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RESEARCH ARTICLE

Amino acid sulfonamides based on 4-(1-oxo-1*H*-isochromen-3-yl)-benzenesulfonyl chloride

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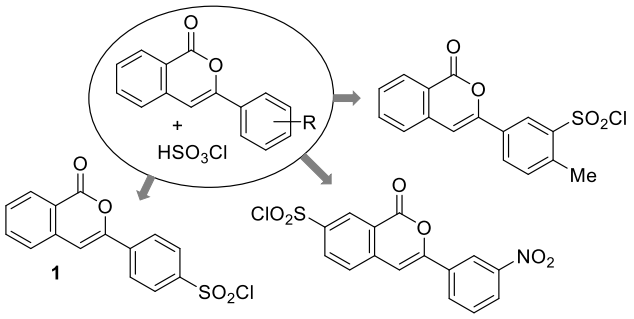
Abstract: The creation of new amino acid derivatives of 4-(1-oxo-1*H*-isochromen-3-yl)benzenesulfonyl chloride **1** was investigated. The interaction of the sulfonyl chloride **1** with amino acid methyl esters (hydrochlorides) in 1,4-dioxane in the presence of triethylamine led to the corresponding amino acid sulfonamide derivatives of isocoumarin. The reaction of the sulfonyl chloride **1** with phenylalanine in the basic aqueous solution was complicated by the lactone system disclosure and led to 2'-carboxydeoxybenzoin ultimately (namely, 2-(2-(4-(*N*-(1-carboxy-2-phenylethyl)sulfamoyl)phenyl)-2-oxoethyl)benzoic acid). Similar product was obtained by the alkali hydrolysis of methyl ((4-(1-oxo-1*H*-isochromen-3-yl)phenyl)sulfonyl)leucinate.

Keywords: sulfonamides; amino acids; 3-phenylisocoumarin; sulfochlorination.

Introduction

Synthetic [1-2] and natural [2-3] compounds that contain the isocoumarin (1*H*-isochromen-1-one) fragment are well known group of oxygen containing heterocycle. These substances have a tremendous potential as starting materials in synthetic organic chemistry (synthesis of isoquinolines [4]) or as bioactive compounds [5-6]. However, isocoumarins can be found in the scientific literature not as often as isomeric chromones and coumarins. It can be explained by the fact that the existing methods for synthesis of isocoumarins and their derivatives [1, 7] do not allow obtaining structures with certain functional groups. Moreover, different polyfunctionalized chromones and coumarins can be easily constructed using phenols as a starting material [8, 9] whereas the synthesis of isocoumarins requires prefunctionalized and not readily available compounds. The electrophilic substitution reactions for isocoumarin compounds have not been widely explored as a possible route for their chemical modification. It can be viewed as an opportunity to tackle the problem. [10-12].

One of the promising electrophilic substitution reactions for the isocoumarin system is a chlorosulfonation. The reaction medium for the chlorosulfonation combines the high activity of the electrophilic particle and weak oxidizing properties, that is especially important for the electron deficient and disposed to oxidative degradation of isocoumarin system. The possibility of preparative



Scheme 1. The basic directions of chlorosulfonation in the 3-aryl-isocoumarins [14].

