. In the refinement 2694 reflections were utilized with $I > 2\sigma(I)$, 240 refined parameters, number of reflections per parameter 6.7, weight scheme was used $\omega = 1/[\sigma^2(Fo^2) + (0.0442P)^2 + 1.8675P]$, where $P = (Fo^2 + 2Fc^2)/3$, the ratio of the maximal (average) shift to the error in the last cycle 0.081 (0.002). The final values of divergence factors are $R_1(F)$ 0.0463, $wR_2(F^2)$ 0.1030, for reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0813, $wR_2(F^2)$ 0.1218, *GOF* 1.004 for all reflections. The residual electron density from the difference Fourier series after the last refinement cycle 0.25 and –0.32 *e*/Å^3.

5-Arylsulfanyl-1-R-6-phenylpiperidin-2-ones IIIa–IIIk and N-[5-(arylsulfanyl)-6-phenyltetrahydro-2*H*-pyran-2-ylidene]propan-2-iminium perchlorates IVb, IVc. To a solution of 2.2 mmol of amide **Ia–Ig** in 10 ml of acetic acid was added in succession while stirring a solution of 0.23 g (2.2 mmol) of lithium perchlorate in 5 ml of acetic acid and a solution of 2.2 mmol of arylsulfenyl chloride **IIa–IIc** in 3 ml of acetic acid. The reaction mixture was stirred at room temperature for 4 h, the solvent was distilled off in a vacuum, the residue was treated with 10 ml of water. The organic products were extracted into chloroform (2×10 ml), the extract was dried with anhydrous magnesium sulfate, filtered, and evaporated. Compounds **IIIa–IIIk** were purified by recrystallization from ethanol. Compounds **IV** were used without further purification.

5-[(4-Methylphenyl)sulfanyl]-6-phenylpiperidin-2-one (IIIa). Yield 88%, mp 154–155°C. IR spectrum, ν, cm^{-1}: 3340 (N–H), 1655 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.65–1.72 m (1H, CH), 1.85–1.94 m (1H, CH), 2.32 s (3H, CH_3), 3.34–3.37 m (2H, CH_2), 3.58–3.60 m (1H, CH), 4.42 d (1H, CH, *J* 6 Hz), 7.18–7.36 m (9H$_{arom.}$), 7.87 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.30 (CH_3), 22.85 (C^4), 28.42 (C^3), 47.96 (C^5), 59.10 (C^6), 126.60, 127.35, 128.19, 129.63, 132.16, 129.72, 137.03, 141.92 (C$_{arom.}$), 169.42 (C^2). Found, %: C 72.62; H 6.34; N 4.62. $[M + 1]^+$ 298. $C_{18}H_{19}NOS$. Calculated, %: C 72.70; H 6.44; N 4.71. *M* 297.4.

1-Butyl-6-phenyl-5-(phenylsulfanyl)piperidin-2-one (IIIb). Yield 81%, mp 54–55°C. IR spectrum, ν, cm^{-1}: 1650 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.81 t (3H, CH_3), 1.12–1.41 m (4H, 2CH_2), 1.59–1.72 m (1H, CH), 1.86–2.01 m (1H, CH), 2.18–2.30 m (1H, CH), 2.37–2.56 m (2H, CH_2), 3.79–3.93 m (2H, CH + CH), 3.85–3.90 m (1H, CH), 4.61 d (1H, CH, *J* 3.3 Hz), 7.18 d (2H$_{arom}$, *J* 6.9 Hz), 7.31–7.45 m (6H$_{arom.}$), 7.54 d (2H$_{arom.}$, *J* 7.5 Hz). ^{13}C NMR spectrum, δ, ppm: 13.39 (CH_3), 19.42 (CH_2), 20.59 (CH_2), 27.77 (C^4), 28.80 (C^3), 44.72 (CH_2N), 47.92 (C^5), 63.41 (C^6), 126.41, 127.21, 127.61, 128.57, 129.18, 131.37, 133.49, 140.04 (C$_{arom.}$), 167.84 (C^2). Found, %: C 74.45; H 7.38; N 4.10; S 9.30. $[M + 1]^+$ 340. $C_{21}H_{25}NOS$. Calculated, %: C 74.28; H 7.41; N 4.12; S 9.42. *M* 339.5.

