SYNTHESIS OF C-GLYCOSYL HETERO CYCLES FOR INHIBITION OF GLYCOGEN PHOSPHORYLASE

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1. Introduction

Type two *diabetes mellitus* is a severe metabolic disease of carbohydrate metabolism with economic and social consequences. Since there is no cure for this disease, the primary goal of the treatment is to keep the blood sugar concentration at a desirable level. A new possible treatment is the suppression of hepatic glucose output by the inhibition of glycogen phosphorylase, the main regulatory enzyme of glycogen degradation.

*N*-Acyl-β-D-glucopyranosylamines (1) and *N*-acyl-β′-D-glucopyranosyl ureas (2) are efficient competitive inhibitors of GP (Table 1). X-ray crystallographic studies showed that a direct hydrogen bond exists between the amide NH of *N*-acyl-β-D-glucopyranosylamines and the enzyme, and plays a significant role in the strong binding. This hydrogen bridge is missing in the case of *N*-acyl-β′-D-glucopyranosyl ureas, the good inhibition is the result of the more extensive favourable interactions of the aglycone and the β-channel.

Former studies pointed out that replacing the NHCO moiety of *N*-acyl-β-D-glucopyranosylamines with non-classical bioisosteric heterocycles (3-7) resulted in chemically more stable molecules, which were similarly efficient in terms of inhibition.

<table>
<thead>
<tr>
<th>Table 1: Glucose analogue inhibitors of GP (RMGPb, $K_i$ [μM])</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>a</td>
</tr>
<tr>
<td>b</td>
</tr>
<tr>
<td>d</td>
</tr>
</tbody>
</table>

6 $K_i = 9$ μM

7 $K_i = 76$ μM
The aim of our research was the preparation of azole type C-glycosyl heterocycles (Scheme 1) representing a formal replacement of the NHCO moiety of N-acyl-β-D-glucopyranosylamines (1) with pyrrole (A, B), indole (C), pyrazole (D), isoxazole (E), 1,3,4-oxadiazole (F), 1,2,3-triazole (G) and 1,2,4-triazole (H), as well as the double replacement of NHCO units in N-acyl-N’-β-D-glucopyranosyl ureas (2) with 1,3,4-oxadiazole and 1,2,3-triazole (I, J).

![Scheme 1: Inhibitor design](image)

2. Methods

In the course of the synthetic work, macro, semimicro 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 one or two-dimensional $^1$H and $^{13}$C NMR methods as well as mass spectrometry.
3. Results

3.1. Synthesis of 2-(β-D-glucopyranosyl)-pyrroles

Pyrrole (9) and 2- and 3-aryl-pyrroles (12, 15), synthesised by literature methods, were C-glycosylated with trichloroacetimidate 8 to give 2-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-pyrroles 10, 13, and 16, respectively (Scheme 2). From 3-aryl-pyrroles 15 the sterically crowded 2-glucosyl-3-aryl pyrroles 16 were formed instead of the expected 4-aryl-2-glucosyl-pyrroles. Acetyl protecting groups were cleaved by the Zemplén method to yield 11, 14, and 17.

![Scheme 2: Synthesis of 2-(β-D-glucopyranosyl)-pyrroles](image)

3.2. Synthesis of 2-(β-D-glucopyranosyl)-1H-indole

The Pd-catalyzed cross-coupling of ethyne 18 with N-tosyl-2-iodoaniline followed by a ring closure furnished the protected indole derivative 19 (Scheme 3). Removal of the tosyl and benzyl groups resulted in 2-β-D-glucopyranosyl-indole 20.
3.3. Synthesis of 3-(β-D-glucopyranosyl)-5-phenyl-1H-pyrazole and 3-(β-D-glucopyranosyl)-5-phenyl-isoxazole

These target compounds were synthesised from ethynyl-ketone 22 as a common starting material. Under the widely used basic conditions (a) for the synthesis of ethynyl-ketones, acid-chloride 21 gave glycal 23. To avoid the elimination, base free conditions and flash chromatography were utilized (c) to get the desired product 22 in medium yield.

![Scheme 3: Synthesis of 2-(β-D-glucopyranosyl)-indole](image)

Transformations of 22 and 23 with binucleophiles gave pyrazoles 24 and 29, isoxazole 26 and benzodiazepine 28 (Scheme 5). Protecting groups of 24 and 26 were removed by NaOMe catalyzed transesterification to yield 25 and 27.¹

![Scheme 4: Synthesis of phenylethynyl-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-ketone](image)

¹ Compound 27 was obtained from a batch of 26 synthesized independently in our research group.
Scheme 5: Synthesis of heterocycles from phenylethynyl-ketones

3.5. Synthesis of 2-(β-D-glucopyranosyl)-2-substituted-1,3,4-oxadiazoles

To avoid chromatographic purification in larger scale preparations new reaction conditions were applied for the formation of tetrazoles from anhydro-aldonitriles (Scheme 6). Cyanides 30-32 were converted to tetrazoles with azidotrimethylsilane and dibutyltin oxide. The method proved scalable and per-O-acylated β-D-gluco-, galacto- and xylopyranosyl-tetrazoles 33-35 could be isolated by crystallization.

