Thesis of doctoral (Ph.D.) dissertation

Synthesis of *C*-glycosyl- and glycosylamino-heterocycles

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DEBRECENI EGYETEM

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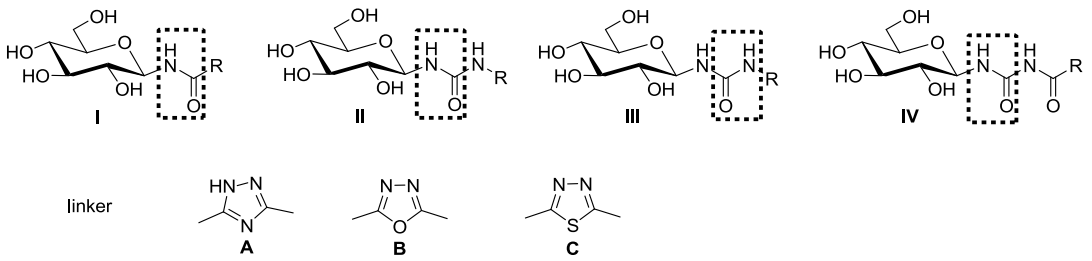
1. Introduction

Diabetes mellitus has become one of the most severe disease nowadays. At the end of the 20th century a dramatic increase could be observed in the number of patients diagnosed with diabetes worldwide. Its symptoms and complications can be originated from abnormally increased blood glucose levels (hyperglycemia) due to absolute insulin deficiency (insulin dependent or type 1 *diabetes mellitus*) or insulin resistance and/or abnormal insulin secretion (non insulin dependent or type 2 *diabetes mellitus*). Current treatment of *diabetes mellitus* is possible only symptomatically; mainly diet, exercise, oral hypoglycemic agents and exogenous insulin are used to restore normal physiological glucose levels. Approx. 90-95% of the patients suffer from type 2 diabetes (T2DM). Because of inefficiency and detrimental side effects of present treatments several new therapeutic possibilities have been intensively investigated for T2DM. The hepatic glucose output could among others be reduced by the inhibition of glycogen phosphorylase (GP, catalysing the degradation of glycogen), whose inhibition may directly influence blood glucose levels.

In our research group synthesis of glucose analogue glycogen phosphorylase inhibitors has been studied for 15 years. As a part of this work I prepared new potential GP inhibitors, which may contribute to a new therapy of type 2 diabetes.

The glucose analogue inhibitors of GP bind to the catalytic site of the enzyme. The *N*-acyl-β-D-glucopyranosylamines, the *N*-aryl-β-D-glucopyranosyl ureas and the *N*-acyl-β-D-glucopyranosyl ureas are efficient GPIs. The binding modes of these molecules were studied by X-ray crystallography. In case of *N*-acyl amines and *N*-aryl ureas a specific hydrogen bond was observed from the amide nitrogen to the carbonyl O of His377, which interaction increased the inhibition efficiency of these compounds. This hydrogen bond is not formed between the *N*-acyl-β-D-glucopyranosyl ureas and the enzyme. However, *N*-acyl-β-D-glucopyranosyl ureas are good inhibitors of GP, because of the well oriented aromatic parts of the molecules in the β-channel of the enzyme. The *N*-(2-naphthoyl)-β-D-glucopyranosyl urea is a nanomolar inhibitor of the enzyme.

The aim of our work was to replace the NHCO moiety of *N*-acyl-β-D-glucopyranosyl amines **I**, *N*-aryl-β-D-glucopyranosyl ureas **II, III**, and the first amide moiety of *N*-acyl-β-D-glucopyranosyl urea **IV** with non-classical heterocyclic bioisosters such as 1,2,4-triazole **A**, 1,3,4-oxadiazole **B**, and 1,3,4-thiadiazole **C** rings (Scheme 1.). Heterocyclic compounds were designed and prepared to get insight into their structure–activity relationships.



Scheme 1. The target molecules of my work

2. Methods

In the course of the synthetic work, macro, semi micro, and micro methods of modern preparative organic chemistry were applied. Reactions were monitored by thin-layer chromatography. Products of the reactions were purified by column chromatography and/or crystallization.