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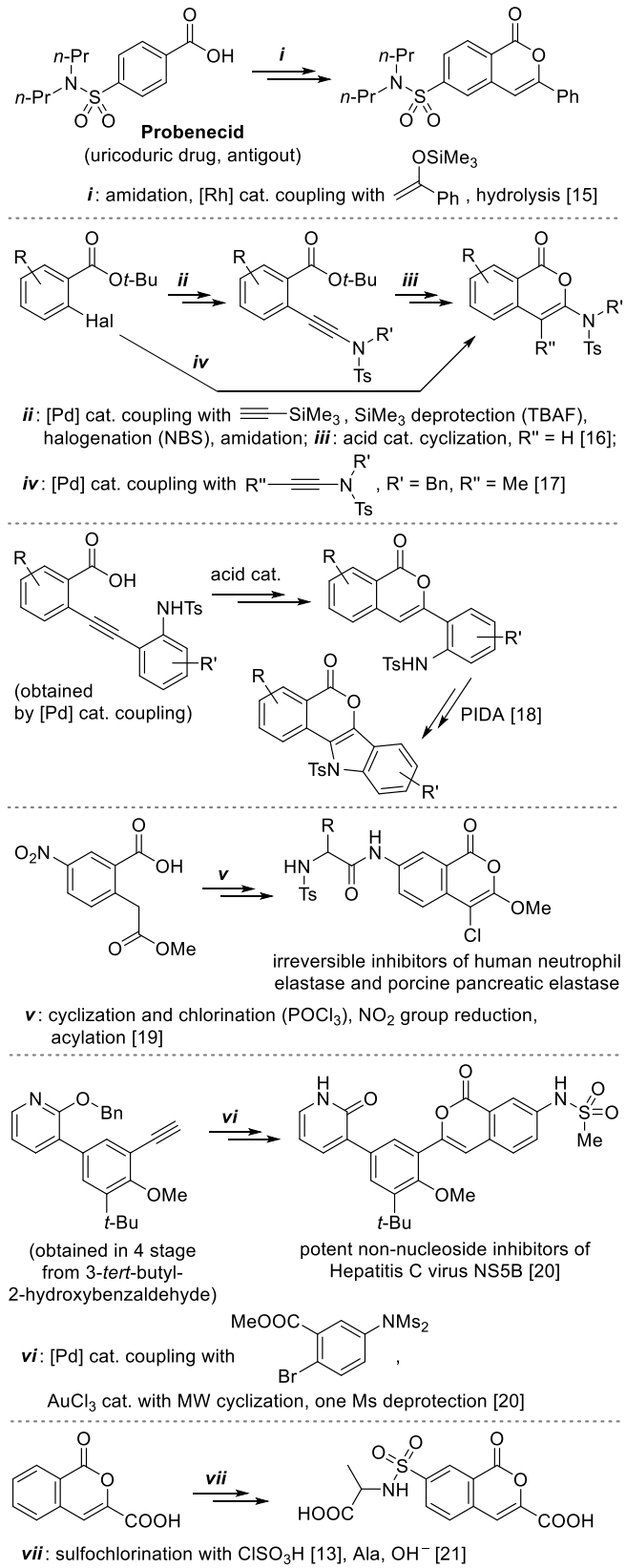
chlorosulfonation of isocoumarin derivatives was confirmed by the preparation of 7-chlorosulfonylisocoumarin-3-carboxylic acid in this way [13].



Scheme 2. Previously reported methods for the synthesis of sulfonamide-containing isocoumarins [15-21].

Earlier, we investigated the basic directions of chlorosulfonation in the 3-arylisocoumarins [14]. For unsubstituted 3-phenylisocoumarin, this reaction proceeds on the 4-position of the phenyl substituent and leads to the sulfonyl chloride **1** (Scheme 1).

The formation of sulfonamides in the reaction of sulfonyl chlorides with selected aromatic and aliphatic amines was also reported [14]. Only several examples of isocoumarins with a sulfonamide group are known to date. The synthetic methods that was developed for obtaining such compounds often required specific substrates, numerous steps, expensive reagents and catalysts (Scheme 2) [15-20]. Moreover, the sulfonamide fragment is attached to isocoumarin mainly by the nitrogen atom and just a few cases of reaction of chlorosulfonyl isocoumarins with amines have been described [21].

The isocoumarins with fragments of amino acid have been attracting significant attention due to their high biological activity [22]. The most known representatives of this class of compounds are ochratoxins [5] and amicoumacins [6] (Figure 1). Therefore, we chose amino acids as an amino component to continue developing synthetic methods and to understand the reactivity of isocoumarins in the following row: isocoumarin – chlorosulfonyl isocoumarin – sulfonamide isocoumarin.

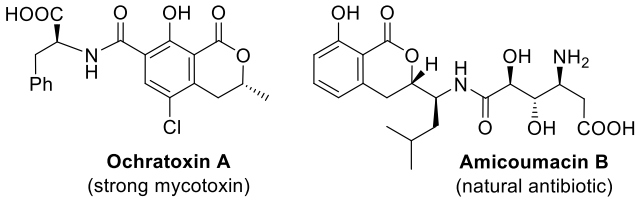


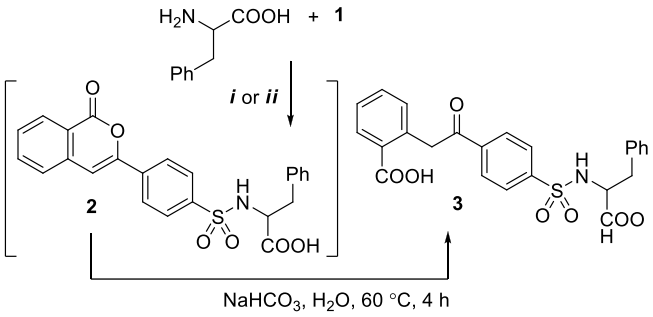
Figure 1. Natural amino-acids derivatives of 3,4-dihydroisocoumarins.

