**Short thesis for the degree of doctor of philosophy (PhD)**

# Transformations of ulosonic acid derivatives into glycosylidene-spiro-morpholinones and *O*-, *N*- and *S*-glycosides under Mitsunobu conditions

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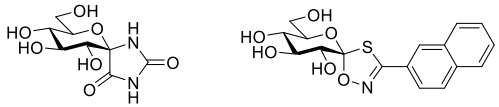
## 1. Introduction and aims of the dissertation

The importance of the morpholine ring in pharmaceutical chemistry cannot be questioned, since this moiety can be found in countless natural and synthetic bioactive molecules and drugs. As a consequence, it is not surprising that the literature of morpholine derivatives is enormous. However, compounds that contain a spiro-morpholine ring system are much less well-explored, as only a few bioactive examples exist in the literature from this family. Even less common are gylcosylidene-spiro-morpholines, in which the carbohydrate ring shares a common atom (the anomeric carbon atom) with the morpholine unit.

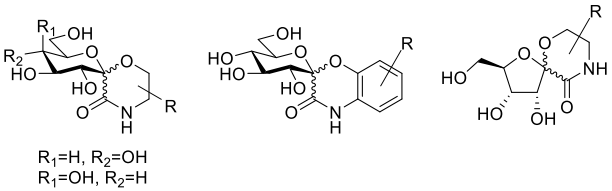
In our group, researchers have been working on the synthesis of various glycosylidene-spiro-heterocycles for decades. Among these molecules, quite a few examples were found to have a significant inhibitory effect against glycogen-phosphorylase (GP) and sodium-dependent glucose cotransporter (SGLT) enzymes. For example, hydantoin **A** and oxathiazoline **B** showed an inhibitor constant of 3.1 and 0.16 μM against GP, respectively (scheme 1). These compounds, as well as the vast majority of other molecules discovered in our group, contain aglycon rings consisting of five atoms. However, synthesis and bioactivity of spiro-compounds with a six-membered aglycon unit have not been extensively studied.




**Scheme 1:** Examples for effective gylcogen phosphorylase inhibitors

The aim of this research was to explore the synthetic possibilities of glycosylidene-spiro-morpholines and -benzoxazines, leading to a novel family of compounds that are unknown in the literature. The generalised structure of these target molecules are shown on scheme 2. After successfully developing the synthetic methods using glucose, the most common carbohydrate configuration, I have also repeated some

of the syntheses using galactose and ribose derivatives, in order to extend the circle of possibilities for biological studies.




**Scheme 2:** General structure of the target compounds

We intended to examine our products with a glucose unit for glycogen phosphorylase inhibition, whereas galactosylidene-spiro-morpholines were subjected to galectin inhibition studies. Molecules with a ribose moiety will be sent for adenylosuccinate syntethase inhibition studies, which, in case of a positive result, has a potential for being an effective antibacterial agent against *Helicobacter pylori*.

During the synthesis of some glycosylidene-spiro-benzoxazines, application of the Mistunobu-reaction have proved to be the necessary method. Hydroxyl groups at the anomeric position of ketoses have a resemblance to tertiary alcohols, therefore the applicability of the Mitsunobu-protocol is limited due to steric hindrance. Not surprisingly, there are only two examples in the literature for a Mitsunobu-type substitution involving a tertiary hydroxyl group of a carbohydrate, and none of these examples investigated the applicability of N-, S- and C-nucleophiles as reaction partners. A further aim of this thesis was to explore the possibility of a Mitsunobu-substitution with a wide range of nucleophiles using a carbohydrate with a tertiary hydroxyl gruop. For the purposes of these studies, heptulopyranosonic ester **204b**[1] was used as substrate.

[1]In this short thesis, the same compound numbers are used as in the dissertation.

## 2. Methods

During the course of this synthetic work, macro-, semimicro- and micro methods of modern preparative organic chemistry were applied. Monitoring the conversion of reactions were carried out by using thin layer chromatography (TLC), the products were purified by coloumn chromatography and/or crystallization. Purity of the isolated products were checked by TLC and their $^{1}H$ and $^{13}C$-NMR spectra. For the characterisation of new compounds, physical constants such as melting point and optical rotatory power were measured, their structure was elucidated based on their NMR and MS spectra.

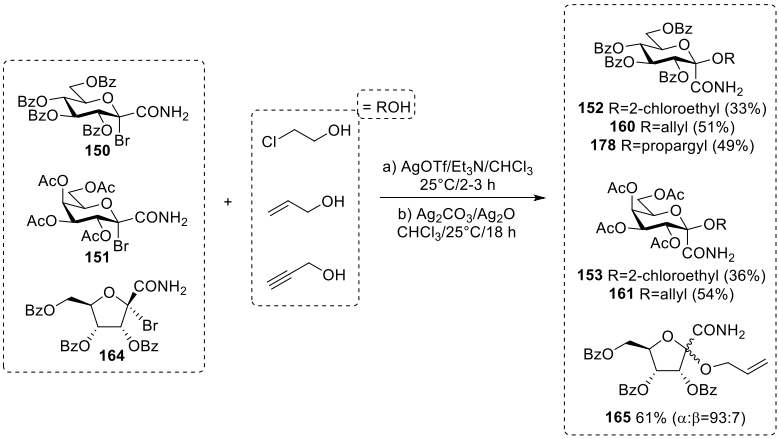
## 3. Results

### 3.1. Synthesis of novel glycosylidene-spiro-morpholines

*Methods were developed for the synthesis of 1',5'-anhydro-2',3',4',6'-tetra-O-benzoyl-D-glucitol-spiro-[1',2]-morpholine-3-one (**153**), 1',5'-anhydro-2',3',4',6'-tetra-O-benzoyl-D-glucitol-spiro-[1',2]-5-hydroxy-morpholine-3-one (**162**), 1',5'-anhydro-2',3',4',6'-tetra-O-benzoyl-D-glucitol-spiro-[1',2]-morpholine-3,5-dione (**179**) and 1',5'-anhydro-2',3',4',6'-tetra-O-benzoyl-D-glucitol-spiro-[1',2]-(2H-1,4-oxazine-3[4H]-one (**184**), and in some cases their analogs containing galactose and ribose moieties.*

