DOI 10.1007/s10593-018-2215-0

*Chemistry of Heterocyclic Compounds* **2017**, *53*(12), 1335–1339

# Reaction of *N*-(3-oxoalkenyl)chloroacetamides with sodium *p*-toluenesulfinate – synthesis of 3-tosylpyridin-2(1*H*)-ones

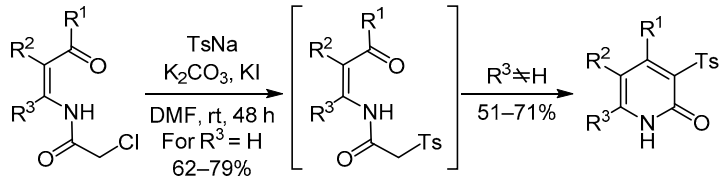
**Dmitry S. Goncharov[1], Ivan V. Kulakov[1], Alexander S. Fisyuk[1,2]***

[1] *F. M. Dostoevskii Omsk State University, 55a Mira Ave., Omsk 644077, Russia; e-mail: fisyuk@chemomsu.ru*

[2] *Omsk State Technical University, 11 Mira St., Omsk 644050, Russia*

Translated from Khimiya Geterotsiklicheskikh Soedinenii, 2017, *53*(12), 1335–1339

Submitted August 31, 2017
Accepted October 6, 2017




$R^1$ = Me, Ph; $R^1 + R^2 = (CH_2)_3$; $R^1 + R^2 = (CH_2)_4$; $R^2 = H$
$R^2 + R^3 = (CH_2)_4$; $R^3$ = H, Me

A series of *N*-(3-oxoalkenyl)chloroacetamides was prepared by acylation of β-enaminoketones with chloroacetyl chloride. A reaction of these compounds with sodium *p*-toluenesulfinate in dimethylformamide in the presence of potassium carbonate led to 3-tosylpyridin-2(1*H*)-ones. The limitations of this reaction were studied.

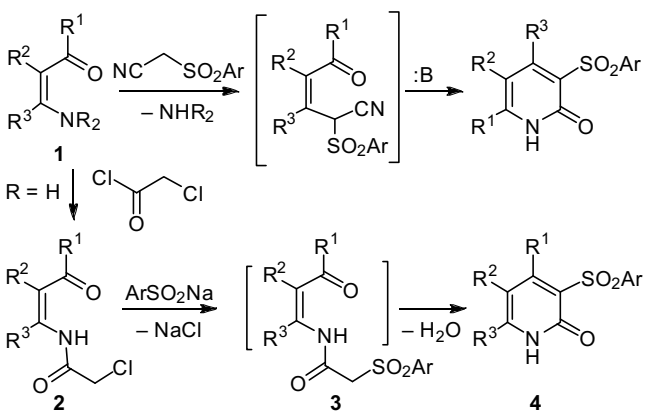
**Keywords**: enaminoketones, *N*-(3-oxoalkenyl)chloroacetamides, 3-tosylpyridin-2(1*H*)-ones, intramolecular cyclization.

Pyridin-2(1*H*)-ones are the privileged scaffolds in medicinal chemistry. The structural motif of pyridin-2(1*H*)-ones is widely represented in natural compounds.[1–3] Compounds of this type include biologically active molecules that have shown anticancer,[4,5] antiviral (including antiHIV),[6,7] cardiotonic,[8] anticonvulsant,[9] and other types of biological effects.[10,11] For this reason, it is important to continue the development of new methods for the preparation of pyridin-2(1*H*)-ones.

We have previously reported that intramolecular cyclization of *N*-(3-oxoalkyl)amides and *N*-(3-oxoalkenyl)-amides provides a convenient method for the synthesis of pyridin-2(1*H*)-ones functionalized at position 3,[12–15] as well as their hydrogenated derivatives.[16–18] The aforementioned method was used to obtain various compounds of this class,[14,15,19,20] including 3-tosyl-3,4-dihydropyridin-2(1*H*)-ones.[21]