Results and Discussion

The simple 3-phenylisocoumarin (Scheme 1, R = H) as a convenient and available substrate for its transformation into sulfonamide derivative was selected. The chlorosulfonation of this substance occurs easily over a wide temperature range (from room temperature up to 60 °C) [14], and the sulfonyl chloride **1** was obtained without any by-products (Scheme 1). Only the mechanical losses during the isolation process can decrease the reaction yield at this stage.

However, the formation of sulfonamides by the reaction of sulfochloride **1** with phenylalanine in a slightly alkaline solution at room temperature is accompanied by a partial opening of the lactone ring. To increase solubility of amino acids during reaction water has to be used as a solvent. At first, we carried out this reaction in an aqueous solution using sodium bicarbonate as a base, so the observed hydrolysis of the lactone was not surprising. However, when a 1,4-dioxane-water solution (5 : 1, respectively) in the presence of triethylamine was used the mixture of

isocoumarin **2** and deoxybenzoin **3** (Scheme 3) was obtained.

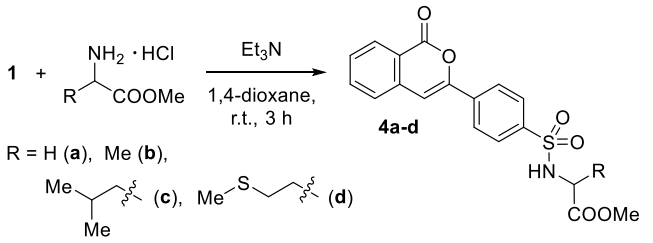


Scheme 3. The interaction of 4-(1-oxo-1*H*-isochromen-3-yl)-benzenesulfonyl chloride (**1**) with glycine.

The fast hydrolysis of **2** is atypical for these lactones. It can be explained by both the electron-withdrawing effect of sulfonyl group and the higher solubility of **2** due to the amino acid fragment. Interestingly, the addition of racemic alanine to 7-chlorosulfonylisocoumarin-3-carboxylic acid under mild basic conditions (K_2CO_3) in the water-acetone mixture occured without opening the lactone cycle (Scheme 2) [21].

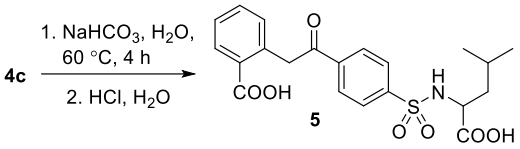
According to LCMS analysis, substances **2** and **3** are formed in approximately equal proportions. The two are very difficult to separate because they have similar physicochemical properties. The additional heating of this mixture in an aqueous solution with the presence of sodium bicarbonate yields the pure deoxybenzoin **3** (Scheme 3). It is worth noting that the isocoumarin cycle of the sulfonamide derivative was opened under stronger conditions (heating with KOH in a water-alcohol solution) while saving of the sulfonamide fragment [15].

Therefore, making the reaction of sulfonyl chloride **1** with methyl esters of amino acids in an anhydrous 1,4-dioxane in the presence of Et_3N solved this problem and gave sulfonamides **4a-d** easily and without undesirable by-products (Scheme 4). The yields of compounds **4** did not depend on the nature of substituent in the amino acid fragment.



Scheme 4. Reaction of 4-(1-oxo-1*H*-isochromen-3-yl)-benzenesulfonyl chloride (**1**) with amino acid esters.

To confirm the higher hydrolytic stability of sulfonamide group compare to ester or lactone fragments, the leucine methyl ester derivative **4c** was heated in an aqueous solution with a large excess of $NaHCO_3$ for 4 h. After acidification the sulfonamide **5** with two carboxylic groups was isolated with high yield (Scheme 5).



Scheme 5. Hydrolysis reaction of isochromone cycle of the compound **4c**.