1-Butyl-5-(4-methylphenylsulfanyl)-6-phenylpiperidin-2-one (IIIc). Yield 87%, mp 63–64°C. IR spectrum, ν, cm^{-1}: 1650 (C=O). ^{1}H NMR spectrum, δ, ppm: 0.81 t (3H, CH_3, *J* 7.8 Hz), 1.10–1.47 m (4H, 2CH_2), 1.54–1.66 m (1H, CH), 1.82–1.96 m (1H, CH), 2.17–2.25 m (1H, CH), 2.32 s (3H, CH_3), 2.40–2.55 m (2H, CH_2), 3.73–3.75 m (1H, CH), 3.80–3.90 m (1H, CH), 4.57 d (1H, CH, *J* 3.1 Hz), 7.15 d (2H$_{arom.}$, *J* 7.5 Hz), 7.23 d (2H$_{arom.}$, *J* 7.8 Hz), 7.32–7.46 m (5H$_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 13.60 (CH_3), 19.45 (CH_2), 20.54 (CH_3), 20.55 (CH_2), 27.77 (C^4), 28.82 (C^3), 44.74 (CH_2N), 48.39 (C^5), 63.44 (C^6), 126.50, 127.60, 128.69, 129.73, 129.85, 131.97, 137.14, 140.14 (C$_{arom.}$), 167.91 (C^2). Found, %: C 74.63; H 7.63; N 3.84. $[M + 1]^+$ 354. $C_{22}H_{27}NOS$. Calculated, %: C 74.73; H 7.69; N 3.94. *M* 353.5.

1-Benzyl-6-phenyl-5-(phenylsulfanyl)piperidin-2-one (IIId). Yield 80%, mp 68–69°C. IR spectrum, ν, cm^{-1}: 1645 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.65–1.78 m (1H, CH), 1.96–2.13 m (1H, CH), 2.44–2.61 m (2H, CH_2), 3.24 d (1H, CH, *J* 10.0 Hz), 3.66–3.75 m (1H, CH), 4.40 d (1H, CH, *J* 3.0 Hz), 5.35 d (1H, CH, *J* 9.0 Hz), 7.07 d (2H$_{arom}$, *J* 8.2 Hz), 7.16 d (2H$_{arom}$, *J* 9 Hz), 7.25–7.44 m (11H$_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 20.67 (C^4), 27.89 (C^3), 47.40 (CH_2N), 48.46 (C^5), 63.30 (C^6), 126.52, 127.05, 127.52, 127.84, 127.91, 128.32, 128.82, 129.16, 132.02, 132.94, 136.85, 139.55 (C$_{arom.}$), 168.41 (C^2). Found, %: C 77.10; H 5.91; N 3.83. $[M + 1]^+$ 374. $C_{24}H_{23}NOS$. Calculated, %: C 77.17; H 5.96; N 3.91. *M* 373.5.

1-Benzyl-5-[(4-methylphenyl)sulfanyl]-6-phenylpiperidin-2-one (IIIe). Yield 73%, mp 104–105°C. IR spectrum, ν, cm^{-1}: 1660 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.60–1.73 m (1H, CH), 2.01–2.09 m (1H, CH), 2.27 s (3C, CH_3), 2.55–2.61 m (2H, CH_2), 3.25 d (1H, CH, *J* 9.0 Hz), 3.55–3.63 m (1H, CH), 4.40 d (1H, CH, *J* 3.1 Hz), 5.38 d (1H, CH, *J* 9.0 Hz), 7.06–7.19 m (8H$_{arom.}$), 7.29–7.42 m (6H$_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 20.54 (CH_3), 20.63 (C^4), 27.86 (C^3),

47.38 (CH_2N), 49.08 (C^5), 62.88 (C^6), 126.42, 127.05, 127.76, 127.89, 128.25, 128.80, 129.21, 129.76, 132.62, 136.88, 137.30, 139.63 ($C_{arom.}$), 168.39 (C^2). Found, %: C 77.75; H 6.24; N 3.34. $[M + 1]^+$ 388. $C_{25}H_{25}NOS$. Calculated, %: C 77.69; H 6.34; N 3.27. *M* 387.5.