#### 3.1.1. Synthesis of glycosylidene-spiro-morpholine precursors via glycosilations of aliphatic alcohols

Peracylated 1-bromoglycosyl-formamides (**150**-**151**, **164**) were prepared according to literature methods, then reacted with 2-chloroethanol, allyl and propargyl alcohols under regular glycosylation conditions (scheme 3). These experiments yielded six *O*-glycosides (**152**-**153**, **160**-**161**, **165**, **178**) that are potentially useable for the synthesis of a morpholine moiety.

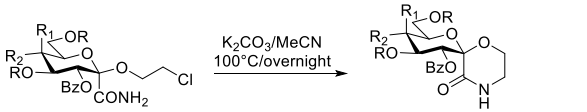



**Scheme 3:** Synthesis of glycosylidene-spiro-morpholine precursors

Experiments involving a substrate with a pyranose ring exclusively yielded the α-anomers of the desired products (**152-153**, **160-161**, **178**), which was proven using the comparison of their $^{1}$H-NMR spectra with reference molecules of known anomeric configuration. Ribose derivative **165** was isolated as a 93:7 mixture of α:β anomers.

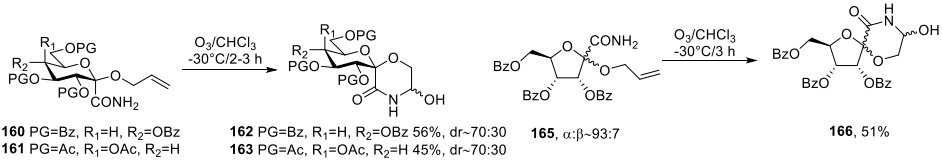
### 3.1.2. Constructing the morpholine ring: synthesis of glycosylidene-spiro-morpholines

Ring closure reactions of peracylated *C*-[1-(2-chloroethoxy)-α-D-glycopyranosyl]-formamides **152-153** were carried out as shown on scheme 4. In this case the intramolecular nucleophilic substitution of the chloroethyl group to the amide nitrogen could be easily performed in the presence of potassium-carbonate.



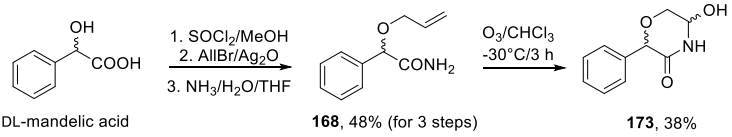

**Scheme 4:** Ring closure of peracylated *C*-[1-(2-chloroethoxy)-α-D-glycopyranosyl]-formamides

Ozonolysis of the peracylated *C*-(1-allyloxy-α-D-glycosyl)-formamides (**160-161**, **165**) yielded three new 5-hydroxy-spiro-morpholine derivatives (**162-163**, **166**) as shown on scheme 5. The intermediate product in this reaction contains an aldehyde group, which further reacts *in situ* with the amide nitrogen to form the desired morpholine ring, without having to isolate the aldehyde. This step is not stereoselective, products **162-163** were formed as a 70:30 ratio of the two possible stereoisomers. Ribosylidene-spiro-morpholine **166** contains four isomers, therefore it has a complex $^1$H-NMR spectrum which rendered the calculation of its diastereomeric ratio impossible.




**Scheme 5:** Ozonolysis of peracylated *C*-(1-allyloxy-α-D-glycosyl)-formamides

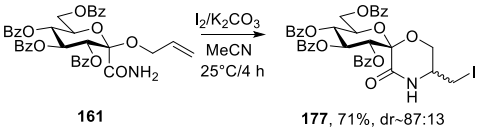
Ozonolysis of 2-allyloxy-amides in general is an unprecedented technique in the literature for synthesizing morpholine derivatives. Therefore we intended to demonstrate the generalisation of this method using a non-carbohydrate substrate. For this purpose, synthesis of *O*-allyl-mandelamide (**168**) was developed from the commercially available DL-madelic acid, after wich its ozonolysis yielded the desired **173** phenylmorpholine derivative (scheme 6).




**Scheme 6:** Synthesys and ozonolysis of 2-allyloxy-2-phenylacetamide

Another ring closure reaction of **160** was performed using elemental iodine and potassium-carbonate (scheme 7), which successfully gave the **177** iodomethly-spiro-

morpholine in a one-pot reaction. However, attempts to form a morpholine ring using the **178** *O*-propargyl-glycoside have failed.