The sulfonamides **4a** as well as deoxybenzoins **3** and **5** are the colorless crystalline solids. The structures of compounds **4a-d** were confirmed ^1H, ^{13}C and IR spectroscopic data that correlated with a previously known data for isochromone derivatives. The ^1H NMR resonance signal for the sulfonamide proton appeared as a broad dublet or broad singlet in a weak field at ~ 8.4 ppm and the methyl ester group appeared as a singlet at 3.4-3.5 ppm. Characteristically, the ^1H NMR spectra of deoxybenzoins **3** and **5** showed a resonance signal for the CH_2 group of $CH_2C{=}O$ fragment at ~ 4.7 ppm.

The characteristic absorption bands associated with N–H, C=O, and S=O bonds of compounds **3-4** can be easily identified in the IR spectra; the absorption bands associated with two (compounds **4**) or three (acids **3**, **5**) C=O groups can appears as two separated bands or appears as one very strong broad band at 1693 (compound **3**) or 1721 (compounds **4b,d**) cm^{-1}.

Conclusions

The reaction of 4-(1-oxo-1*H*-isochromen-3-yl)benzenesulfonyl chloride with amino acids in the alkaline water-containing solution occurred with the opening of the lactone ring and can be recommended for synthesis of 2'-carboxydeoxybenzoins that contains the amino acid sulfamide group. At the same time, the reaction of this sulfochloride with amino acid esters in 1,4-dioxane in the presence of triethylamine yielded the corresponding isocoumarin sulfonamide derivatives.

Experimental section

All solvents were purified according to the standard procedures [23]. All materials were purchased from commercial sources and used without further purification. ^1H and ^{13}C NMR spectra were recorded on a Mercury-400 spectrometer (400 and 100 MHz respectively) in DMSO-d_6 solutions. Chemical shifts are reported in ppm downfield from TMS as internal standards. FT-IR (KBr pellet) spectra were performed on a Bruker VERTEX 70 spectrometer. Melting points were determined by using a Kofler-type Leica Galen III micro hot stage microscope and are uncorrected. LC-MS/MS analyses were performed using an Agilent 1200 LCMSD SL system equipped with DAD/ELSD/LCMS-6120 diode matrix and mass-selective detector (chemical ionization (APCI), electrospray

ionization (ESI)). Elemental analyses for C, H, and N were determined using Perkin-Elmer CHN Analyzer. All the experiment values are in a good agreement (±0.4%) with the calculation results.

*Synthesis of the mixture of isocoumarin **2** and deoxybenzoin **3**.*

Method 1. To a solution of 330 mg (2 mmol) of phenylalanine and 504 mg (6 mmol) of $NaHCO_3$ in 10 mL of water 321 mg (1 mmol) of sulfonyl chloride **1** was added by three portion with a vigorous stirring at room temperature. The reaction mixture was stirred at room temperature for 3 h to a clear solution formation; the medium should remain alkaline all the time. The solution was acidified by 1N HCl to pH 4-5 and leaved for a night. The precipitate was filtered, washed with water, and dried.

Method 2. To a solution of 321 mg (1 mmol) of sulfonyl chloride **1** in 7.5 mL of 1,4-dioxane 330 mg (2 mmol) of phenylalanine, 1.5 mL of water, and 0.55 mL (4 mmol) of Et_3N were added. The reaction mixture was heated slightly (up to 40 °C) with stirring to a homogeneous condition, and was stirred at room temperature for 30 min. Then the mixture was poured into ice and acidified by 1N HCl to pH 4-5. The precipitate was filtered, washed with water, and dried.

*2-(2-(4-(N-(1-carboxy-2-phenylethyl)sulfamoyl)phenyl)-2-oxoethyl)benzoic acid (**3**).*