1,6-Diphenyl-5-(phenylsulfanyl)piperidin-2-one (IIIf). Yield 61%, mp 99–100°C. IR spectrum, ν, cm^{-1}: 1660 (C=O). ^1H NMR spectrum, δ, ppm: 1.76–1.93 m (1H, CH), 2.04–2.20 m (1H, CH), 2.56–2.75 m (2H, CH_2), 3.90–3.98 m (1H, CH), 4.92 d (1H, CH, *J* 3.0 Hz), 7.06 d ($2H_{arom}$, *J* 7.2 Hz), 7.14–7.41 m ($11H_{arom}$), 7.60 d ($2H_{arom}$, *J* 6.8 Hz). ^{13}C NMR spectrum, δ, ppm: 21.16 (C^4), 28.43 (C^3), 48.38 (C^5), 67.78 (C^6), 126.42, 126.85, 127.27, 127.42, 127.66, 128.53, 128.57, 129.35, 131.45, 133.36, 139.66, 142.52 (C_{arom}), 168.37 (C^2). Found, %: C 76.73; H 5.76; N 3.76. $[M + 1]^+$ 360. $C_{23}H_{21}NOS$. Calculated, %: C 76.83; H 5.88; N 3.89. *M* 359.5.

1,6-Diphenyl-5-[(4-methylphenyl)sulfanyl] piperidin-2-one (IIIg). Yield 71%, mp 135–136°C. IR spectrum, ν, cm^{-1}: 1655 (C=O). ^1H NMR spectrum, δ, ppm: 1.74–1.87 m (1H, CH), 2.04–2.14 m (1H, CH), 2.31 c (3H, CH_3), 2.57–2.67 m (2H, CH_2), 3.80–3.87 m (1H, CH), 4.89 d (1H, CH, *J* 3.3 Hz), 7.06 d ($2H_{arom}$, *J* 7.5 Hz), 7.14–7.38 m ($10H_{arom}$), 7.49 d ($2H_{arom}$, *J* 7.8 Hz). ^{13}C NMR spectrum, δ, ppm: 20.49 (CH_3), 21.07 (C^4), 28.39 (C^3), 48.84 (C^5), 67.62 (C^6), 126.44, 126.85, 127.32, 127.65, 128.53, 128.60, 129.59, 130.02, 132.12, 137.29, 139.75, 142.57 ($C_{arom.}$), 168.39 (C^2). Found, %: C 77.19; H 6.03; N 3.63. $[M + 1]^+$ 374. $C_{24}H_{23}NOS$. Calculated, %: C 77.16; H 6.21; N 3.73. *M* 373.5.

1,6-Diphenyl-5-[(4-nitrophenyl)sulfanyl]piperidin-2-one (IIIh). Yield 74%, mp 203–205°C. IR spectrum, ν, cm^{-1}: 1655 (C=O). ^1H NMR spectrum, δ, ppm: 1.93–2.05 m (1H, CH), 2.14–2.30 m (1H, CH), 2.58–2.60 m (2H, CH_2), 4.26–4.33 m (1H, CH), 5.08 d (1H, CH, *J* 3.6 Hz), 7.07–7.43 m ($10H_{arom}$), 7.75 d ($2H_{arom.}$ *J* 8.8 Hz), 8.20 d ($2H_{arom}$, *J* 8.7 Hz). ^{13}C NMR spectrum, δ, ppm: 21.59 (C^4), 28.60 (C^3), 46.67 (C^5), 67.78 (C^6), 123.96, 126.37, 127.09, 127.26, 127.78, 128.49, 128.57, 128.74, 139.19, 142.24, 144.31, 145.24 (C_{arom}), 168.16 (C^2). Found, %: C 68.12; H 4.88; N 6.80. $[M + 1]^+$ 405. $C_{23}H_{20}N_2O_3S$. Calculated, %: C 68.28; H 4.97; N 6.91. *M* 404.5.

