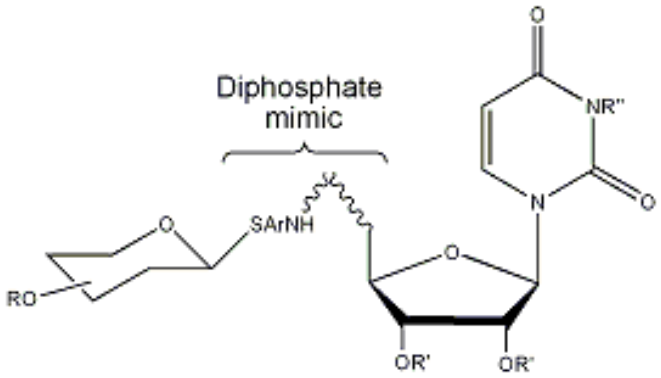
the three different moieties composing NDP sugar natural substrates: carbohydrate part, the diphosphate linkage and the nucleoside moiety [1].



We present herein a part of our current program on the synthesis of some kind of analogues of sugar nucleotides, which were designed to act as GTs inhibitors particularly donor substrate analogues. Such inhibitors contain a glycosyl unit (usual glucose or galactose) and a nucleoside diphosphate mimic, which is essential for binding to the enzyme. We construct analogues of GTs inhibitors using aryl and heteroaryl 1-thioglycosides as glycosyl units which are connected to uridine with or without a spacer. We used succinic, glutaric and malonic acid as a spacer. We believe that presence of sulfur atom instead of glycosidic oxygen atom increases the stability of sugar-aglycon linkage against enzymatic cleavage [2]. This way we obtained several uridine derivatives containing different types of diphosphate mimic linkers.

Acknowledgement

Financial support from the Polish State Committee for Scientific Research (Grant No. 1 T09A 08630) is gratefully acknowledged.

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Uridine derivatives of heteroaryl 1-thioglycosides: synthesis and biological activity against CSFV glycoproteins

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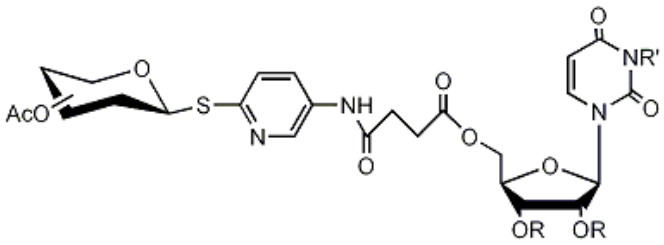
In search for effective inhibitors of sugar processing enzymes the uridine derivatives of (5-amino-2-pyridyl) 1-thioglycosides attract our attention as substrate analogs. Along this line, we have reported different methodology for the synthesis of compounds in which heteroaryl 1-thioglycosides derivatives of D-glucose and D-galactose were connected to selectively protected uridine by amide bond. As a spacer between these two parts we have chosen a succinic acid. In order to obtain uridine with ester bond connected succinic acid in good yield we applied microwave irradiation. The construction of amide bonds was performed using DCC/DMAP [1], ethyl chloroformate [2] or DMTMM as condensing agent [3]. This way we obtained uridine derivatives **GP-U1**, **GP-U2** and **GP-U3** and then we tested their biological activity.



The three inhibitors tested by us exhibited relatively low toxic effect on cells in *in vitro* tests using swine kidney (SK6) cells. High antiviral activity against classical swine fever virus (CSFV) was demonstrated by inhibiting the propagation of the virus. We have investigated the formation of envelope glycoproteins of CSFV after inhibitor treatment by immunoperoxidase monolayer assay and by immunoblotting. We showed that they can influence, not only glycosylation, but also the stability of E2 protein, effectively inhibiting the formation of glycoprotein complexes.

Acknowledgement

Financial support from the Polish State Committee for Scientific Research (Grant No. 1 T09A 08630) is gratefully acknowledged.

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Crystal structure of β-adrenergic receptor as a new template in homology modeling of GPCR. Application to serotonin 5-HT$_{1A}$ and 5-HT$_7$ receptors

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When dificulties in receiving crystal structures appear, homology modeling aproach is the best way to obtain three dimensional structure of a protein. Procedure is realtively simple, but results depend on degree of similarity between a target and a template sequence. Since 2000 there was one available crystal structure of transmembrane domain of GPCR protein: the bovine rhodopsin. We, and others have previously shown that regardless of relatively low sequence identity, it was possible to obtain useful rhodopsin based models of serotonin receptors, such as 5-HT$_{1A}$ and 5HT$_7$. In October 2007, a high resolution structure of another GPCR, beta-2 adrenergic receptor, was solved. Very close evolutionary relationships between 5-HT

receptors and beta adrenoreceptors give us possibility to improve comparative models of serotonin receptors and to verify our previous results. New homology models will be used in a process of drug design and virtual screening.