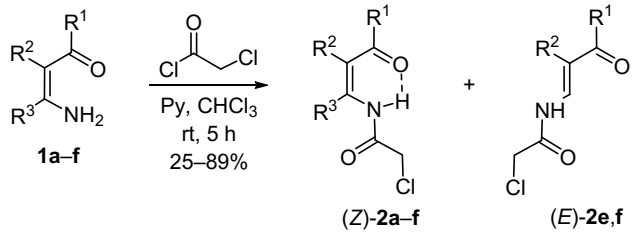
This approach was used to synthesize only one 3-tosyl-substituted pyridin-2(1*H*)-one.[15] During the nucleophilic substitution of halide with a tosyl group in *N*-(3-oxoalkenyl)chloroacetamide **2**, an intramolecular cyclization of *p*-toluenesulfonyl derivative **3** occurred with the formation of the corresponding pyridin-2(1*H*)-one **4**. It is important to note that the earlier method for the preparation of 3-arylsulfonylpyridin-2(1*H*)-ones was based on the condensation of arylsulfonylacetonitrile with β-enaminoketones **1** (Scheme 1).[22,23] These approaches complement each other by allowing to convert the same starting β-enaminoketone into the isomeric pyridin-2(1*H*)-ones with different arrangement of the $R^1$ and $R^3$ substituents in the ring.

**Scheme 1**



For the purpose of studying the limitations of *N*-(3-oxoalkenyl)chloroacetamide reactions with sodium *p*-toluenesulfinate (TsNa), we performed the synthesis of 3-tosylpyridin-2(1*H*)-ones both with the previously known compounds **2a**–**c**[12,15,24] and the new *N*-(3-oxoalkenyl)-chloroacetamides **2d**–**f**, which were obtained in 25–81% yields according to a published procedure[15] by acylation of the respective enaminoketones **1** with chloroacetyl chloride. Compounds **2e**,**f** lacking a substituent at the α-position relative to the nitrogen atom were formed as mixtures of isomers (84:16 ratio of isomers (*Z*)/(*E*)-**2f** and 63:37 ratio of isomers (*Z*)/(*E*)-**2e**). At the same time, for *N*-(3-oxoalkenyl)chloroacetamide **2d** containing the methyl group ($R^3$ = Me) in the α-position to the nitrogen atom, unlike its structural isomer **2e**, no formation of the (*E*)-configuration was observed. The individual (*Z*)- and (*E*)-isomers **2e** were isolated by silica gel column chromatography. The (*E*)-isomer was separated by crystallizing a mixture of (*Z*)- and (*E*)-isomers of compound **2f** from EtOAc (Scheme 2).

**Scheme 2**




**a** $R^1 = R^3 = Me$, $R^2 = H$; **b** $R^1 = Ph$, $R^2 = H$, $R^3 = Me$
**c** $R^1 = Me$, $R^2 + R^3 = (CH_2)_4$; **d** $R^1 + R^2 = (CH_2)_3$, $R^3 = Me$
**e** $R^1 + R^2 = (CH_2)_4$, $R^3 = H$; **f** $R^1 + R^2 = (CH_2)_3$, $R^3 = H$

The composition and structure of the obtained products were confirmed by data of elemental analysis, $^1H$, $^{13}C$ NMR and IR spectroscopy. The (*Z*)-isomers of compounds **2a**–**f** showed a broad absorption band in IR spectra at 3150–3250 $cm^{-1}$ due to the stretching vibrations of the hydrogen-bonded N–H group. The NH proton was observed in $^1H$ NMR spectra of compounds **2a**–**f** in $CDCl_3$ solution in the range of 12.1–13.4 ppm as a result of intramolecular hydrogen bond with the oxygen atom of carbonyl group, confirming its (*Z*)-configuration. At the same time, IR spectra of (*E*)-isomers featured a narrow absorption band at 3410 $cm^{-1}$ due to the stretching vibrations of N–H bond, while $^1H$ NMR spectra showed the NH proton signal at 8.3 ppm. These observations were in a good agreement with literature data on (*E*)- and (*Z*)-isomers of *N*-acyl-β-enaminoketones.[25]

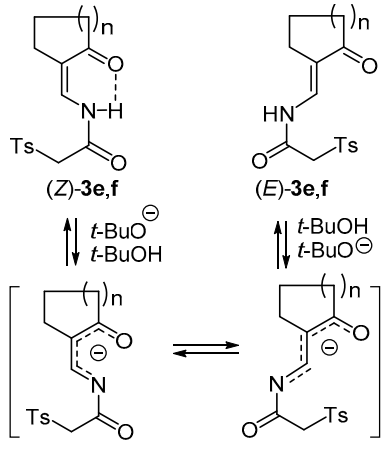
The experiments regarding nucleophilic substitution of chloride in *N*-(3-oxoalkenyl)chloroacetamides **2a**–**d** with a tolylsulfonyl group by the action of TsNa showed that the obtained 3-tosylacetamides **3a**–**d** cyclized under the reaction conditions, forming 3-tosylpyridin-2(1*H*)-ones **4a**–**d** already at room temperature according to TLC data. Performing the reaction in the presence of $K_2CO_3$ in DMF for 1–2 days allowed to obtain 3-tosylpyridin-2(1*H*)-ones **4a**–**c** in 51–71% yields (Scheme 3).