The obtained mixture of isocoumarin **2** and deoxybenzoin **3** was suspended in 20 mL water with 336 mg (4 mmol) of $NaHCO_3$, and was stirred at 60 °C to a clear solution formation. The solution was cooled to room temperature and acidified by 1N HCl to pH 4-5. The precipitate was filtered and washed with water obtaining pure deoxybenzoin **3**. Yield: 257 mg, 55% (after two stage through *Method 1*) or 313 mg, 68% (after two stage through *Method 2*), mp 114-115 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.50 (br d, *J* 8.2 Hz, 1H, N*H*), 8.01 (d, *J* 8.0 Hz, 2H, *H*-3',5'), 7.97 (d, *J* 7.8 Hz, 1H, *H*-6), 7.66 (d, *J* 8.0 Hz, 2H, *H*-2',6'), 7.55 (t, *J* 7.4 Hz, 1H, *H*-4), 7.42 (t, *J* 7.4 Hz, 1H, *H*-5), 7.37 (d, *J* 7.4 Hz, 1H, *H*-3), 7.20-7.14 (m, 3H, C_6H_5), 7.14-7.08 (m, 2H, C_6H_5), 4.75 (s, 2H, CH_2CO), 3.99-3.89 (m, 1H, CH_2CH), 3.01-2.92 (m, 1H, CH_2CH), 2.78-2.65 (m, 1H, CH_2CH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 197.2, 172.7, 168.6, 145.1, 139.8, 137.1, 133.3, 132.5, 131.0, 129.6, 128.8, 128.6, 127.6, 127.0, 126.9, 58.0, 45.3, 38.2. IR (KBr) *v* 3539 (br), 3304 (br, NH), 3069, 3034, 2963, 2928, 2911, 1693 (vs, br, C=O), 1602, 1577, 1496, 1454, 1423, 1400, 1349 (S=O), 1294, 1235, 1211, 1162 (S=O), 1094, 1079, 999, 952, 832, 749, 727, 702, 651, 621, 584, 549. LC/MS (CI) m/z $(M+H)^+$ 468.

*General procedure for preparation of sulfonamides **4a-d**.*

To a solution of 321 mg (1 mmol) of sulfonyl chloride **1** in 5 mL of 1,4-dioxane 2 mmol of hydrochloride of amino acid methyl ester, and 0.55 mL (4 mmol) of Et_3N were added. The reaction mixture was stirred vigorously at room temperature for 3 h; then 30 mL of water was added. The forming precipitate was filtered, washed with water, and recrystallized from isopropyl alcohol (5-10 mL).

*Methyl ((4-(1-oxo-1H-isochromen-3-yl)phenyl)sulfonyl)-glycinate (**4a**).*

Yield: 209 mg, 56 %, mp 196-197 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35 (br s, 1H, N*H*), 8.19 (d, *J* 7.5 Hz, 1H, *H*-8), 8.09 (d, *J* 8.5 Hz, 2H, *H*-3',5'), 7.95-7.85 (m, 3H, *H*-6,2',6'), 7.74 (d, *J* 7.6 Hz, 1H, *H*-5), 7.70-7.60 (m, 2H, *H*-4,7), 3.76 (s, 2H, CH_2), 3.51 (s, 3H, COO*Me*). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 160.8, 151.3, 142.1, 137.3, 136.0, 135.7, 129.8, 129.5, 127.7, 127.5, 126.0, 120.7, 104.7, 52.3, 44.2. IR (KBr) *v* 3335 (br, NH), 3100, 2987, 2955, 1751 (s, C=O), 1720 (vs, C=O), 1637, 1603, 1485, 1455, 1407, 1328 (S=O), 1239, 1207, 1162 (S=O), 1112, 1066, 977, 830, 756, 727, 686, 630, 612, 540. LC/MS (CI) m/z $(M+H)^+$ 374.

*Methyl ((4-(1-oxo-1H-isochromen-3-yl)phenyl)sulfonyl)-alaninate (**4b**).*

Yield: 195 mg, 50 %, mp 177-178 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.45 (br d, *J* 5.6 Hz, 1H, N*H*), 8.19 (d, *J* 8.1 Hz, 1H, *H*-8), 8.09 (d, *J* 7.6 Hz, 2H, *H*-3',5'), 7.93-7.84 (m, 3H, *H*-6,2',6'), 7.74 (d, *J* 7.6 Hz, 1H, *H*-5), 7.70-7.61 (m, 2H, *H*-4,7), 3.99-3.89 (m, 1H, C*H*CH_3), 3.39 (s, 3H, COO*Me*), 1.18 (d, *J* 6.4 Hz, 3H, CHCH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 161.3, 151.4, 142.1, 137.1, 136.1, 135.5, 129.8, 129.5, 127.7, 127.5, 125.7, 120.6, 104.8, 54.5, 52.4, 17.1. IR (KBr) *v* 3286 (br, NH), 3097, 2957, 1721 (vs, C=O), 1638, 1604, 1485, 1454, 1434, 1408, 1339 (S=O), 1237, 1212, 1168 (S=O), 1131, 1093, 1065, 1014, 972, 834, 756, 727, 686, 631, 614, 560. LC/MS (CI) m/z $(M+H)^+$ 388.