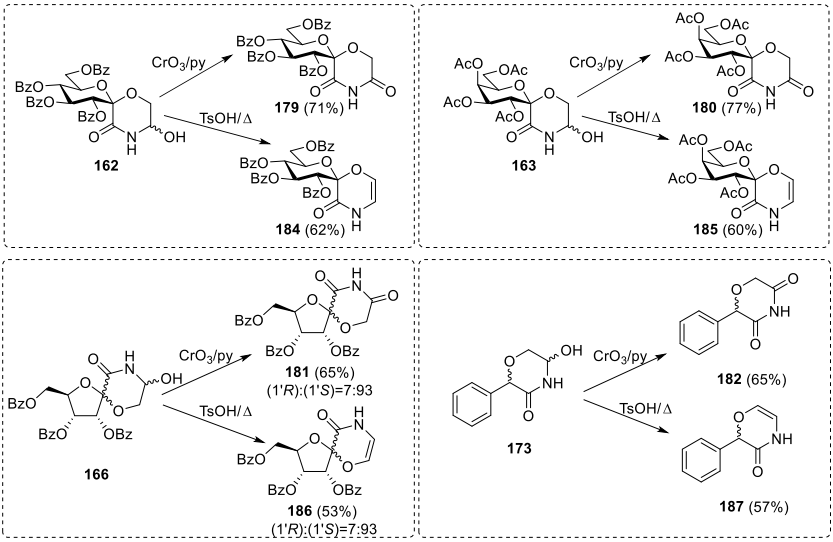



**161** **177**, 71%, dr~87:13

**Scheme 7:** Synthesis of a spiro-morpholine derivative with an iodomethyl group

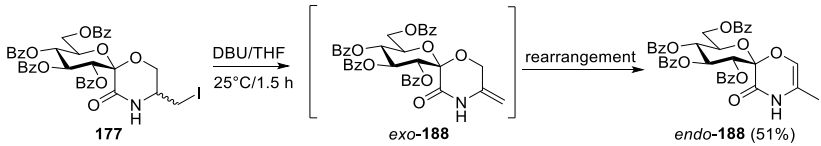
### 3.1.3. Further transformations of glycosylidene-spiro-morpholines

In order to achieve stereouniform products from the above synthesized spiro-morpholines, we aimed for transformations which would eliminate the new stereogenic centre formed in the ring closure reaction. For this reason, hydroxy-spiro-morpholines **162-163**, **166** were subjected to oxidation with chromium-trioxide, as well as acid catalysed water elimination. All of these experiments resulted in the expected spiro-morpholine-diones (**179-181**) and unsaturated spiro-morpholines (**184-186**) with acceptable to good yields (scheme 8). Continuing the generalization of the methods, phenylmorpholine **173** was also converted into analogous products (**182**, **187**).




**Scheme 8:** Elimination of the new stereogenic centre of the hydroxy-(spiro)-morpholines

In case of our spiro-morpholine with an iodomethyl group (**177**), the new stereogenic centre can be eliminated by treating the compound with DBU. However, instead of the expected *exo*-**188**, the product with the endocyclic double bond (*endo*-**188**) was formed due to a rearrangement reaction (scheme 9).

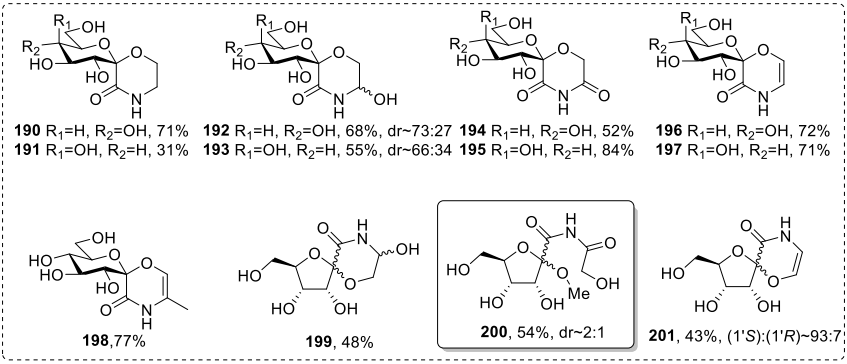



**Scheme 9:** Elimination of hydrogen-iodide from spiro-morpholine **177**

### 3.1.4. Removing the protecting groups from the spiro-morpholines

Over the course of this work, a total of 12 novel glycosylidene-spiro-morpholines were synthesized. In order to make the compounds available for biological studies, removal of the ester protecting groups was necessary, which could be preformed

according to the Zemplén protocol. The structures of the unprotected final products are summarised on scheme 10.

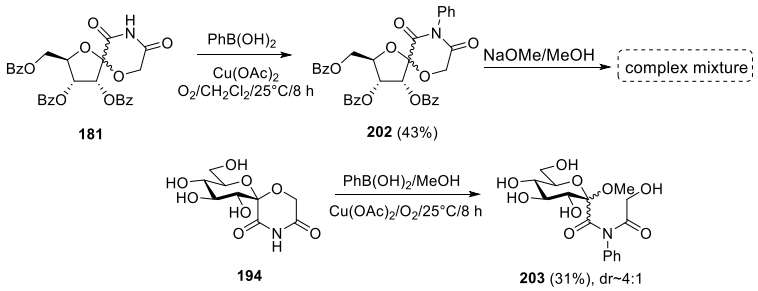



**Scheme 10:** Products after removal of protecting groups

Purification of these products by coloumn chromatography has proven difficult, because these spiro-morpholines have a tendency to react with methanol in the eluent, resulting in the ring opening of the morpholine moiety. In most cases, this phenomenon could be avoided using basic conditions (e.g. adding 0.5% triethylamine to the eluent), however in one case (**200**), the ring opening reaction could not be circumvented by any attempted means. As a result, only a total of 11 spiro-morpholines were isolated successfully.