At the same time, the reaction of chloroacetamide **2d** with TsNa under these conditions did not proceed to completion according to TLC analysis. It could be completed by subsequent heating of the reaction mixture to 70°C for 5 h or by performing the reaction at room temperature for 4 days. The longer reaction time required in the case of compound **2d** was apparently associated with the lower activity of carbonyl group in the five-membered ring.

Attempts to convert *N*-(3-oxoalkenyl)chloroacetamides (*Z*)-**2e**,**f** to the corresponding 3-(tolylsulfonyl)pyridin-2-ones **4e**,**f** were unsuccessful neither by heating in the presence of $K_2CO_3$ nor by treatment with potassium *tert*-butoxide. The only major products of the reaction were the (*E*)-isomers of tosylacetamides **3e**,**f**, obtained in 62 and 79% yields, respectively. Decreasing the steric bulk of the substituent $R^3$ at the α-position relative to the nitrogen atom in *N*-(3-oxoalkenyl)amide should stabilize the (*E*)-isomer by minimizing the steric interaction with carbonyl group at the double bond. On the other hand, increasing the steric bulk of substituent $R^3$ favored the (*Z*)-isomer *via* additional stabilization by intramolecular hydrogen bond.

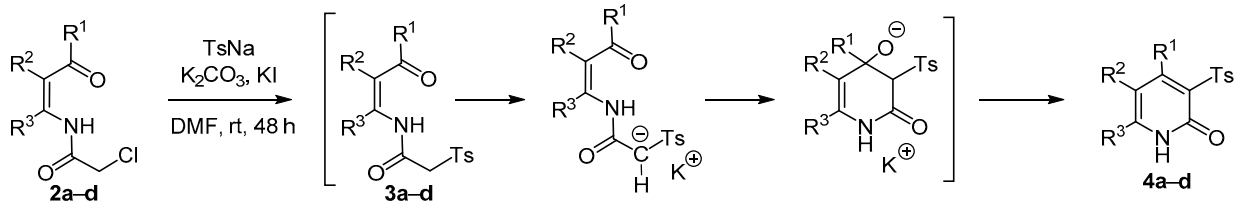
Deprotonation of the nitrogen atom by the action of bases resulted in the control of equilibrium between the isomers (tautomers) only through steric factors, increasing the stability of (*E*)-isomers in the case of compounds **3e**,**f** ($R^3$ = H), the cyclization of which is impossible (Scheme 4).

**Scheme 4**




**e** n = 2, **f** n = 1

**Scheme 3**




**a** $R^1 = R^3 = Me$, $R^2 = H$; **b** $R^1 = Ph$, $R^2 = H$, $R^3 = Me$; **c** $R^1 = Me$, $R^2 + R^3 = (CH_2)_4$; **d** $R^1 + R^2 = (CH_2)_3$, $R^3 = Me$

We observed a similar substituent effect during the cyclization of *N*-(3-oxoalkenyl)arylacetamides to 6-arylpyridin-2(1*H*)-ones.[13]

Thus, intramolecular cyclization of *N*-(3-oxoalkenyl)-tosylacetamides can be successfully used for the synthesis of 3-tosylpyridin-2-ones, including derivatives with alicyclic rings fused at the C(4)–C(5) and C(5)–C(6) bonds. At the same time, this method failed to provide 3-tosylpyridin-2(1*H*)-ones lacking substituents at the C(6) position. However, the diversity of suitable starting materials and the simple experimental procedure make *N*-(3-oxoalkenyl)chloroacetamides convenient precursors for the preparation of 3-tosyl-substituted pyridin-2-ones.

## Experimental

IR spectra were recorded on an Infralum FT-801 spectrometer in KBr pellets. $^1$H and $^{13}$C NMR spectra were acquired on a Bruker DRX-400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ solution, with TMS as internal standard. $^{13}$C NMR spectra were acquired in JMOD mode. Elemental analysis was performed on a Carlo Erba EA 1106 automatic CHN-analyzer. The reaction progress and purity of the obtained compounds were controlled by TLC method on Sorbfil AF-A-UF plates, visualization with iodine vapor and under UV light. The separation and purification of the obtained compounds were performed by column chromatography, using L 40/100 silica gel or alumina as the stationary phase.