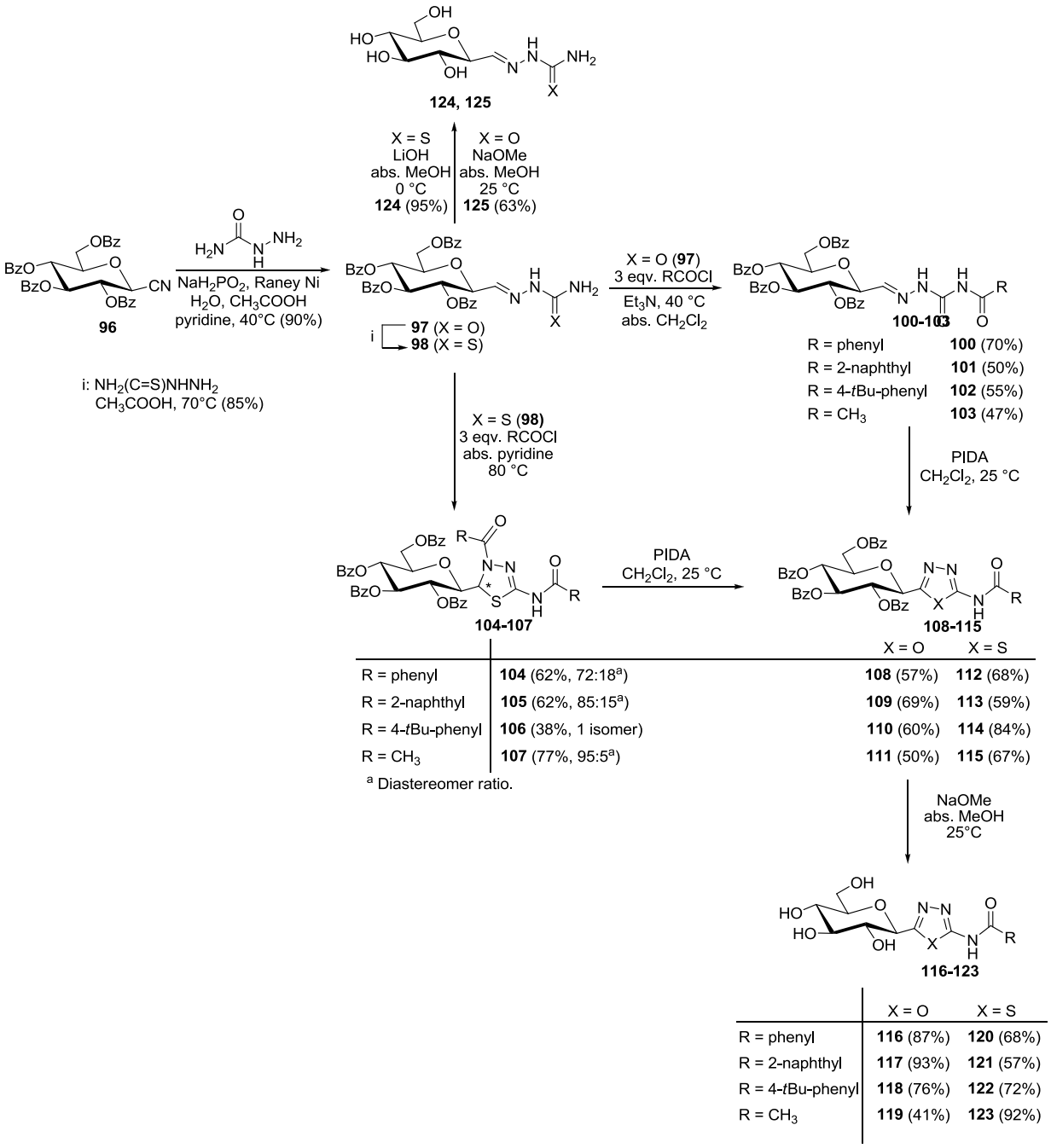
New compounds were characterized by their physical properties (melting point, optical rotation) and their structures were elucidated by ^{1}H NMR and ^{13}C NMR methods as well as mass spectrometry.

3. Results

3.1. Synthesis of 2-acylamino-5-(β-D-glucopyranosyl)-1,3,4-oxa- and -thiadiazoles

The protected *C*-(β-D-glucopyranosyl)formaldehyde-semicarbazone (**97**) was prepared by the reaction of *O*-perbenzoylated β-D-glucopyranosyl cyanide **96** with semicarbazide in the presence of Raney Ni and NaH_2PO_2 at 40°C. Thiosemicarbazone **98** was obtained by the acid catalysed transimination of **97**.