1-(4-Methoxyphenyl)-6-phenyl-5-(phenylsulfanyl) piperidin-2-one (IIIi). Yield 83%, mp 114–115°C. IR spectrum, ν, cm^{-1}: 1665 (C=O). ^1H NMR spectrum, δ, ppm: 1.76–1.92 m (1H, CH), 2.04–2.21 m (1H, CH), 2.56–2.73 m (2H, CH_2), 3.67 s (3H, CH_3O), 3.89–3.95 m (1H, CH), 4.85 d (1H, CH, *J* 2.1 Hz), 6.80 d ($2H_{arom}$, *J* 8.8 Hz), 6.96 d ($2H_{arom.}$, *J* 8.7 Hz), 7.24–7.45 m ($8H_{arom.}$), 7.59 d ($2H_{arom.}$, *J* 8.8 Hz). Found, %: C 73.87; H 5.86; N 3.46. $[M + 1]^+$ 390. $C_{24}H_{23}NO_2S$. Calculated, %: C 73.99; H 5.94; N 3.59. *M* 389.5.

1-(4-Methoxyphenyl)-5-[(4-methylphenyl) sulfanyl]-6-phenylpiperidin-2-one (IIIj). Yield 79%, mp 122–123°C. IR spectrum, ν, cm^{-1}: 1655 (C=O). ^1H NMR spectrum, δ, ppm: 1.71–1.85 m (1H, CH), 2.01–2.16 m (1H, CH), 2.31 s (3H, CH_3), 2.54–2.63 m (2H, CH_2), 3.66 s (3H, CH_3O), 3.79–3.83 m (1H, CH), 4.82 d (1H, CH, *J* 3.0 Hz), 6.80 d ($2H_{arom.}$, *J* 8.7 Hz), 6.96 d ($2H_{arom.}$, *J* 8.7 Hz), 7.22–7.38 m ($7H_{arom.}$), 7.49 d ($2H_{arom.}$ *J* 8.7 Hz). ^{13}C NMR spectrum, δ, ppm: 20.52 (CH_3), 21.04 (C^4), 28.36 (C^3), 48.74 (C^5), 54.84 (CH_3O), 67.94 (C^6), 113.66, 126.87, 127.62, 128.41, 128.51, 129.64, 130.00, 132.08, 135.29, 137.27, 139.86, 157.41 ($C_{arom.}$), 168.44 (C^2). Found, %: C 74.27; H 6.11; N 3.28. $[M + 1]^+$ 404. $C_{25}H_{25}NO_2S$. Calculated, %: C 74.39; H 6.23; N 3.45. *M* 403.5.

1-(4-Methoxyphenyl)-5-[(4-nitrophenyl)sulfanyl]-6-phenylpiperidin-2-one (IIIk). Yield 58%, mp 159°C. IR spectrum, ν, cm^{-1}: 1665 (C=O). ^1H NMR spectrum, δ, ppm: 1.89–1.99 m (1H, CH), 2.17– 2.31 m (1H, CH), 2.54–2.79 m (2H, CH_2), 3.67 s (3H, CH_3O), 4.28 m (1H, CH), 5.01 d (1H, CH, *J* 3.0 Hz), 6.81 d ($2H_{arom.}$, *J* 8.4 Hz), 6.98 d ($2H_{arom.}$, *J* 8.4 Hz), 7.25–7.40 m ($5H_{arom.}$), 7.74 d ($2H_{arom.}$ *J* 8.4 Hz), 8.19 d ($2H_{arom.}$ *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 22.03 (C^4), 29.01 (C^3), 47.46 (C^5), 55.66 (CH_3O), 68.89 (C^6), 114.22, 124.65, 127.75, 128.38, 128.95, 129.09, 129.33, 135.49, 139.80, 144.77, 145.73, 157.91 ($C_{arom.}$), 168.64 (C^2). Found, %: C 66.31; H 5.02; N 6.37. $[M + 1]^+$ 435. $C_{24}H_{22}N_2O_4S$. Calculated, %: C 66.34; H 5.10; N 6.45. *M* 434.5.