The starting β-enaminoketones **1a**–**d**[26] and **1e**,**f**[27] were obtained according to published procedures. The synthesis of *N*-(3-oxoalkenyl)chloroacetamides **2a**–**c** was described in our earlier work.[24]

**Synthesis of *N*-(3-oxoalkenyl)chloroacetamides 2d–f** (General method). A solution of enaminoketone **1d**–**f** (11 mmol) in anhydrous $CHCl_3$ (15 ml) and pyridine (1.58 g, 20 mmol) was cooled and treated by dropwise addition of chloroacetyl chloride (1.9 g, 17 mmol) solution in $CHCl_3$ (5 ml). The reaction mixture was stirred for 5 h at room temperature and left overnight. The solution was then washed with aqueous 10% HCl solution, several times with $H_2O$, dried over anhydrous $Na_2SO_4$, and the solvent was removed by evaporation at reduced pressure.

**2-Chloro-*N*-[1-(2-oxocyclopentylidene)ethyl]acetamide (2d)**. The product was purified by column chromatography ($Al_2O_3$, $CH_2Cl_2$–hexane, 5:1). Yield 1.97 g (89%), light-yellow oil. IR spectrum, ν, cm$^{-1}$: 3200–3100 (NH), 1692 (C=O), 1675 (C=O), 1613 (NC=O). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.89–1.98 (2H, m, H-4); 2.39 (3H, s, $CH_3$); 2.42 (2H, t, $^3J$ = 7.9, H-5); 2.61–2.67 (2H, m, H-3); 4.08 (2H, s, $CH_2Cl$); 12.61 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 18.3 ($CH_3$); 19.7 (C-4); 27.2 (C-5); 39.6 (C-3); 43.2 ($CH_2$); 116.3 (C-1); 146.2 ($\underline{C}CH_3$); 165.7 (NHCO); 208.3 ($\underline{C}OCH_3$). Found, %: C 53.75; H 5.76; N 6.72. $C_9H_{12}ClNO_2$. Calculated, %: C 53.61; H 6.00; N 6.95.

**2-Chloro-*N*-[(2-oxocyclohexylidene)methyl]acetamide (2e)** (a mixture of (*Z*)- and (*E*)-isomers). The dark residue was purified by silica gel flash chromatography ($CHCl_3$–EtOAc, 1:1). Chloroacetamide **2e** was obtained as a light-yellow oil (0.55 g, 25%) containing a mixture of (*Z*)- and (*E*)-isomers at 84:16 ratio according to the data of $^1$H NMR spectroscopy. The individual isomers were isolated by silica gel column chromatography, using 1:1 $CHCl_3$–EtOAc as eluent.

**Compound (*Z*)-2e**. Colorless crystals, mp 62–64°C (hexane). $R_f$ 0.56 ($CHCl_3$–EtOAc, 1:1). IR spectrum, ν, cm$^{-1}$: 3254 (NH), 1697 (C=O), 1663, 1587 (NC=O). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.71–1.88 (4H, m), 2.41–2.54 (4H, m, $(CH_2)_4$); 4.13 (2H, s, $CH_2Cl$); 7.19 (1H, dt, $^3J$ = 10.6, $^4J$ = 1.5, C$\underline{H}$NH); 12.16 (1H, m, NH). $^{13}$C NMR spectrum, δ, ppm: 22.3; 23.3; 28.9; 39.6 ($4CH_2$); 42.3 ($CH_2Cl$); 115.4 ($\underline{C}$=CHN); 132.2 (CHN); 165.7 (NHCO); 203.9 (C=O). Found, %: C 53.87; H 6.29; N 6.71. $C_9H_{12}ClNO_2$. Calculated, %: C 53.61; H 6.00; N 6.95.