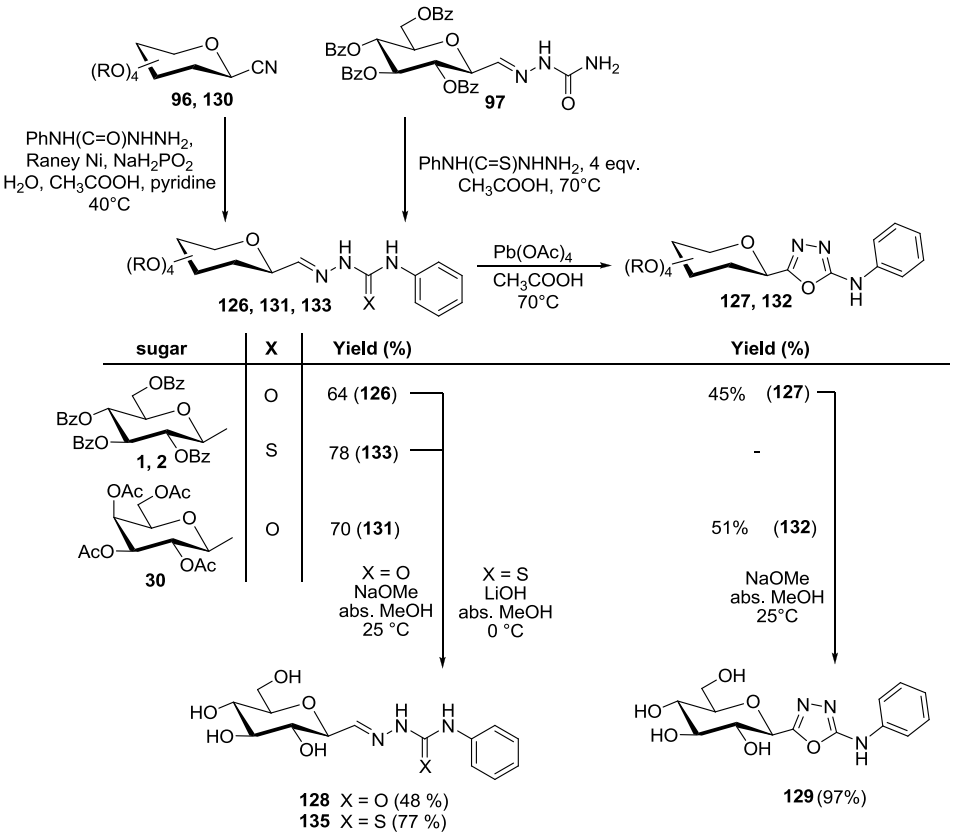
Semicarbazone **97** was treated with acyl chlorides in the presence of Et_3N in CH_2Cl_2 to give 4-acyl-[*C*-(β-D-glucopyranosyl)formaldehyde]semicarbazones (**100-103**). Acylation of thiosemicarbazone **98** in dry pyridine at 80°C resulted in 4-acyl-2-acylamino-5-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-Δ^2-1,3,4-thiadiazolines (**104-107**). Semicarbazones **100-103** were reacted with phenyliodonium diacetate (PIDA) in CH_2Cl_2 at room temperature to get 2-acylamino-5-(β-D-glucopyranosyl)-1,3,4-oxadiazoles (**108-111**). Thiadiazolines **104-107** were oxidized in a similar way to result in 2-acylamino-5-(β-D-glucopyranosyl)-1,3,4-thiadiazoles (**112-115**). Deprotections were performed by the Zemplén protocol (NaOMe/abs. MeOH) or LiOH in abs. MeOH to give molecules **116-123** and **124**, **125**.



Scheme 2. Synthesis of 2-acylamino-5-(β-D-glucopyranosyl)-1,3,4-oxadiazoles and -thiadiazoles

3.2. Synthesis of 2-arylamino-5-(β-D-glycopyranosyl)-1,3,4-oxa- and -thiadiazoles

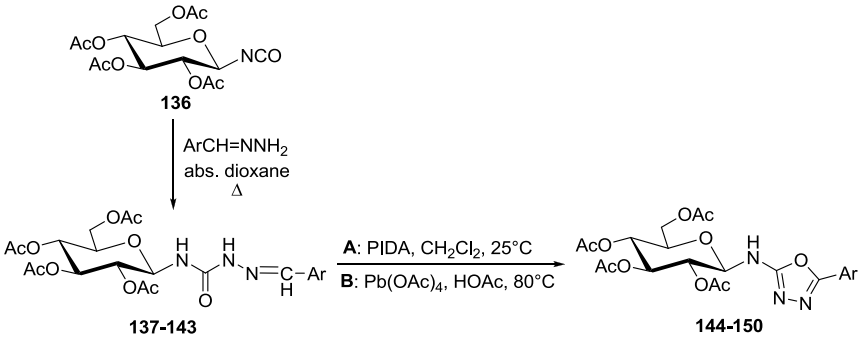
4-Phenyl-[*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde]-semicarbazone (**126**) was prepared by the reaction of *O*-perbenzoylated β-D-glucopyranosyl cyanide (**96**) with 4-phenylsemicarbazide in the presence of Raney Ni and NaH_2PO_2 at 40°C. Semicarbazone **126** was reacted with $Pb(OAc)_4$ in glacial AcOH at 70 °C to furnish 2-phenylamino-5-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-1,3,4-oxadiazole (**127**). 4-Phenyl-[*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-formaldehyde]-semicarbazone (**131**) was prepared by the reaction of *O*-peracetylated β-D-galactopyranosyl cyanide (**130**) with 4-phenylsemicarbazide in the presence of Raney Ni and NaH_2PO_2 at 40°C. To obtain 2-phenylamino-5-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-1,3,4-oxadiazole (**132**) semicarbazone **131** was reacted with $Pb(OAc)_4$ in glacial AcOH. 4-Phenyl-[*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)formaldehyde]thiosemicarbazone (**133**) was prepared by the acid catalysed transimination of semicarbazone **126** with 4-phenylthiosemicarbazide. 2-Phenylamino-5-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-1,3,4-thiadiazole could not be prepared under oxidative conditions. Deprotected compounds **128**, **129** were formed from **126**, **127** by the Zemplén method. Removal of the *O*-benzoyl protecting groups of thiosemicarbazone **133** was carried out by using LiOH in dry MeOH to result thiosemicarbazone **135** (Scheme 3.).