***N*-[6-Phenyl-5-(phenylsulfanyl)-tetrahydro-2*H*-pyran-2-ylidene]propan-2-iminium perchlorate (IVb).** Yield 50%, mp 81–82°C. IR spectrum, ν, cm^{-1}: 1705 (C=N). ^1H NMR spectrum, δ, ppm: 1.10–1.16 m ($2CH_3$, 6H), 2.18–2.55 m (1H, CH), 2.57–2.63 m (1H, CH), 2.84–2.91 m (1H, CH), 3.05–3.12 m (1H, CH), 3.64–3.72 m (1H, CH), 4.98 d (1H, CH, *J* 3.9 Hz), 5.52–5.60 m (1H, CH), 7.31–7.48 m ($9H_{arom.}$), 11.77 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.55 (CH_3), 20.85 (CH_3), 25.65 (C^4), 30.23 (C^3), 53.64 (C^5), 74.23 (CH), 92.36 (C^6), 127.56, 128.02, 128.46, 128.59, 129.17, 130.46, 136.24, 137.51 ($C_{arom.}$), 178.22 (C=N). Found, %: Cl 8.24; S 7.42. $C_{20}H_{24}ClNO_5S$. Calculated, %: Cl 8.32; S 7.53.

***N*-{[5-(4-Methylphenyl)sulfanyl]-6-phenyltetra-**

hydro-2*H*-pyran-2-ylidene}propan-2-iminium perchlorate (IVc). Yield 48%, mp 110–112°C. IR spectrum, ν, cm^{-1}: 1710 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.07–1.20 m (6H, 2CH_3), 2.11–2.35 m (1H, CH), 2.28 s (3H, CH_3), 2.47–2.63 m (1H, CH), 2.79–2.98 m (1H, CH), 3.03–3.20 m (1H, CH), 3.60–3.77 m (1H, CH), 4.88 d (1H, CH, *J* 3.9Hz), 5.45–5.61 m (1H, CH), 7.22–7.47 m (9$H_{arom.}$), 11.68 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.51 (CH_3), 20.70 (CH_3), 20.77 (CH_3), 25.64 (C^4), 30.22 (C^3), 54.20 (C^5), 73.80 (CH), 92.36 (C^6), 127.89, 128.34, 128.42, 129.01, 129.74, 132.06, 137.15, 137.46 ($C_{arom.}$), 178.25 (C=N). Found, %: Cl 10.26; S 9.29. $C_{21}H_{26}ClNO_5S$. Calculated, %: Cl 10.42; S 9.41.

5-(Arylsulfanyl)-6-phenyltetrahydro-2*H*-pyran-2-ones Va–Vc. A solution of 1.5 mmol of salt **IVb–IVd** in 5 ml of a mixture ethanol–water, 4:1, was stirred at room temperature over 8 h, the solvent was evaporated, the residue was purified by chromatography on silica gel (eluent ethyl acetate–hexane, 2:3).

6-Phenyl-5-(phenylsulfanyl)tetrahydropyran-2-one (Va). Yield 51% from salt **IVb**, 48% from salt **IVe**, mp 72–73°C. IR spectrum, ν, cm^{-1}: 1775 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.90–2.06 m (1H, CH), 2.08–2.21 m (1H, CH), 2.29–2.50 m (2H, CH_2), 4.73 d (1H, CH, *J* 4.2 Hz), 4.89–5.03 m (1H, CH), 7.21–7.44 m (10$H_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 25.70 (C^3), 27.90 (C^4), 54.87 (C^5), 80.51 (C^6), 127.06, 127.48, 128.17, 128.63, 128.91, 131.07, 133.45, 137.95 ($C_{arom.}$), 176.42 (C^2). Found, %: C 71.68; H 5.54; S 11.13. [*M* + 1]$^+$ 285. $C_{17}H_{16}O_2S$. Calculated, %: C 71.80; H 5.67; S 11.25. *M* 284.4.