**Compound (*E*)-2e**. Colorless crystals, mp 115–117°C (EtOAc). $R_f$ 0.56 ($CHCl_3$–EtOAc, 1:1). IR spectrum, ν, cm$^{-1}$: 3411 (NH), 1710 (C=O), 1687, 1598 (NC=O). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.80–1.89 (4H, m), 2.32–2.57 (4H, m, $(CH_2)_4$); 4.20 (2H, s, $CH_2Cl$); 7.90 (1H, d, $^3J$ = 12.1, C$\underline{H}$NH); 8.28 (1H, d, $^3J$ = 12.1, NH). $^{13}$C NMR spectrum, δ, ppm: 22.6; 22.7; 24.5; 39.6 ($4CH_2$); 42.6 ($CH_2Cl$); 118.6 ($\underline{C}$=CHN); 128.4 (CHN); 163.8 (NHCO); 199.1 (C=O). Found, %: C 53.93; H 5.72; N 7.26. $C_9H_{12}ClNO_2$. Calculated, %: C 53.61; H 6.00; N 6.95.

**2-Chloro-*N*-[1-(2-oxocyclopentylidene)methyl]acetamide (2f)** (mixture of (*E*)- and (*Z*)-isomers). The obtained dark residue (1.68 g, 81%) containing a mixture of (*Z*)- and (*E*)-isomers of chloroacetamide **2f** (63:37 ratio according to the data of $^1$H NMR spectroscopy) was first purified by silica gel flash chromatography ($CHCl_3$–EtOAc, 1:1), followed by removal of the solvent and recrystallization from EtOAc. The product was pure (*E*)-isomer of chloroacetamide **2f** (300 mg, 15% yield) isolated as light-yellow crystals. The evaporation of mother liquors afforded viscous yellow oil containing the (*Z*)-isomer with a small amount of the (*E*)-isomer.

**Compound (*E*)-2f**. Light-yellow crystals, mp 164–165°C. $R_f$ 0.45 (EtOAc–hexane, 1:1). IR spectrum, ν, cm$^{-1}$: 3408 (NH), 1710 (C=O), 1632 (NC=O). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.99–2.07 (2H, m, 4-$CH_2$); 2.38 (2H, t, $^3J$ = 8.0, 5-$CH_2$); 2.63 (2H, td, $^3J$ = 7.3, $^4J$ = 2.7, 3-$CH_2$); 4.19 (2H, s, $CH_2Cl$); 7.78 (1H, dt, $^3J$ = 11.9, $^4J$ = 2.5, C$\underline{H}$NH); 8.31 (1H, br. d, $^3J$ = 11.0, NH). $^{13}$C NMR spectrum, δ, ppm: 19.8 (C-4); 25.4 (C-5); 38.6 (C-3); 42.4 ($CH_2Cl$); 119.9 (C-1); 125.3 (CHN); 164.4 (NHCO); 206.8 (C-2). Found, %: C 51.59; H 5.74; N 7.18. $C_8H_{10}ClNO_2$. Calculated, %: C 51.21; H 5.37; N 7.47.

**Compound (*Z*)-2f**. Yellow oil. $R_f$ 0.65 (EtOAc–hexane, 1:1). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.99–2.07 (2H, m, 4-$CH_2$); 2.41 (2H, t, $^3J$ = 7.8, 5-$CH_2$); 2.67 (2H, td, $^3J$ = 7.3, $^4J$ = 1.8, 3-$CH_2$); 4.15 (2H, s, $CH_2Cl$); 7.26 (1H, dt, $^3J$ = 10.5, $^4J$ = 2.1, C$\underline{H}$NH); 11.77 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm (obtained by subtracting the signals of (*E*)-isomer from the spectrum of isomer mixture): 21.1 (C-4); 27.4 (C-5); 39.5 (C-3); 42.2 ($CH_2Cl$); 117.7 (C-1); 127.9 (CHN); 165.1 (NHCO); 210.2 (C-2).

**Synthesis of (4-methylphenyl)sulfonylpyridones 4a–d** (General method). A mixture of compound **2** (1.0 mmol), $K_2CO_3$ (207 mg, 1.5 mmol), TsNa monohydrate (294 mg,

1.5 mmol), and KI (17 mg, 0.10 mmol) in anhydrous DMF (3 ml) was stirred for 2 days at room temperature, then poured into cold water (12 ml). The precipitate was filtered off and recrystallized.