### 3.1.5. Experiments for the arylation of the nitrogen atom

The reaction of ribofuranosylidene-spiro-morpholine-dione **181** with phenylboronic acid and copper(II)-acetate resulted in the desired *N*-phenyl derivative (**202**), however, deprotection of this compound was unsuccessful. I have also attempted to perform the arylation reaction on an already deprotected spiro-morpholine-dione (**194**), and altough the phenyl group was present in the product, a similar ring opening side reaction as discussed above also occured (scheme 11).




**Scheme 11:** Experiments for *N*-arylation of spiro-morpholine-diones

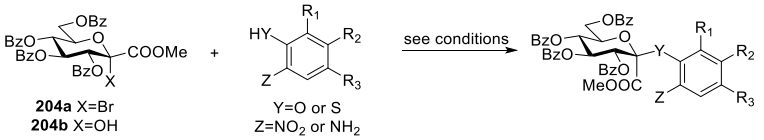
### 3.2. Synthesis of glycosylidene-spiro-benzoxazines and -benzothiazines

*Methods for the synthesis of 1',5'-anhydro-D-glucitol-spiro-[1',2]-benzo[b][1,4]-oxazinones* ***(214-217)*** *and 1',5'-anhydro-D-glucitol-spiro-[1',2]-benzo[b][1,4]-thiazinones* ***(222-223)*** *were developed.*

#### 3.2.1. Synthesis of glycosylidene-spiro-benzoxazine and -benzothiazine precursors via glycosylation of phenols and benzenethiols

During the course of this research, 3 new methyl *C*-[2,3,4,6-tetra-*O*-benzoyl-1-(2-nitroaryloxy)-α-D-glucopyranosyl]formates (**209-211**) and 2 new methyl *C*-[2,3,4,6-tetra-*O*-benzoyl-1-(2-nitroarylsulfanyl)-α-D-glucopyranosyl]formates (**220-221**) have been synthesized. The starting material for these experiments were bromo-ester **204a** or hydroxy-ester **204b**, both of which can be prepared according to literature methods. The optimal reaction conditions depended on the nucleophilic reagents, resulting in a different optimal method for each *O*- or *S*-glycoside, the results of these experiments are summarised in table 1.

**Table 1:** Synthesys of glycosylidene-spiro-benzoxazine and -benzothiazine precursors




**204a** X=Br
**204b** X=OH

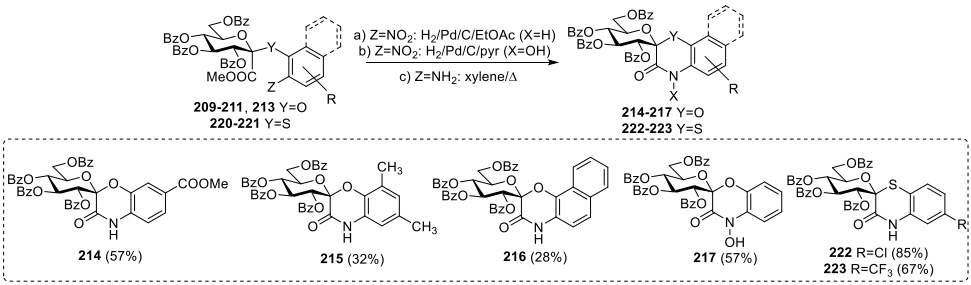
Y=O or S
Z=$NO_2$ or $NH_2$

| | X= | Y= | Z= | $R_1/R_2/R_3$ | Conditions | Product (yield) |
|---|---|---|---|---|---|---|
| 1. | Br | O | $NO_2$ | $R_2$=COOMe | a) $K_2CO_3$/acetone/rt<br>b) AgOTf/$Et_3N$/$CHCl_3$/rt | **209**<br>(a: 53%)<br>(b: 60%) |
| 2. | OH | O | $NO_2$ | $R_1$=$R_3$=Me | DEAD/$Ph_3P$/THF/rt | **210**<br>(76%) |
| 3. | OH | O | $NO_2$ | $R_1$, $R_2$=  | DEAD/$Ph_3P$/THF/rt | **211**<br>(87%) |
| 4. | Br | S | $NH_2$ | $R_3$=Cl | 1. NaOMe/MeOH+thiol<br>2. **204a**/acetone/rt | **220**<br>(59%) |
| 5. | Br | S | $NH_2$ | $R_3$=$CF_3$ | $K_2CO_3$/acetone/reflux<br>thiol added in small portions | **221**<br>(48%) |

### 3.2.2. Synthesis of glycosylidene-spiro-benzoxazines and -benzothiazines via the ring closure reactions of the *O*- and *S*-aryl-glycosides

The 5 precursors shown above were converted into spiro-benzoxazine or -benzothiazine derivatives using different ring closing metods. Intermediates containing a nitro gruop (**209**-**211**) were subjected to Pd-catalysed hydrogenation, which not only reduced the nitro group into an amino group, but it also catalysed the ring closure reaction between the amine and the ester, therefore the synthesis of spiro-benzoxazines turned out to be a one-pot reaction. The *S*-aryl-glycosides (**220**-**221**) already contained amino groups, therefore the simple heating of their solutions in xylene was sufficient to

yield the desired spiro-benzothiazines **222-223** (scheme 12). Another *O*-aryl-glycoside (**213**), which was previously synthesized in our group, has also been converted into a spiro-hydroxamic acid derivative (**217**) by performing the partial reduction of the amino group using pyridine as solvent.