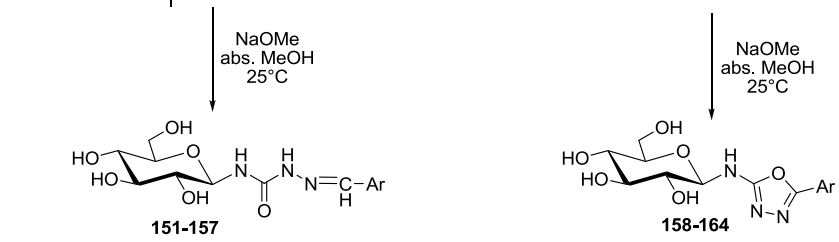
Scheme 3. Synthesis of 2-phenylamino-5-(β-D-glycopyranosyl)-1,3,4-oxadiazoles and its precursores

3.3. Synthesis of 2-(β-D-glucopyranosylamino)-5-substituted-1,3,4-oxadiazoles

For the synthesis of 2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamino)-5-substituted-1,3,4-oxadiazoles (**144-150**) the oxidative ring closure of aromatic aldehyde-[4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)]semicarbazones (**137-143**) was investigated (Scheme 4.). Semicarbazones **137-143** were prepared by the reaction of β-D-glucopyranosyl isocyanate **136** with aldehyde hydrazones in dry 1,4-dioxane at reflux temperature. Semicarbazones **137-143** were reacted with phenyliodonium diacetate (PIDA) in CH_2Cl_2 at 25 °C (method **A**) or with $Pb(OAc)_4$ in glacial AcOH at 80°C (method **B**) to furnish the corresponding 1,3,4-oxadiazoles **144-150**. Deacetylations were performed by the Zemplén protocol to give unprotected products **151-164**.



Ar		A	B
phenyl	**137** (83%)	**144** 45%	85%
4-Me-phenyl	**138** (72%)	**145** -	66%
4-NO_2-phenyl	**139** (66%)	**146** 43%	53%
4-F-phenyl	**140** (76%)	**147** 24%	88%
3-Cl-phenyl	**141** (71%)	**148** 52%	64%
1-naphthyl	**142** (89%)	**149** -	89%
2-naphthyl	**143** (80%)	**150** 49%	-



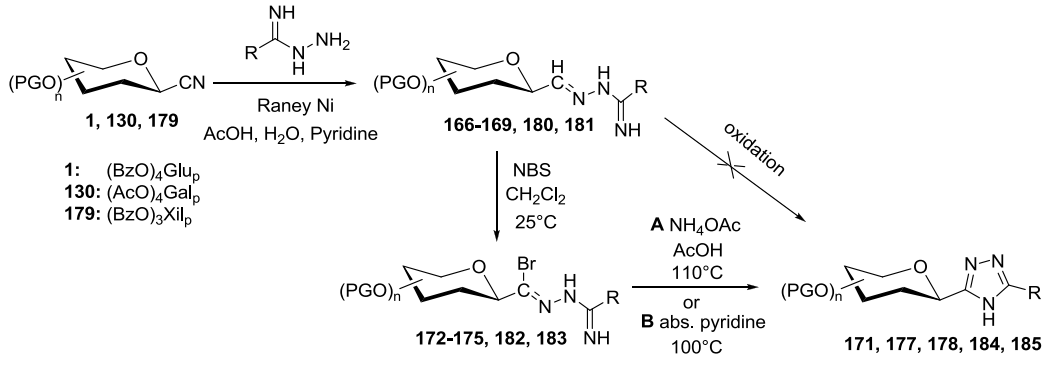
Ar		
phenyl	**151** (99%)	**158** (70%)
4-Me-phenyl	**152** (98%)	**159** (33%)
4-NO_2-phenyl	**153** (93%)	**160** (79%)
4-F-phenyl	**154** (98%)	**161** (83%)
3-Cl-phenyl	**155** (94%)	**162** (74%)
1-naphthyl	**156** (80%)	**163** (84%)
2-naphthyl	**157** (98%)	**164** (84%)

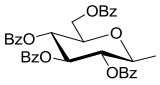
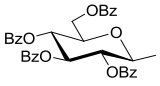
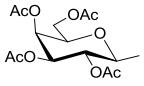
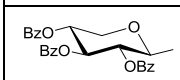
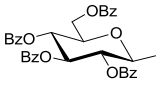
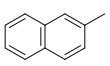
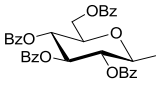
Scheme 4. Synthesis of 2-(β-D-glucopyranosylamino)-5-substituted-1,3,4-oxadiazoles

3.4. Synthesis of 3-(β-D-glycopyranosyl)-5-substituted-1,2,4-triazoles

A new method for the synthesis of 3-(*O*-peracylated-β-D-glycopyranosyl)-5-substituted-1,2,4-triazoles (**171**, **177**, **178**, **184, 185**) was elaborated (Table 1.). *N*-[*C*-(*O*-peracylated-β-D-glycopyranosyl)methylideneamino]arene-carboximidamides and guanidine (**166-169**, **180**, **181**) were synthesized by the Raney Ni catalysed reaction of β-D-glycopyranosyl cyanides **96**, **130**, **179** with aromatic amidrazones or guanidine.