**4,6-Dimethyl-3-[(4-methylphenyl)sulfonyl]-2(1*H*)-one (4a)**. Yield 70%, colorless crystals, mp 268–270°C (decomp.). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.16 (3H, s, 4-$CH_3$); 2.36 (3H, s, 6-$CH_3$); 2.62 (3H, s, Ar$CH_3$); 6.07 (1H, s, 5-H); 7.33–7.80 (2H, m, H Ar); 12.01 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 18.37 (6-$CH_3$); 20.91 (4-$CH_3$); 21.14 (Ar$\underline{C}H_3$); 109.15 (C-5); 122.70 (C-3); 127.55; 128.68; 139.46; 142.95 (C Ar); 151.29 (C-6); 156.33 (C-4); 158.29 (C-2). $^1$H and $^{13}$C NMR spectra, as well as melting point were in agreement with the previously reported data for compound **4a**.[15]

**6-Methyl-3-[(4-methylphenyl)sulfonyl]-4-phenylpyridin-2(1*H*)-one (4b)**. Yield 205 mg (60%), colorless crystals, mp 244–245°C (EtOH). IR spectrum, ν, cm$^{-1}$: 3250 (NH), 1643, 1617 (C=O), 1308, 1149 ($SO_2$). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.32 (3H, s, 6-$CH_3$); 2.39 (3H, s, Ar$C\underline{H}_3$); 6.06 (1H, s, H-5); 7.17–7.24 (2H, m, H Ar); 7.33–7.53 (5H, m, H Ph); 7.78–7.90 (2H, m, H Ar); 13.41 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 19.0 (6-$CH_3$); 21.6 (Ar$\underline{C}H_3$); 110.9 (C-5); 124.0 (C-3); 127.3; 127.7; 128.5; 128.6 (2C); 128.8 (2C); 138.1; 138.8; 143.5; 150.3 (C-4); 159.1 (C-6); 161.3 (C-2). Found, %: C 67.49; H 5.21; N 4.38. $C_{19}H_{17}NO_3S$. Calculated, %: C 67.24; H 5.05; N 4.13.

**4-Methyl-3-[(4-methylphenyl)sulfonyl]-5,6,7,8-tetrahydroquinolin-2(1*H*)-one (4c)**. Yield 226 mg (71%), colorless crystals, mp 237–238°C (EtOH). IR spectrum, ν, cm$^{-1}$: 3300–3240 (NH), 1639, 1614 (NC=O), 1304, 1156 ($SO_2$). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.69–1.85 (4H, m, 2$CH_2$); 2.38 (3H, s, Ar$C\underline{H}_3$); 2.42–2.51 (4H, m, 2$CH_2$); 2.71 (3H, s, 4-$CH_3$); 7.18–7.23 (2H, m, H Ar); 7.83–7.89 (2H, m, H Ar); 12.95 (1H, br. s, NH). $^{13}$C NMR spectrum, δ, ppm: 16.1 (4-$CH_3$); 20.8 ($CH_2$); 21.6 (Ar$\underline{C}H_3$); 22.6, 24.5, 27.5 (3$CH_2$); 115.6 (C-4a); 124.9 (C-3); 128.1 (2C Ar); 128.5 (2C Ar); 140.1 (C Ar); 143.1 (C Ar); 148.6 (C-4); 157.5 (C-8a); 159.7 (C-2). Found, %: C 64.04; H 5.86; N 4.63. $C_{17}H_{19}NO_3S$. Calculated, %: C 64.33; H 6.03; N 4.41.

**1-Methyl-4-[(4-methylphenyl)sulfonyl]-2,5,6,7-tetrahydro-3*H*-cyclopenta[*c*]pyridin-3-one (4d)** was obtained according to the general method, but after stirring for 1 day at room temperature the reaction mixture was heated to 70°C and maintained for 5 h. Yield 154 mg (51%), colorless crystals, mp 262–263°C (EtOH). IR spectrum, ν, cm$^{-1}$: 3290–3240 (NH), 1631 (NC=O), 1317, 1151 ($SO_2$). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.05–2.14 (2H, m, $CH_2$); 2.22 (3H, s, 1-$CH_3$); 2.38 (3H, s, Ar$C\underline{H}_3$); 2.63–2.69 (2H, m), 3.50 (2H, t, $^3J$ = 7.7, 2$CH_2$); 7.19–7.23 (2H, m, H Ar); 7.88–7.92 (2H, m, H Ar). $^{13}$C NMR spectrum, δ, ppm: 17.3 (1-$CH_3$); 21.6 (Ar$\underline{C}H_3$); 24.8, 28.0, 34.5 (3$CH_2$); 121.7 (C-4); 122.6 (C-7a); 128.5 (2C Ar); 128.7 (2C Ar); 139.0 (C Ar); 143.6 (C Ar); 145.4 (C-4a); 160.9 (C-1); 164.2 (C-3). Found, %: C 63.65; H 5.84; N 4.48. $C_{16}H_{17}NO_3S$. Calculated, %: C 63.34; H 5.65; N 4.62.