Acknowledgement
This study was partly supported by the Network "Synthesis, structure and therapeutic properties of compounds and organic substances" coordinated by the Institute of Organic Chemistry Polish Academy of Sciences.

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New rosiglitazone salts

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The description of the new pharmaceutical salts of rosiglitazone was presented.

Rosiglitazone is an oral drug that reduces the glucose level in the blood. It is used for treating patients with type 2 diabetes and is in a class of anti-diabetic drugs called thiazolidinediones.

The possibilities to obtain of rosiglitazone salts with pharmaceutically acceptable organic acids were tested. The conditions of the synthesis for three possible new salts to obtain and also the technology for one of them were worked out.

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Syntheses of N,S-substituted 4-chloro-2-mercapto-5-methylbenzenesulfonamide derivatives with potential biological activity

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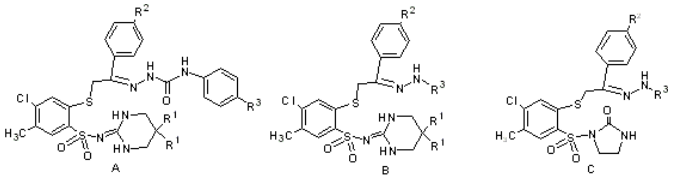
As a part of our research on chemical and biological properties of 2-mercaptobenzenesulfonamides with potential anticancer and/or anti-HIV activities [1-4], the syntheses of *N,S*-substituted benzenesulfonamide derivatives were performed. Reactions of the previously described 2-(2-mercaptobenzenesulfonylimino)tetrahydropyrimidines [5] or 1-(2-mercaptobenzenesulfonyl)-2-imidazolidinone [6] with the appropriate 2-bromoacetophenones afforded 4-chloro-*N*-(tetrahydropyrimidin-2-ylidene) -5-methyl-2-[2-oxo-2-(4-R^2-phenyl)ethylsulfanyl]benzenesulfonamides **1-3** and 1-{4-chloro-5-methyl-2-[2-oxo-2-(4-R^2-phenyl)ethylsulfanyl]benzenesulfonyl}imidazolidin-2- ones **4-5**, respectively. The subsequent reactions of sulfonamides **1-3** with suitable semicarbazones or hydrazines and **4,5** with hydrazines led to the target title compounds of type **A, B** and **C**. The structures of new compounds were determined by analytical and spectral methods.



Ten of the obtained compounds were screened at Institute of Pharmacy University of Greifswald for their in vitro activity against a panel of 12 human cancer cell lines. The prominent benzenesulfonamide showed the selective activity toward cell lines of bladder cancer (IC_{50} values in range 2.9-8.1 μM).

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Development of HPLC and GC methods for analysis of Zolmitriptan of pharmaceutical purity

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Zolmitriptan (4(S)-4-[3-2-dimethyl aminoethyl)-1H-5-indolyl-methyl]-1,3-oxazolan-2-one) belongs to group of medicines known as Serotonin 5-HT1D receptor antagonist. Zolmitriptan is used to treat severe migraine headaches. This cure is available on market as convetional tablets (Zomig), or nasal spray (Zomig nasal spray).

For the determination of pharmaceutical purity of Zolmitriptan, high performance liquid chromatography with spectrophotometric detection is recommended as an analytical technique. The chromatographic separation was achieved on a Waters XTerra RP Column, (250mm, x 4,6 mm, x 5μm) column using linear gradient solutions. As mobile phase – 20 mM ammonium hydrogen orthophosphate and acetonitrile was chosen. In the developed HPLC method, the resolution between Zolmitriptan and its potential impurities, ZL3, ZL4, ZL5, ZL7, werefound to be greater than 3. Obtained product, as pharmaceutical substance, should contain less than 0.5% of total impurities, and no more than 0.10 % of an individual unidentified impurities (acc. ICH). The detection limit (0.5 mg mL^{-1}) for compoud ZL7 obtained using the developed HPLC method with spectrophotometric detection is unsatisfactory. Because of that, for determination of this compound the different method of analysis need to be used. The developed GC method gave an accepted limit of detection for analysis of this potential impurity (75 ppm). The proposed methods, owing to its satisfactory precision and accuracy as well as selectivi-