Table 1. Synthesis of 3-(β-D-glycopyranosyl)-5-substituted-1,2,4-triazoles



R	(RO)n	Yield (%)			
		166-169, 180, 181	**172-175, 182, 183**	**171, 177, 178, 184, 185**	
NH_2		64 (**166**)	30 (**172**)	-	-
		48 (**167**)	74 (**173**)	56 (**171**) **A**	58 (**171**) **B**
		64 (**180**)	66 (**182**)	64 (**184**) **A**	-
		65 (**181**)	not isolated (**183**)	32 (**185**) **A**	-
		49 (**168**)	64 (**174**)	32 (**177**) **A**	55 (**177**) **B**
		51 (**169**)	70 (**175**)	55 (**178**) **A**	-

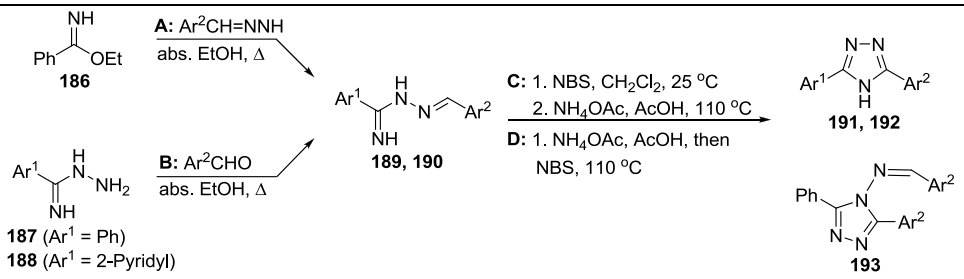
First, oxidative ring closure of carboximidamides **166-169**, **180**, **181** was investigated, but these reactions failed. The syntheses of 1,2,4-triazoles **171**, **177**, **178**, **184**, **185** were carried out from *N*-[arenecarboximidoyl-*C*-(*O*-peracylated-β-D-glycopyranosyl)]carbohydrazonoyl bromides (**172-175**, **182**, **183**) which were obtained from carboximidamides **166-169**, **180**, **181** by NBS in CH_2Cl_2 at room temperature. Carbohydrazonoyl bromides (**172-175**, **182**, **183**) were reacted with NH_4OAc in AcOH,

at 110 °C (method **A**) or with dry pyridine at 100 °C (method **B**) to give 3-(*O*-peracylated-β-D-glycopyranosyl)-5-substituted-1,2,4-triazoles (**171**, **177**, **178**, **184**, **185**) (Table 1).

3.5. Synthesis of asymmetric 3,5-diaryl-1,2,4-triazoles

The method applied for the synthesis of 3-(β-D-glycopyranosyl)-5-substituted-1,2,4-triazoles was extended for the preparation of asymmetric 3,5-diaryl-1,2,4-triazoles (Table 2.). Two series of 3,5-disubstituted-1,2,4-triazoles were synthesized. First, *N*-[aryl-methylideneamino]benzene-carboximidamides (**189**) were prepared in two different ways. Carboximidamides **189** were obtained by the reaction of ethylbenzimidate (**186**) with aromatic hydrazones (method **A**) or by the reaction of benzamidrazone (**187**) with aromatic aldehydes (method **B**). The latter one proved to be better, because in this case no formation of any side products were observed. *N*-[Aryl-methylideneamino]pyridine-2-carboximidamides (**190**) were synthesized from amidrazone derivative **188** with aromatic aldehydes (method **B**).

Table 2. Synthesis of asymmetric 3,5-diaryl-1,2,4-triazoles



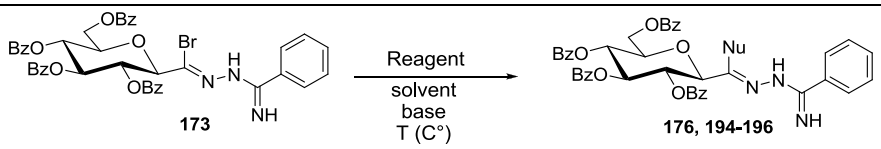
		Ar^1 = Ph					Ar^1 = 2-Piridil	
Ar^2		amidrazone (**189**)		triazole (**191**)		triazole (**193**)	amidrazone (**190**)	triazole (**192**)
		A	**B**	**C**	**D**	**C**	**B**	**D**
a	4-Br-phenyl	39%	85%	22%	60%	not isolated	85%	40%
b	4-F-phenyl	86%	93%	22%	68%	14%	75%	59%
c	3-Cl-phenyl	-	81%	34%	64%	not isolated	61%	45%
d	4-NO_2-phenyl	59%	94%	-	34%	-	87%	-
e	4-MeO-phenyl	47%	90%	-	60%	-	79%	58%
f	4-pyridyl	-	77%	-	40%	-	81%	30%
g	4-Me-phenyl	-	82%	17%	50%	38%	74%	58%
h	4-OH-phenyl	-	93%	-	-	-	79%	-
i	4-MeS-phenyl	-	80%	30%	61%	not isolated	82%	4-MeS(O)-phenyl 56%
j	4-AcNH-phenyl	74%	82%	-	56%	-	95%	61%
k	4-CN-phenyl	84%	78%	-	35%	-	81%	40%

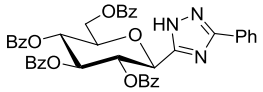
Preparation of 1,2,4-triazoles **191** were carried out by the reaction of carboximidamides **189** with NBS in CH_2Cl_2 and NH_4OAc in AcOH at 110 °C (method **C**) to result in the target molecules in low yields (17-30%). However, by changing the order of addition of the reactants (method **D**), 3,5-disubstituted-1,2,4-triazoles **191**, **192** were obtained in moderate and good yields (34-68%) without formation of 1,3,5-trisubstituted-1,2,4-triazoles **193**.