**(*E*)-2-[(4-Methylphenyl)sulfonyl]-*N*-[(2-oxocyclohexylidene)methyl]acetamide (3e)** was obtained according to the general method for the synthesis of compounds **4**. Yield 199 mg (62%), colorless crystals, mp 142–143°C (EtOH–$H_2O$). IR spectrum, ν, cm$^{-1}$: 3263 (NH), 1714 (C=O), 1678, 1570 (NC=O), 1330, 1152 ($SO_2$). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.76–1.99 (4H, m), 2.42–2.46 (2H, m, 3$CH_2$); 2.47 (3H, s, $CH_3$); 2.51–2.57 (2H, m, $CH_2$); 4.13 (2H, s, $CH_2SO_2$); 7.37–7.41 (2H, m, H Ar); 7.72–7.76 (2H, m, H Ar); 7.84–7.90 (1H, m, C$\underline{H}$NH); 8.69 (1H, m, NH). $^{13}$C NMR spectrum, δ, ppm: 21.8 ($CH_3$); 22.6, 22.7, 24.6, 39.7 (4$CH_2$); 61.9 ($CH_2SO_2$); 118.7; 128.0 (2C Ar); 128.5 (CHN); 130.5 (2C Ar); 134.6 (C Ar); 146.4 (C Ar); 158.7 (NHCO); 199.3 (C=O). Found, %: C 59.55; H 5.71; N 4.59. $C_{16}H_{19}NO_4S$. Calculated, %: C 59.79; H 5.96; N 4.36.

**(*E*)-2-[(4-Methylphenyl)sulfonyl]-*N*-[(2-oxocyclopentylidene)methyl]acetamide (3f)**. A solution of acetamide (*E*)-**2f** (150 mg, 0.8 mmol) in *i*-PrOH (5 ml) was treated by the addition of TsNa hydrate (230 mg, 1.2 mmol) and refluxed for 24 h. The precipitated salt was filtered off, the solvent was evaporated, the residue was triturated with hexane, and the amorphous hygroscopic powder was recrystallized three times from 1:1 mixture of $H_2O$–EtOH. Yield 195 mg (79%), white crystals, mp 152–153°C. IR spectrum, ν, cm$^{-1}$: 3275 (NH); 1697 (C=O), 1607, 1526 (NC=O), 1323, 1153 ($SO_2$). $^1$H NMR spectrum, δ, ppm (*J*, Hz): 1.96–2.06 (2H, m, 4-$CH_2$); 2.38 (2H, t, $^3J$ = 7.8, 5-$CH_2$); 2.43 (3H, s, $CH_3$); 2.65 (2H, td, *J* = 7.2, *J* = 2.6, 3-$CH_2$); 4.20 (2H, s, $CH_2SO_2$); 7.39 (2H, d, *J* = 7.9, H-3,5); 7.69–7.77 (3H, m, C$\underline{H}$NH, H-2,6); 8.75 (1H, br. d, *J* = 11.6, NH). $^{13}$C NMR spectrum, δ, ppm: 19.9 (C-4); 21.8 ($CH_3$); 25.6 (C-5); 38.8 (C-3); 62.1 ($CH_2SO_2$); 120.3 (C-1); 125.4 (CHN); 128.1 (2C Ar); 130.3 (2C Ar); 134.8 (C Ar); 146.2 (C Ar); 159.5 (NHCO); 207.3 (C-2). Found, %: C 58.97; H 5.85; N 4.88. $C_{15}H_{17}NO_4S$. Calculated, %: C 58.61; H 5.57; N 4.56.

*This work was performed with financial support from the Ministry of Education and Science of the Russian Federation (project No. 4.1657.2017/4.6*).