**Scheme 12:** Cyclizations into glycosylidene-spiro-benzoxazines and -benzothiazines

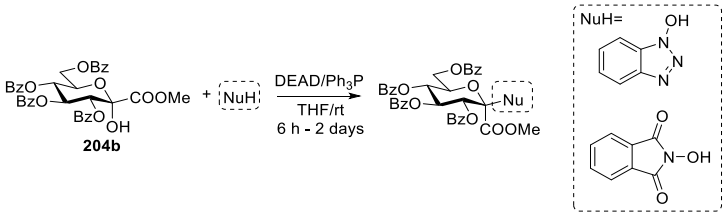
Removal of the ester protecting groups under Zemplén conditions have also been performed on all 6 spirocycles with varied yields (32-85%). The unprotected products were not prone to ring opening reactions with methanol like the spiro-morpholines, and as a result, their purification and isolation proceeded without problems.

### 3.3. Extending the Mitsunobu-protocol for glycosylations with ulosonic acid esters

*Studies involving the Mitsunobu-reactions of methyl C-(2,3,4,6-tetra-O-benzoyl-1-hydroxy-β-D-glucopyranosyl)formate (**204b**) and methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glicero-D-galacto-2-nonulopyranosonate (**128**) were carried out using O-, N-, S- and C-nucleophiles that are unprecedented in the literature in the presence of ketose type carbohydtates.*

### 3.3.1. Reaction of methyl *C*-(2,3,4,6-tetra-*O*-benzoyl-1-hydroxy-β-D-glucopyranosyl)formate (**204b**) with O-nucleophiles

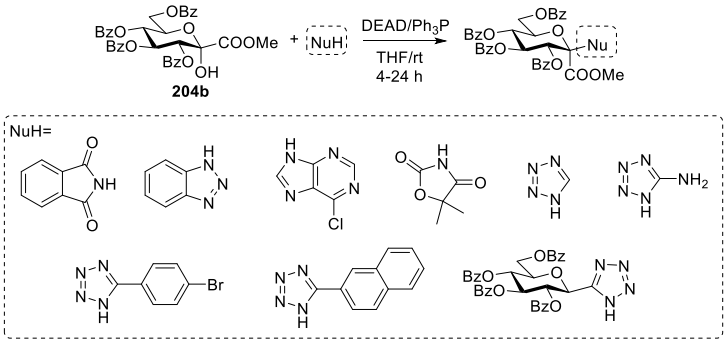
Besides the above mentioned two phenol derivatives, a further 10 O-nucleophiles have been attempted as reaction partners of **204b** under Mitsunobu conditions. Out of these experiments, only two reactions yielded the desired *O*-glycosides (scheme 13). The conclusion of this study is that the optimal $pK_a$ range of the nucleophiles is between 5-8. Reactivity of reagents with a higher value seems to be insufficient, while more acidic nucleophiles cause the decomposition of **204b**.




**Scheme 13:** Successful Mitsunobu-reactions of **204b** with O-nucleophiles

### 3.3.2. Reaction of methyl *C*-(2,3,4,6-tetra-*O*-benzoyl-1-hydroxy-β-D-glucopyranosyl)formate (**204b**) with N-nucleophiles

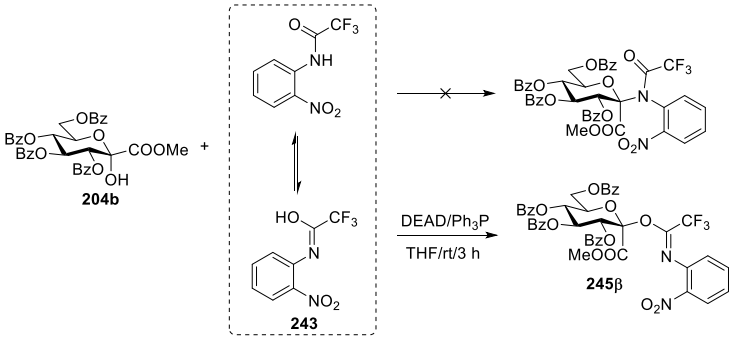
Mitsunobu-substitutions of a tertiary hydroxyl group of a carbohydrate are scarce in the literature, and the few examples we know of only mention O-nucleophiles. Therefore, the aim of this work was to examine the scope and limitations of this protocol, and extend its application to N-, S- and C-nucleophiles as well. For this purpose, 20 different N-nucleophiles were subjected to glucopyranosonic ester **204b** with a $pK_a$ range of 4-12. In this series of experiments, 9 *N*-glycosides have been isolated successfully (scheme 14).




**Scheme 14:** Successful Mitsunobu-reactions of **204b** with N-nucleophiles

Once again, our observation was consistent with what we experienced with the O-nucleophiles: the $pK_a$ range of the reagent proved to be important, with an optimal range of 4-8. In some cases (e.g. xanthine and uric acid), the reactions were unsuccessful despite the correct $pK_a$ value, which could be explained with the large steric hindrance of these compounds. An interesting result was observed in the case of tetrazole: in this experiment, two different products were isolated, which is a result of the two tautomer forms of the reagent, leading to 1*N*- and 2*N*-substituted derivatives. Tetrazoles with a substituted carbon atom did not produce a similar phenomenon, only the 2*N*-glycosides were isolated in those cases.