3.6. Nucleophilic substitution reactions of *N*-[benzenecarboximidoyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)]carbohydrazonoyl bromide

Nucleophilic substitution reactions of *N*-[benzenecarboximidoyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)]carbohydrazonoyl bromide (**173**) were also investigated (Table 3.). *N*-[(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)(*N*-benzylamino)methylideneamino]benzene-carboximidamide (**194**), *N*-[(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)(*N*-cyanoamino)methylideneamino]benzene-carboximidamide (**195**) and *N*-[(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)(phenylsulfanyl)methylideneamino]benzene-carboximidamide (**196**) were prepared by the reaction of carbohydrazonoyl bromide **173** with benzylamine, cyanamide, and thiophenol in dry acetonitrile at 82 °C, respectively. Application of water as nucleophile resulted in 3-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-5-phenyl-1,2,4-triazole (**171**). Reactions with *C*-nucleophiles (AgCN, HgCN) provided complex reaction mixtures.

Table 3. Reaction of *N*-[benzenecarboximidoyl-*C*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)]carbohydrazonoyl-bromide with nucleophiles



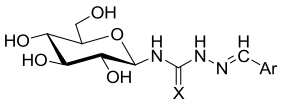
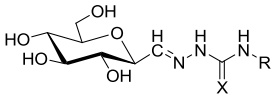
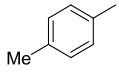
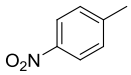
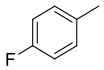
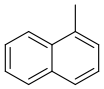
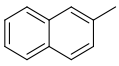
reagent	base	solvent	temperature (°C)	product	
				Nu	Yield (%)
NH_3		MeOH	25→reflux	OMe	35 (**176**)
$BnNH_2$	Et_3N	abs CH_3CN	reflux	BnNH	77 (**194**)
NH_2CN	Et_3N	abs. CH_3CN	reflux	NHCN	53 (**195**)
PhSH	Et_3N	abs. CH_3CN	reflux	PhS	34 (**196**)
H_2O	-		reflux	 37 (**171**)	
AgCN	-	abs. CH_3NO_2	25	CN	complex reaction mixture
$Hg(CN)_2$	-	abs. CH_3NO_2	25	CN	complex reaction mixture

4. Structure-activity relationships

The inhibition efficiency of the synthesized molecules against RMGP*b* was measured in the Department of Medical Chemistry, Medical and Health Science Centre in the University of Debrecen.

According to the kinetic results, aromatic aldehyde-[4-(β-D-glucopyranosyl)]semicarbazones **151-157** proved to be low micromolar inhibitors of GP. Among semicarbazones **151-157** the 4-nitrophenyl derivative **153** was the best one (K_i = 4.5 μM). A comparison of **151** to compound **128**, wherein the semicarbazone linker is formally reversed between the carbohydrate ring and the phenyl group, shows a moderate strengthening of the inhibition that may refer to the higher contribution of the second carbonyl unit to the binding. A formal reversal of the thiosemicarbazone linker as in **135** makes a very large decrease in the binding strength most probably because the thiocarbonyl in the position of the 'second amide' moiety is much less suitable to make strong interactions to the enzyme. Semicarbazones **124** and **128** are better inhibitors than the thiosemicarbazones **125** and **135**. Phenyl derivatives **128** and **135** are more efficient than the unsubstituted compounds **124** and **125**, because of the larger aromatic part in the aglycon (Table 4.).

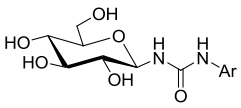
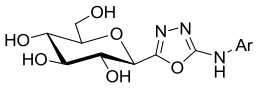
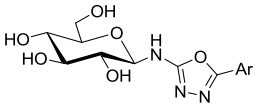
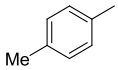
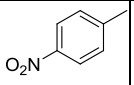
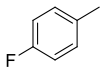
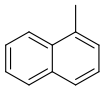
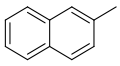
Table 4. Aromatic aldehyde-[4-(β-D-glucopyranosyl)]semicarbazones, 4-phenyl-[*C*-(β-D-glucopyranosyl)formaldehyde]-(thio)semicarbazone, and *C*-(β-D-glucopyranosyl)-formaldehyde-(thio)semicarbazone as inhibitors of rabbit muscle glycogen phosphorylase *b* (RMGP*b*) (K_i = [μM])

					
Ar	**X = O**	**X = O**		**X = S**	
	**151** 38	**R**			
		H	Ph	H	Ph
	**152** 136[3]	**124** 332	**128** 29	**125** no inhibition	**135** 300
	**153** 4.5	-			
	**154** 48	-			
	**155** 30	-			
	**156** 124	-			
	**157** 5.5	-			

The 2-(β-D-glucopyranosyl)-5-substituted-1,3,4-oxadiazoles (**158-164**) were moderate GPIs (K_i = 12-33 μM) (Table 5.). A comparison of **25** to compound **158**, and **26** to compound **163** shows similar GPI efficiency.