## References

1. Jessen, H. J.; Gademann, K. *Nat. Prod. Rep*. **2010**, *27*, 1168.
2. Jessen, H. J.; Schumacher, A.; Shaw, T.; Pfaltz, A.; Gademann, K. *Angew. Chem.*, *Int. Ed.* **2011**, *50*, 4222.
3. Nagarajan, M.; Xiao, X. S.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. *J. Med. Chem.* **2003**, *46*, 5712.
4. Mathijssen, R. H.; Loos, W. J.; Verweij, J.; Sparreboom, A. *Curr. Cancer Drug Targets* **2002**, *2*, 103.
5. Chen, T.; Luo, Y; Sheng L.; Li, J.; Hu, Y.; Lu, W. *Mol. Diversity* **2013**, *17*, 435.
6. Medina-Franco, J. L.; Martinez-Mayorga, K.; Juarez-Gordiano, C.; Castillo, R. *ChemMedChem* **2007**, *2*, 1141.
7. Liu, N.; Rai, D.; Zhao; F.; Jia, H.; Zhan, P.; Liu, X. *Med. Chem. Commun.* **2015**, *6*, 521.
8. Ravinder, M.; Mahendar, B.; Mattapally, S; Hamsini, K. V.; Reddy, T. N.; Rohit, C.; Srinivas, K.; Banerjee, S. K.; Rao, V. J. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 6010.
9. Hibi, S.; Ueno, K.; Nagato, S.; Kawano, K.; Ito, K.; Norimine, Y.; Takenaka, O.; Hanada, T.; Yonaga, M. *J. Med. Chem.* **2012**, *55*, 10584.
10. Loughlin, W. A.; Jenkins, I. D.; Karis, N. D.; Healy, P. C. *Eur. J. Med. Chem*. **2017**, *127*, 341.

11. Jia, H.; Song, Y.; Yu, J.; Zhan, P.; Rai, D.; Liang, X.; Ma, C.; Liu, X. *Eur. J. Med. Chem*. **2017**, *136*, 144.
12. Kulakov, I. V.; Matsukevich, M. V.; Shulgau, Z. T.; Sergazy, S.; Seilkhanov, T. M.; Puzari, A.; Fisyuk, A. S. *Chem. Heterocycl. Compd*. **2015**, *51*, 991. [*Khim. Geterotsikl. Soedin.* **2015**, *51*, 991.]
13. Goncharov, D. S.; Garkushenko, A. K.; Savelieva, A. P.; Fisyuk, A. S. *ARKIVOC* **2015**, (v), 176.
14. Fisyuk, A. S.; Bogza, Y. P.; Poendaev, N. V.; Goncharov, D. S. *Chem. Heterocycl. Compd.* **2010**, *46*, 844. [*Khim. Geterotsikl. Soedin.* **2010**, 1044.]
15. Goncharov, D. S.; Kostuchenko, A. S.; Fisyuk, A. S. *Chem. Heterocycl. Compd*. **2009**, *45*, 793. [*Khim. Geterotsikl. Soedin.* **2009**, 1005.]
16. Fisyukm, A. S.; Poendaev, N. V. *Molecules*. **2002**, *7*, 119.
17. Fisyuk, A. S.; Poendaev, N. V. *Molecules* **2002**, *7*, 124.
18. Fisyuk, A. S.; Vorontsova, M. A. *Chem. Heterocycl. Compd.* **1998**, *34*, 195. [*Khim. Geterotsikl. Soedin.* **1998**, 220.]
19. Fisyuk, A. S.; Poendaev, N. V.; Bundel', Y. G *Mendeleev Commun*. **1998**, *8*, 12.
20. Fisyuk, A. S.; Bundel', Y. G. *Chem. Heterocycl. Compd*. **1999**, *35*, 125. [*Khim. Geterotsikl. Soedin.* **1999**, 147.]
21. Fisyuk, A. S.; Poendaev, N. V. *Chem. Heterocycl. Compd*. **2003**, *39*, 895. [*Khim. Geterotsikl. Soedin.* **2003**, 1037.]
22. Bondavalli, F.; Bruno, O.; Lo Presti, E.; Menozzi, G.; Mosti, L. *Synthesis* **1999**, 1169.
23. Alberola, A.; Andrés, C.; Ortega, A. G.; Pedrosa, R.; Vicente, M. *J. Heterocycl. Chem.* **1987**, *24,* 709.
24. Fisyuk, A. S.; Kulakov, I. V.; Goncharov, D. S.; Nikitina, O. S.; Bogza, Y. P.; Shatsauskas, A. L. *Chem. Heterocycl. Compd.* **2014**, *50*, 217. [*Khim. Geterotsikl. Soedin.* **2014**, 241.]
25. Shabanas, R.; Rasmussen, J. B.; Lawesson, S.-O. *Tetrahedron* **1981**, *37*, 1819.
26. Baraldi, P. G.; Simoni, D.; Manfredini, S. *Synthesis* **1983**, 902.
27. Thummel, R. P.; Kohli, D. K. *J. Org. Chem.* **1977**, *42*, 2742.