The reaction with 2-nitrotrifluoroacetanilide (**243**) also produced an interesting result, as it did not act as an N-nucleophile, contrary to what we expected. Instead, the tautomer form of this compound formed an O-glycoside with **204b**, leading to the trifluoroacetimidate **245β** (scheme 15). These type of compounds are important glycosyl donors in carbohydrate chemistry, and their synthesis have not previously been described in the literature using trifluoroacetanilides, therefore this discovery has a synthetic significance.




**Scheme 15:** Reaction of **204b** with 2-nitrotrifluoroacetanilide (**243**)

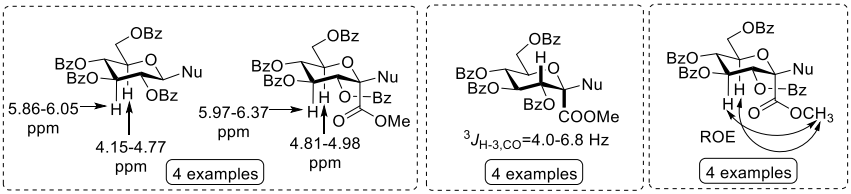
### 3.3.3. Reaction of methyl *C*-(2,3,4,6-tetra-*O*-benzoyl-1-hydroxy-β-D-glucopyranosyl)formate (**204b**) with S- and C-nucleophiles

To further extend the list of possible reagents, **204b** was subjected to 3 S-nucleophiles and 10 C-nucleophiles under Mitsunobu conditions. Unfortunately, only benzenethiol proved to be reactive, yielding one *S*-glycoside (**246**). All other reagents had an unsuitable $pK_a$ value, or its steric hindrance was too great. In these unsuccessful experiments, only the formation of glycal **212** was observed.

### 3.3.4. Verification of the anomeric configuration of the products

Over the course of the above experiments, a total of 14 new glucopyranosonic esters with disubstituted anomeric carbon atoms have been synthesized. These compounds were all found to be stereouniform, the nucleophile took up equatorial position in all products. This can be confirmed using three different NMR techniques (scheme 16). Firstly, four products (**232-233**, **235**, **246**) were compared to reference compounds known from the literature. These molecules have a similar structure to our products, except the methoxycarbonyl group is absent from the anomeric position. Comparing the chemical shifts of H-4 and H-6 in these pairs of compounds, we found that these protons have a chemical shift 0.1-0.4 ppm higher in the presence of the ester group. This phenomenon can only be observed if the carbonyl group is axial, because it

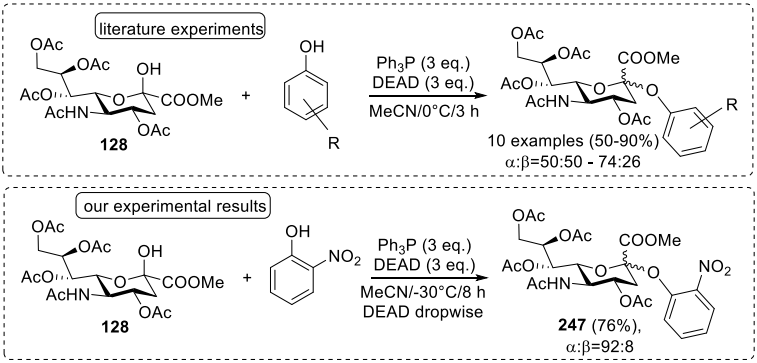
needs to be *cis*-configured with H-4 and H-6 to cause their deshielding. Secondly, using four of our compounds (**233-234**, **237**, **238b**), the three-bond heteronuclear coupling constant between H-3 and the carbonyl group has been measured by HSQMBC-NMR technique, which in all cases was in accordance with the axial ester group ($J \geq 4{,}0$ Hz). Finally, the same four compounds have been subjected to 1D-ROESY NMR measurement, which successfully detected ROE-effect between H-4, H-6 and the methyl group of the ester moiety, proving their close proximity to each other, and therefore the presence of an axial carbonyl group.




**Scheme 16:** Confirmation of the anomeric configuration of the Mitsunobu-products

### 3.3.5. Mitsunobu-reactions of methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glicero*-D-*galacto*-2-nonulopyranosonate (**128**)

Apart from glucopyranosonic ester **204b**, neuraminic ester **128** also has a tertiary-like hydroxyl group at its anomeric centre. This compound is known to react with phenols under Mitsunobu-conditions, but no other nucleophiles have been attemped with **128**. At first, we have tried to reproduce these literature experiments, however, only the formation of glycal **249** was observed. Optimization of the reaction conditions revealed that adding the DEAD dropwise, and changing the temperature to -30°C, the results can not only be reproduced, but the anomeric ratio can also be improved in favour of the α-product (scheme 17).




**Scheme 17:** Optimization of the conditions for the Mitsunobu-reaction of **128**

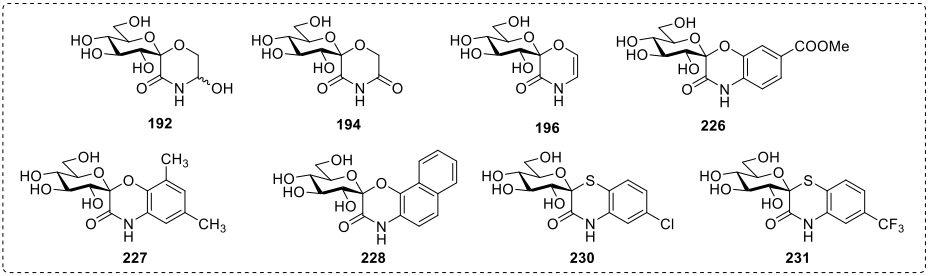
Neuraminic ester **128** was then subjected to 9 different nucleophiles under the improved conditions, however, only benzotriazole yielded the expected product, whereas glycal **249** was detected in all other cases as main product. A possible explanation of this is that **128** is a 2-deoxysugar, therefore it may be more susceptible to eliminations leading to glycal formation. Also worth noting is that **128** might have a vastly different conformation compared to **204b**, which may lead to completely different steric interactions with the nucleophile. From these experiments, it can be concluded that Mitsunobu-substitutions of ketose-type substrates largely depend on the structure of the starting material, but the size and $pK_a$ value of the nucleophilic patner are also important.