5-[(4-Methylphenyl)sulfanyl]-6-phenyltetrahydropyran-2-one (Vb). Yield 64% from salt **IVc**, 53 % from salt **IVf**, mp 106–107°C. IR spectrum, ν, cm^{-1}: 1765 (C=O). ^{1}H NMR spectrum, δ, ppm 1.89–2.07 m (1H, CH), 2.11–2.21 m (1H, CH), 2.26 s (3H, CH_3), 2.33–2.49 m (2H, CH_2), 4.60 d (1H, CH, *J* 3.9 Hz), 4.86–5.01 m (1H, CH), 7.11 d (2$H_{arom.}$, *J* 7.8 Hz), 7.20–7.41 m (7$H_{arom.}$). ^{13}C NMR spectrum, δ, ppm: 20.30 (CH_3), 25.82 (C^3), 27.95 (C^4), 55.44 (C^5), 80.62 (C^6), 127.41, 127.84, 128.12, 128.59, 129.60, 131.86, 136.98, 138.11 ($C_{arom.}$), 176.48 (C^2). Found, %: C 72.55; H 6.02; S 10.64. [*M* + 1]$^+$ 299. $C_{18}H_{18}O_2S$. Calculated, %: C 72.45; H 6.08; S 10.75. *M* 298.4.

5-[(4-Nitrophenyl)sulfanyl]-6-phenyltetrahydropyran-2-one (Vc). Yield 52% from salt **IVd**, 49% from salt **IVg**, mp 130–131°C. IR spectrum, ν, cm^{-1}: 1770 (C=O). ^{1}H NMR spectrum, δ, ppm 1.96–2.12 m (2H, CH_2), 2.30–2.55 m (2H, CH_2), 4.99–5.07 m (1H, CH), 5.11–5.14 m (1H, CH), 7.26–7.39 m (3$H_{arom.}$), 7.50–7.61 m (4$H_{arom.}$), 8.09 d (2$H_{arom.}$, *J* 8.6 Hz). ^{13}C NMR spectrum, δ, ppm: 27.73 (C^4), 28.65 (C^3), 52.77 (C^5), 80.54 (C^6), 124.06, 126.50, 127.95, 128.84, 139.21, 142.27, 144.37, 144.50 ($C_{arom.}$), 176.31 (C^2). Found, %: C 61.84; H 4.48; N 4.12; S 9.53. [*M* + 1]$^+$ 330. $C_{17}H_{15}NO_4S$. Calculated, %: C 61.99; H 4.59; N 4.25; S 9.73. *M* 329.4.

5-{[4-(Nitrophenyl)sulfanyl](phenyl)methyl}-dihydro-3*H*-furan-2-one (VIc). To a solution of 0.2 g of unpurified salt **IVc** in 3 ml of acetone was added 0.05 g of anhydrous sodium acetate, and the mixture was left standing for 24 h. The solvent was evaporated, the organic substance insoluble in water was extracted with chloroform (2 × 20 ml), the extract was dried with anhydrous magnesium sulfate, filtered, and evaporated. The residue was crystallized from hexane. Yield 68%, mp 125°C. IR spectrum, ν, cm^{-1}: 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.01–2.15 m (1H, CH), 2.27–2.39 m (1H, CH), 2.73–2.85 m (2H, CH_2), 4.21–4.33 m (1H, CH), 5.45 d (1H, CH, *J* 9 Hz), 7.28–7.45 m (7$H_{arom.}$), 7.99 d (2$H_{arom.}$, *J* 8.7 Hz). ^{13}C NMR spectrum, δ, ppm: 25.68 (C^4), 28.63 (C^3), 44.13 ($C^{Ph–CH}$), 82.63 (C^5), 123.53, 127.53, 128.22, 128.64, 128.71, 137.37, 143.91, 145.03 ($C_{arom.}$), 169.95 (C^2). Found, %: C 61.83; H 4.47; N 4.46; S 9.61. [*M* + 1]$^+$ 330. $C_{17}H_{15}NO_4S$. Calculated, %: C 61.99; H 4.59; N 4.25; S 9.73. *M* 329.4.