*Methyl ((4-(1-oxo-1H-isochromen-3-yl)phenyl)sulfonyl)-leucinate (**4c**).*

Yield: 338 mg, 79 %, mp 194-195 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (br d, *J* 8.2 Hz, 1H, N*H*), 8.20 (d, *J* 7.9 Hz, 1H, *H*-8), 8.10 (d, *J* 8.4 Hz, 2H, *H*-3',5'), 7.94-7.84 (m, 3H, *H*-6,2',6'), 7.75 (d, *J* 7.8 Hz, 1H, *H*-5), 7.69 (s, 1H, *H*-4), 7.65 (t, *J* 8.1 Hz, 1H, *H*-7), 3.87-3.73 (m, 1H, NHC*H*), 3.37 (s, 3H, COO*Me*), 1.62-1.50 (m, 1H, C*H*$(CH_3)_2$), 1.50-1.33 (m, 2H, CH_2), 0.82 (d, *J* 6.5 Hz, 3H, CHCH_3), 0.72 (d, *J* 6.4 Hz, 3H, CHCH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 161.5, 151.2, 142.0, 137.2, 136.0, 135.5, 129.7, 129.4, 127.6, 127.4, 125.8, 120.7, 104.7, 54.4, 52.3, 41.0, 24.3, 22.9, 21.4. IR (KBr) *v* 3314 (br, NH), 3281 (br, NH), 3097, 2956, 2935, 2870, 1739 (s, C=O), 1720 (vs, C=O), 1617, 1586, 1512, 1469, 1414, 1340 (S=O), 1311, 1297, 1237, 1169 (S=O), 1141, 1091, 1065, 1012, 966, 887, 833, 756, 685, 634, 569, 537. LC/MS (CI) m/z $(M+H)^+$ 430.

*Methyl ((4-(1-oxo-1H-isochromen-3-yl)phenyl)sulfonyl) methioninate (**4d**).*

Yield: 288 mg, 64 %, mp 182-183 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.52 (br. d, *J* 8.8 Hz, 1H, N*H*), 8.20 (d, *J* 7.6 Hz, 1H, *H*-8), 8.11 (d, *J* 8.2 Hz, 2H, *H*-3',5'), 7.92-7.84 (m, 3H, *H*-6,2',6'), 7.75 (d, *J* 7.6 Hz, 1H, *H*-5), 7.70-7.61 (m, 2H, *H*-4,7), 4.04-3.98 (m, 1H, NHC*H*), 3.38

(s, 3H, COO*Me*), 2.44-2.26 (2H, m, CH_2CH$_2$SCH$_3$), 1.93 (s, 3H, SCH_3), 1.88-1.72 (2H, m, CH$_2$CH_2SCH$_3$). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 161.6, 151.1, 141.8, 137.1, 135.8, 135.6, 129.6, 129.5, 127.6, 127.2, 126.0, 120.6, 104.8, 54.2, 52.0, 24.4, 22.8, 21.3. IR (KBr) ν 3272 (br, NH), 3094, 2956, 2917, 1721 (vs, C=O), 1638, 1604, 1485, 1451, 1430, 1408, 1341 (S=O), 1282, 1233, 1209, 1162 (S=O), 1092, 1066, 974, 864, 834, 755, 728, 685, 633, 615, 564. LC/MS (CI) m/z (M+H)$^+$ 448.

*2-(2-(4-(N-(1-carboxy-3-methylbutyl)sulfamoyl)phenyl)-2-oxoethyl)benzoic acid (**5**).*

The sulfonamide **4c** (200 mg, 0.47 mmol) was suspended in 20 mL water with 2 mL of ethanol and 672 mg (8 mmol) of NaHCO$_3$, and was stirred at 60 °C near 4 h to a clear solution formation. The solution was cooled down to room temperature and acidified by 1N HCl to pH 4-5. The precipitate was filtered, washed with water, dried to give deoxybenzoin **5**. Yield: 192 mg, 95 %, mp 188-189 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20-8.10 (m, 3H, *H*-3',5', N*H*), 8.01 (d, *J* 7.5 Hz, 1H, *H*-6), 7.90 (d, *J* 8.2 Hz, 2H, *H*-2',6'), 7.51 (t, *J* 7.0 Hz, 1H, *H*-4), 7.38 (t, *J* 7.0 Hz, 1H, *H*-5), 7.30 (d, *J* 7.2 Hz, 1H, *H*-3), 4.73 (s, 2H, CH_2CO), 3.80-3.70 (m, 1H, NHC*H*), 1.79-1.66 (m, 1H, C*H*(CH$_3$)$_2$), 1.55-1.35 (m, 2H, CH_2), 0.91 (d, *J* 6.5 Hz, 3H, CHCH_3), 0.85 (d, *J* 6.4 Hz, 3H, CHCH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.6, 173.3, 168.4, 145.4, 140.1, 137.2, 133.0, 132.0, 131.1, 130.6, 128.5, 127.2, 127.1, 54.5, 45.2, 41.5, 24.4, 23.1, 21.4. IR (KBr) ν 3604, 3525, 3395 (br), 3240 (br), 2963. 2874, 2629, 1711 (s, C=O), 1691 (vs, C=O), 1400, 1330 (S=O), 1294, 1251, 1214, 1168 (S=O), 1146, 1081, 1000, 934, 842, 811, 752, 729, 715, 624, 582. LC/MS (CI) m/z (M+H)$^+$ 434.