### 3.4. Biological studies

*Several model compounds have been chosen from the previously synthesized glycosylidene-spiro-morpholines, -benzoxazines and -benzothiazines, which have been tested in various biological studies by our partners. Compounds with a glucose unit have been subjected to glycogen phosphorylase inhibition, while galactose-containing molecules have been sent for binding studies to galectins. Ribosylidene-spiro-morpholines will be examined in the future for adenylosuccinate synthetase inhibition.*

### 3.4.1. Inhibition studies for glycogen phosphorylase isolated from rabbit muscle (RMGP*b*)

Three of the glucosylidene-spiro-morpholines (**192**, **194**, **196**), and all five members of the glucosylidene-spiro-benzoxazine and -benzothiazine family (**226-228**, **230-231**) have been studied by Dr. Tibor Docsa and his group at the Department of Medical Chemistry, University of Debrecen (scheme 18). The results indicated that all eight compounds have a weak inhibition effect for RMGP*b*, with 0-28% enzyme inhibition values at 625 μM concentration. Because $K_{di}$ and $IC_{50}$ values are normally measured for relatively strong binders (~100% inhibition at 625 μM or lower concentrations), these values have not been determined for our compounds.

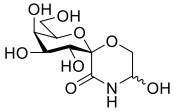
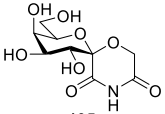
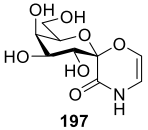



**Scheme 18:** Compounds examined for RMGP*b* inhibition

### 3.4.2. Studies for binding to galectins

Three model compounds (**193**, **195**, **197**) have been chosen and sent for Dr. Ulf Nilsson at Lund University (Sweden), where they have been subjected to different types of galectins. The results are summarised in table 2. Unfortunately, these compounds proved to be weak inhibitors of all galectins, with vastly larger $K_{di}$ values compared to currently known galectin inhibitors.

**Table 2:** Results of the binding studies of galactosylidene-spiro-morpholines to different galectins ($K_{di}$ values, μM)

| | Galectin-1 | Galectin-3 | Galectin-8N |
|---|---|---|---|
|  **193** | 1359 | no inhibition | 6578 |
|  **195** | 1414 | 4482 | 5620 |
|  **197** | 1798 | 4999 | 6479 |

Adenylosuccinate synthetase inhibition studies, involving our ribosylidene-spiro-morpholines, will be carried out by Dr. Agnieszka Bzowska's group at the University of Warsaw. The results of these experiments are still unknown at the time of submitting this dissertation.

## 4. Possible future applications of the results

Despite all glycosylidene-spiro-heterocycles being weak inhibitors of the examined targets, the research still contains important results from a synthetic point of view, which may find its applications in preparative organic chemistry in the future.

A new, unprecedented ring closure reaction was discovered for the synthesis of morpholine derivatives by way of ozonolysis of 2-allyloxyamides. This strategy might prove useful for synthesizing new, bioactive target molecules containing a morpholine moiety in the future.

An extensive study was carried out for the possibility of a Mitsunobu-substitution involving the hydroxyl group at the anomeric position of ulopyranosonic esters. This area of carbohydrate chemistry is not thoroughly studied in the literature, especially in the presence of N-, S- and C-nucleophiles. The results of these experiments might be useful in the future in the synthesis of new nucleosides or their analogues, which is an important family of molecules from a biological and medicinal point of view.

In this same series of experiment, a novel method has been discovered for the synthesis of *O*-glycosyl-trifluoroacetimidates, which are important glycosyl donors. This reaction requires a hydroxyl group at the anomeric position, and trifluoroacetanilide as reagent, as well as Mitsunobu-conditions, which is an unprecedented method in the literature for the synthesis of trifluoroacetimidate-type glycosyl donors.

In case the ribosylidene-spiro-morpholines prove to be effective for adenylosuccinate synthetase inhibition, followed by a possible structure-effect correlation study and optimization of the structure, they might have a potential application against *Helicobacter pylori* infections.

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Subject: PhD Publication List

Candidate: Nándor Kánya
Doctoral School: Doctoral School of Chemistry
MTMT ID: 10054572

**List of publications related to the dissertation**

Foreign language scientific articles in international journals (2)

1. **Kánya, N.**, Kun, S., Batta, G., Somsák, L.: Glycosylation with ulosonates under Mitsunobu conditions: scope and limitations.
   *New J. Chem. 44* (34), 14463-14476, 2020. ISSN: 1144-0546.
   DOI: http://dx.doi.org/10.1039/D0NJ03044A
   IF: 3.591