REFERENCES

1. Kaiser, A., Ulmer, D., Goebel, T., Holzgrabe, U., Saeftel, M., and Hoerauf, A., *Mini-Rev. Med. Chem*., 2006, vol. 6, p. 1231.
2. Pei, Z., Li, X., Geldern, T.W., Longenecker, K., Pirch, O., Ste-wort, K.D., Backers, B.J., Lai, C., Lubben, T.H., Ballaron, S.J., Beno, D.W.A., Kempt-Grote, A.J., Sham, H.L., and Trevilligan, J.M., *J. Med. Chem*., 2007, vol. 50, p. 1983.
3. Nara, S., Tanaka, R., Eishima, J., Hora, M., Takahashi, Y., Otaki, S., Foglesong, R.G., Hugnes, R.F., Turkington, S., and Kanda, Y., *J. Med. Chem*., 2003, vol. 46, p. 2467.
4. Buffat, M.G.P., *Tetrahedron*, 2004, vol. 60, p. 1701.
5. Rodriguez, J., *Stud. Nat. Prod. Chem*., 2000, vol. 24, p. 573.
6. Weintraub, P.M.V., Sabol, J.S., and Kane, J.M., Borcherding, D.R., *Tetrahedron*, 2003, vol. 59, p. 2553.
7. Xu, F., Corley, E., Murry, J.A., and Tschoen, D.M., *Org. Lett*., 2007, vol. 9, p. 2669.
8. Davis, F. and Xang, B.. *Org. Lett*., 2003, vol. 5, p. 5051.
9. Kaveski, R., *Tetrahedron*, 2001, vol. 57, p. 8385.
10. Watson, P.S., Jiang, B., and Scott, B.. *Org. Lett*., 2000, vol. 2, p. 3679.

11. Davis, F., Fang, T., Chao, B., and Burns, D.M.. *Synthesis*, 2000, 2106.
12. Takahashi, K., Yamamoto, S., and Naka, M.. Japan Patent 1447401A1, 2004.
13. Rodrigues, R., Estiarte, M.A., Diez, A., Rubiralta, M., Colell, A., Garsia-Ruiz, C., and Fernander-Checa, J.C. *Tetrahedron*, 1996, vol. 52, p. 7727.
14. Fox, D.J., Morley, T.J., Taylor, S., and Warren, S., *Org. Biomol. Chem*., 2005, vol. 3, p. 1369.
15. Robin, S. and Roussean, G., *Tetrahedron*, 1998, vol. 54, p. 13681.
16. Zefirov, N.S., Cmit, V.A., Bodrikov, I.V., and Krimer, M.Z., *Dokl. Akad. Nauk SSSR*, 1978, vol. 240, p. 858.
17. Krimer, M.Z., Cmit, V.A., and Shamshurin, A.A., *Dokl. Akad. Nauk SSSR*, 1973, 208, 864.
18. Vas'kevich, A.I., Gevaza, Yu.I., Vas'kevich, R.I., and Staninets, V.I., *Khim. Geterotsikl. Soedin*., 2004, p. 1251.
19. Vas'kevich, A.I. and Staninets, V.I., *Ukr. Khim. Zh*., 2006, vol. 72, p. 44.
20. Vas'kevich, A.I., Vas'kevich, R.I., Staninets, V.I., But, S.A., and Chernega, A.I., *Zh. Org. Khim*., 2007, vol. 43, p. 1530.
21. Sheldric, G.M., *SHELXS97. Program for Solution of Crystal Structure*. University of Gottingen Germany, 1997.
22. Sheldric, G.M., *SHELXS97. Program for the Refinement of Crystal Structures*, Univetsity of Gottingen, Germany., 1997.