Notes

The authors declare no conflict of interest.

Author contributions. **A. A. R.**: synthesis of compounds, investigation, formal analysis, writing experimental section. **S. V. S.**: synthesis of compounds, investigation, editing. **O. V. S.**: formal analysis, writing of the most part of the manuscript, editing. **S. A. C.**: synthesis of compounds, investigation, spectral analysis. **V. P. K.**: conceptualization, supervision, writing review & editing**.**

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Одержання амінокислотних сульфонамідів на основі 4-(1-оксо-1*H*-ізохромен-3-іл)бензенсульфонілхлориду

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Резюме: Представлено дослідження особливостей взаємодії 4-(1-оксо-1*H*-ізохромен-3-іл)бензенсульфонілхлориду (**1**) з похідними амінокислот, що веде до утворення відповідних сульфонамінів. На початку статті подано короткий огляд способів синтезу рідкісних на сьогодні 1*H*-ізохромонів (ізокумаринів) із сульфонамідними фрагментами. Ізокумарини та споріднені до них молекули, як синтетичного, так і природного походження – давно знана група оксигеновмісних гетероциклів. Ці речовини цікаві з точки зору їх біоактивності, а також мають дуже великий потенціал використання синтетичній органічній хімії (наприклад, для отримання ізохінолінів). На жаль, існуючі методи синтезу ізокумаринів обмежують можливості побудови молекул з певними функціональними групами. Зокрема, відомо дуже небагато прикладів одержання ізокумаринів із сульфамідними групами; переважно методи синтезу таких похідних базуються на паладій-каталізованих сполученнях із використанням досить вартісних вихідних речовин, а пряма послідовність сульфохлорування ізокумарину – амідування використовувалась лише кілька разів. Раніше нами було показано, що сульфохлорування із наступним утворенням сульфамідів може бути з препаративними виходами проведено в ряду 3-арилізокумаринів. В даній роботі сульфонілхлорид **1** було залучено в реакцію з амінокислотними похідними. Внаслідок взаємодії сульфонілхлориду **1** із фенілаланіном в присутності основи та при наявності навіть невеликих кількостей води в реакційному середовищі утворення сульфонамідного фрагменту ускладнюється частковим розкриттям хромонового циклу. Додаткова обробка такої суміші слабколужним водним розчином завершує розкриття циклу та приводить до утворення похідної дезоксибензоїну **3** – 2-(2-(4-(*N*-(1-карбокси-2-фенілетил)сульфамоїл)феніл)-2-оксоетил)бензойної кислоти. Натомість в результаті реакції сульфонілхлориду **1** з метиловими естерами амінокислот (у формі гідрохлоридів), що була проведена у безводному 1,4-діоксані та з додаванням триетиламіну у якості основи, легко та без побічних продуктів утворюються відповідні сульфонаміди; внаслідок чого було синтезовано ізокумаринові сульфонаміди із фрагментами гліцину, аланіну, лейцину та метіоніну. Щоб продемонструвати більшу, ніж у естеру або лактону, гідролітичну стабільність сульфонамідної групи у синтезованих сполуках, один із естерів **4** (похідна лейцину **4c**) був оброблений водним розчином $NaHCO_3$ при нагріванні. Після підкислення було виділено з майже кількісним виходом сульфонамід **5** з двома карбоксильними групами, спорідненим сполуці **3**.

Ключові слова: сульфонаміди; амінокислоти; 3-фенілізокумарин; сульфохлорування.