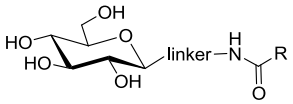
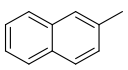
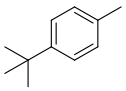
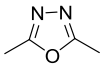
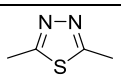
Among the substituted phenyl derivatives **159-161** are better inhibitors than **158**. But compound **162** bind worse to the enzyme than **158**. The 1,3,4-oxadiazole is an acceptable bioisosteric replacement of the NHCO moiety in this system. However, in case of 2-naphtyl derivatives **27 – 164** due to the replacement of NHCO moiety with 1,3,4-oxadiazole ring, the inhibition efficiency decreased. The 2-(phenylamino)-5-(β-D-glucopyranosyl)-1,3,4-oxadiazole (**129**) was inactive against RMGP*b* enzyme (Table 5.).

Table 5. 2-Phenylamino-5-(β-D-glucopyranosyl)-1,3,4-oxadiazole and 2-(β-D-glucopyranosyl)-5-substituted-1,3,4-oxadiazoles as inhibitors of rabbit muscle glycogen phosphorylase *b* (RMGP*b*) (K_i = [μM])

			
Ar			
	**25** 18	**129** no inhibition	**158** 20
	-	-	**159** 12
	-	-	**160** 15
	-	-	**161** 14
	-	-	**162** 33
	**26** 350 (IC_{50})	-	**163** 315 (IC_{50})
	**27** 5.2	-	**164** 27

2-Acylamino-5-(β-D-glucopyranosyl)-1,3,4-oxadiazoles (**116-119**) and 2-acylamino-5-(β-D-glucopyranosyl)-1,3,4-thiadiazoles (**120-123**) were practically inactive against RMGP*b* enzyme (Table 6).

Table 6. 2-Acylamino-5-(β-D-glucopyranosyl)-1,3,4-oxa- and thiadiazoles as inhibitors of rabbit muscle glycogen phosphorylase *b* (K_i = [μM])

	**R**			
linker	CH_3			
NHCO	305	4.6	0.35	0.7
	**116** no inhibition	**117** no inhibition	**118** no inhibition	**119** no inhibition
	**120** no inhibition	**121** no inhibition	**122** no inhibition	**123** no inhibition

5. Possible application of the results

In the course of my work new glucose analogues as potential glycogen phosphorylase inhibitors were prepared. The inhibition efficiency of the synthesized heterocyclic glucose derivatives were measured against rabbit muscle glycogen phosphorylase *b* (RMGP*b*) enzyme. The active compounds may contribute to a new therapy for type two diabetes after subsequent biological studies.

Documented scientific results

Data of scientific articles published (accepted for publication) in peer reviewed international journals

Publications related to the thesis

1. **B. Szőcs**, M. Tóth , T. Docsa, P. Gergely, L. Somsák:
   Synthesis of 2-(β-D-glucopyranosyl)-5-(substituted-amino)-1,3,4-oxa- and -thiadiazoles for the inhibition of glycogen phosphorylase
   Carbohydr. Res., **2013**, *381*,187-195. **IF: 2.044** (2012)

2. M. Tóth, **B. Szőcs**, T. Kaszás, T. Docsa, P. Gergely, L. Somsák:
   Synthesis of 2-(β-D-glucopyranosylamino)-5-substituted-1,3,4-oxadiazoles for inhibition of glycogen phosphorylase
   Carbohydr. Res., **2013**, *381*, 196-204. **IF: 2.044** (2012)

3. L. Somsák; É. Bokor; M. Tóth; L. Juhász; K. Czifrák; B. Kónya; S. Kun; A. Páhi; **B. Szőcs**; G. Varga; L. Kóder; K. Nagy; P. Gergely; T. Docsa:
   Inhibitors of Glycogen Phosphorylase
   P1100602 Hungarian patent application. **2011.**

Other publications

4. D. M. Griffith, **B. Szőcs**, T. Keogh, K. Y. Suponitsky, E. Farkas, P. Buglyó, C. J. Marmion:
   Suberoylanilide hydroxamic acid, a potent histone deacetylase inhibitor; its X-ray crystal structure and solid state and solution studies of its Zn(II), Ni(II), Cu(II) and Fe(III) complexes
   J. Inorg. Biochem. **2011,** *105*, 763–769**. IF: 3.19** (2012)

5. É. Bokor, A. Fekete, G. Varga, **B. Szőcs**, K. Czifrák, I. Komáromi, L. Somsák:
   C-(β-D-Glucopyranosyl)formamidrazones, formic acid hydrazides and their transformations into 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles: a synthetic and computational study
   Tetrahedron **2013**, *69*, 10391-10404. **IF: 2.803** (2012)

6. S. Kun, É. Bokor, G. Varga, **B. Szőcs**, A. Páhi, K. Czifrák, M. Tóth, L. Juhász, T. Docsa, P. Gergely, L. Somsák:
   New synthesis of 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles, nanomolar inhibitors of glycogen phosphorylase
   Eur. J. Med. Chem., submitted. **IF: 3.499** (2012)

Conference participations

Oral presentations

1. L. Somsák, É. Bokor, K. Czifrák, B. Kónya, S. Kun, A. Páhi, **B. Szőcs**, M. Tóth, S. Vidal, J.-P. Praly:
   Heterociklusos glükózszármazékok, mint potenciális antidiabetikumok
   MTA Heterociklusos Kémiai Munkabizottság előadóülése, Balatonszemes, 2010. május 19-21.