2. Kun, S., **Kánya, N.**, Galó, N., Páhi, A., Mándi, A., Kurtán, T., Makleit, P., Veres, S., Sipos, Á., Docsa, T., Somsák, L.: Glucopyranosylidene-spiro-benzo[b][1,4]oxazinones and -benzo[b][1,4]thiazinones: Synthesis and Investigation of Their Effects on Glycogen Phosphorylase and Plant Growth Inhibition.
   *J. Agric. Food Chem. 67* (24), 6884-6891, 2019. ISSN: 0021-8561.
   DOI: http://dx.doi.org/10.1021/acs.jafc.9b00443
   IF: 4.192

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## List of other publications

Foreign language international book chapters (1)

3. Kašáková, M., Bertolotti, B., Moravcová, J., Dong, L., Rousset, A., Vidal, S., **Kánya, N.**: 3-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-prop-1-ene.
In: Carbohydrate Chemistry:. Ed.: Paul Kosma, Tanja M. Wrodnigg, Arnold Stütz, CRC Press, Boca Raton, 153-163, 2021, (Proven Synthetic Methods ; 5.) ISBN: 9780815367888

Foreign language scientific articles in international journals (1)

4. Rapi, Z., Ozohanics, O., Tóth, G., Bakó, P., Höfler, L., Nemcsok, T., **Kánya, N.**, Keglevich, G.: Syntheses and complexing ability of α-d-gluco- and α-d-xylofuranoside-based lariat ethers.
*J. Incl. Phenom. Macrocycl. Chem. 85* (1-2), 19-32, 2016. ISSN: 1388-3127.
DOI: http://dx.doi.org/10.1007/s10847-016-0601-8
IF: 1.095

**Total IF of journals (all publications): 8,878**
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**Conference participations**

***Oral lectures***

1. S. Kun, **N. Kánya**, N. Galó, A. Mándi, P. Makleit, Sz. Veres, T. Kurtán, L. Somsák: Glucopyranosylidene-spiro- benzo[b][1,4]oxazinones and -benzo[b][1,4]thiazinones: synthesis, CD and biological studies, Annual meeting of the Working Committee for Carbohydrates, Nucleic Acids and Antibiotics of the Hungarian Academy of Sciences; Mátraháza, 2017.
2. **N. Kánya**, S. Kun, L. Somsák: A study for the application of the Mitsunobu-reaction on a heptulopyranosonic ester, International Workshop on Chemistry and Chemical Biology of Carbohydrates, Nucleic Acids and Antibiotics, Mátrafüred, 2019.
3. **Kánya N.**, Kun S., Somsák L.: Synthesis of glycosylidene-spiro-morpholines (original title: „Glikozilidén-spiro-morfolinok szintézise"), MTA Online meeting of the Working Committee for Carbohydrate-, Nucleic acid- and Antibiotics Chemistry, 2021. 06. 14.
4. **Kánya N.**, Rapi Zs., Ozohanics O., Tóth G., Bakó P.: Synthesis and application of glucofuranoside-based crown ethers (original title: „Glükofuranozid alapú koronaéterek szintézise és alkalmazása"), XXXVIII. Chemistry Lectures Day, Szeged, 2015.

***Posters***

5. Kun S., Szabó E. K., **Kánya N**., Galó N., Páhi A., Mándi A., Kurtán T., Somsák L.: Glucopyranosylidene-spirocycles with five and six membered heterorings: synthesis, CD studies and inhibition of glycogen phosphorylase (original title: „Glükopiranozilidén spirociklusok öt- és hattagú heterogyűrűvel: szintézis, CD vizsgálatok és glikogén-foszforiláz gátlás"), MKE Chemist's Conference, Hajdúszoboszló, 2017. 06. 19-21. P-27.

6. S. Kun, K. E. Szabó, N. **Kánya, N**. Galó, A. Páhi, A. Mándi, T. Kurtán, L. Somsák: Glucopyranosylidene-spirocycles with five and six membered heterorings: synthesis, CD studies and inhibition of glycogen phosphorylase, 19th European Carbohydrate Symposium, Barcelona, Spain, 2017. July 2-6., P32, Book of abstracts p. 323.
7. **Kánya N**., Kun S., Somsák L.: Modifications of Heptulopyranosonic Acid Esters Using the Mitsunobu-reaction (original title: „Heptulopiranozonsav-észterek átalakításai Mitsunobu-reakcióval"), I. FKF Symposium, Debrecen, Book of abstracts p84., 2019.
8. Sándor Kun, **Nándor Kánya**, Nóra Magos, László Somsák: Novel Bis-C,C-Glycosyl Derivatives: C-glycosides of Heptulosonic acids and their Spyrocyclisation, 20th European Carbohydrate Symposium, Leiden, The Netherlands, 2019. 06.30. - 07. 04. (P119)
9. **Nándor Kánya**, Sándor Kun, László Somsák: Modifications of Heptulopyranosonic Acid Esters Using the Mitsunobu-reaction, 20th European Carbohydrate Symposium, Leiden, The Netherlands, 2019. 06. 30 - 07. 04. (P164)
10. Tóth G., Ozohanics O., Rapi Zs., **Kánya N**., Bakó P., Vékey K., Drahos L.: Examining the complexing abilities and possible applications of lariate ethers (original title: „Lariát-éterek komplexképző tulajdonságainak vizsgálata és felhasználási lehetőségei"), XXI. Bolyai Conference 2016.
11. G. Tóth, O. Ozohanics, Zs. Rapi, P. Bakó, **N. Kánya**, K. Vékey, L. Drahos: Synthesis of sugar-based crown ethers and investigation of complexing abilities with mass spectroscopy, XIII. „Students for Students" International Conference of Students and Young Scientists, 2016.