2. **B. Szőcs**, M. Tóth, L. Somsák:
   Synthesis of C-glycopyranosyl-oxadiazoles and -thiadiazoles
   MTA Szénhidrátkémiai Munkabizottság előadóülése, Mátrafüred, 2010. május 27-28.

3. M. Tóth, **B. Szőcs**, T. Kaszás, E. K. Szabó, T. Docsa, P. Gergely, L.Somsák:
   Synthesis of C-(β-D-glucopyranosyl) heterocycles and 4-(β-D-glucopyranosyl) semicarbazones: potent glycogen phosphorylase inhibitors
   4th German-Hungarian Workshop, Synthesis, Isolation, and Biological Activity of Natural Products and Related Systems, Debrecen, Hungary, July 14-16, 2011, Book of Abstracts OP-7.

4. **B. Szőcs**, T. Kaszás, K. E. Szabó, M. Tóth, L. Somsák:
   Glükózhoz kapcsolt acilhidrazon származékok heterociklizációja
   MTA Szénhidrát, Nukleinsav és Antibiotikum Munkabizottság előadóülése, Debrecen, 2012. máj. 31.-jún. 1.

5. **B. Szőcs**, S. Kun, É. Bokor, K. E. Szabó, M. Tóth, K. Czifrák, L. Juhász, G. Varga, A. Páhi, T. Docsa, P. Gergely, L. Somsák:
   Synthesis of 3-glucopyranosyl-5-substituted-1,2,4-triazoles and their evaluation as glycogen phosphorylase inhibitors
   MTA Szénhidrát, Nukleinsav és Antibiotikum Munkabizottsága előadóülése, Mátrafüred, 2013. máj. 22-24.

6. S. Kun, É. Bokor, **B. Szőcs**, M. Tóth, K. Czifrák, L. Juhász, G. Varga, A. Páhi, T. Docsa, P. Gergely, L. Somsák:
   3-(β-D-Glükopiranozil)-5-szubsztituált-1,2,4-triazolok, a glikogén foszforiláz enzim új nanomólos inhibitorai
   MKE Vegyészkonferencia, Hajdúszoboszló, 2013. jún. 26-28.,O-20.

Posters

7. **B. Szőcs**, M. Tóth, L. Somsák:
   C-Glükopiranozil heterociklusok, mint potenciális glikogén foszforiláz inhibitorok szintézise
   MKE Vegyészkonferencia, Hajdúszoboszló, 2010. jún. 31.-júl 2., P-49.

8. **B. Szőcs**, T. Kaszás. M. Tóth, T. Docsa, P. Gergely, L. Somsák:
   C-(β-D-glucopyranosyl) heterocycles and 4-(β-D-glucopyranosyl) semicarbazones as glycogen phosphorylase inhibitors
   16th European Carbohydrate Symposium, Sorrento, Italy, July 3-7, 2011, Book of abstracts PO 327.

9. **B. Szőcs**, T. Kaszás, K. E. Szabó, M. Tóth, T. Docsa, P. Gergely, L. Somsák:
Synthesis of C-(β-D-glucopyranosyl) heterocycles and 4-(β-D-glucopyranosyl) semicarbazones
4th European Conference on Chemistry for Life Sciences, Budapest Hungary, Aug 31-Sep 3, 2011, Book of abstracts p 254.

10. **B. Szőcs**; M. Tóth; T. Kaszás; T. Docsa; P. Gergely; L. Somsák:
Synthesis of 3-(β-D-glucopyranosyl)-1,3,4-oxa- and -thiadiazoles and 3-(β-D-glucopyrano-sylamino)-1,3,4-oxadiazoles for inhibition of glycogen phosphorylase
26th International Carbohydrate Symposium, Madrid, Spain, July 22-26, 2012, Book of abstracts P399.

11. É. Bokor, S. Kun, **B. Szőcs**, M. Tóth, K. Czifrák, L. Juhász, A. Páhi, M. Polyák, T. Docsa, P. Gergely, L. Somsák:
3-(β-D-Glucopyranosyl)-5-substituted-1,2,4-triazoles as new nanomolar inhibitors of glycogen phosphorylase
5th European Conference on Chemistry for Life Sciences, Barcelona, Spain, June 10-12, 2013, Book of abstracts P021.

12. **B. Szőcs**, K. E. Szabó, M. Tóth, É. Bokor, L. Somsák:
3-(C-Glikozil)-5-aril-1,2,4-triazolok, valamint asszimetrikus3,5-diszubsztituált-1,2,4-triazolok új szintézise
MKE Vegyészkonferencia, Hajdúszoboszló, 2013. jún. 26-28., P-63.