Scheme 6: Synthesis of 5-(β-D-glucopyranosyl)-tetrazoles

<table>
<thead>
<tr>
<th>Products (yields)</th>
<th>33 (95%)</th>
<th>34 (93%)</th>
<th>35 (91%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30,31,32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMSN₃ Bu₂SnO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>abs. toluene 60°C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>33,34,35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acylation and ring transformation of tetrazole 33 yielded 1,3,4-oxadiazoles 36 (Scheme 7). Acylation was carried out by using acid-chlorides (a) or DCC activated carboxylic acids (b), both methods proved efficient. Removal of the ester protecting groups by the Zemplén procedure gave 4b,d,e,f,i. Reduction of the 4-nitrophenyl derivative 4f yielded 4-aminophenyl-1,3,4-oxadiazole 4j.

![Scheme 7: Synthesis of 2-(β-D-glucopyranosyl)-5-substituted-1,3,4-oxadiazoles](image)

<table>
<thead>
<tr>
<th>Products (36)</th>
<th>R’</th>
<th>Method</th>
<th>Yields (%)</th>
<th>Products (4)</th>
<th>R’</th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>b</td>
<td>C₆H₅</td>
<td>b</td>
<td>56</td>
<td>b</td>
<td>C₆H₅</td>
<td>91</td>
</tr>
<tr>
<td>d</td>
<td>4-MeO-C₆H₄</td>
<td>a</td>
<td>40</td>
<td>d</td>
<td>4-MeO-C₆H₄</td>
<td>65</td>
</tr>
<tr>
<td>e</td>
<td>4-CH₃-C₆H₄</td>
<td>a</td>
<td>70</td>
<td>e</td>
<td>4-CH₃-C₆H₄</td>
<td>67</td>
</tr>
<tr>
<td>f</td>
<td>4-NO₂-C₆H₄</td>
<td>a</td>
<td>63</td>
<td>f</td>
<td>4-NO₂-C₆H₄</td>
<td>76</td>
</tr>
<tr>
<td>g</td>
<td>4-AcO-C₆H₄</td>
<td>b</td>
<td>41</td>
<td>i</td>
<td>4-HO-C₆H₄</td>
<td>45</td>
</tr>
<tr>
<td>h</td>
<td>-C≡CH</td>
<td>b</td>
<td>59</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

3.5. Synthesis of 1-aryl-4-(β-D-glucopyranosyl)-1,2,3-triazoles

Copper(I) catalyzed 1,3-dipolar cycloadditions of 2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl-ethyne (18) with aromatic azides (a, b, c) gave 1-aryl-4-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-1,2,3-triazoles 37 (Scheme 8). The benzyl groups of 37a were cleaved by catalytic hydrogenolysis (d) to yield 40a. Formation of a tetraline derivative was observed during the deprotection of 37b. The mixture of products was acylated and separated to yield 39b and 39d (f). To avoid this side reaction 39b and 39c were synthesized by a protecting group change from 37c (e) or by a cycloaddition from 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-ethyne (38) (a, b). Acetyl groups of 39b,c were removed by the Zemplén method (g) to give 40b,c.
Scheme 8: Synthesis of 1-aryl-4-(β-D-glucopyranosyl)-1,2,3-triazoles

3.6. Synthesis of 5-aryl-3-(β-D-glucopyranosyl)-1,2,4-triazoles

N-Benzyl-arenecarboxamides 43 were treated with thionyl chloride to yield the corresponding imidoyl chlorides whose reaction with tetrazole 33 (a or b) resulted in the formation of 4-benzyl-5-aryl-3-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-1,2,4-triazoles 41 (Scheme 9). The benzoyl groups were removed according to the Zemplén procedure (c), the benzyl groups were cleaved by catalytic hydrogenolysis (d, e). The removal of the protecting groups of 41a was carried out in both orders (routes „A” and „B”). Deacylation followed by benzyl cleavage (route „A”) provided higher yields, so later on this sequence was followed for the synthesis of 1,2,4-triazoles 45.
Ar

<table>
<thead>
<tr>
<th></th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>C₆H₅</td>
</tr>
<tr>
<td>b</td>
<td>4-CH₃-C₆H₄</td>
</tr>
<tr>
<td>c</td>
<td>4-(CH₃)₂C₆H₄</td>
</tr>
<tr>
<td>d</td>
<td>4-CF₃-C₆H₄</td>
</tr>
<tr>
<td>e</td>
<td>4-NO₂-C₆H₄</td>
</tr>
<tr>
<td>f</td>
<td>4-NH₂-C₆H₄</td>
</tr>
<tr>
<td>g</td>
<td>3,4,5-(CH₃O)₃C₆H₂</td>
</tr>
<tr>
<td>h</td>
<td>4-COOBn-C₆H₄</td>
</tr>
<tr>
<td>i</td>
<td>4-COOH-C₆H₄</td>
</tr>
<tr>
<td>j</td>
<td>2-Naphthyl</td>
</tr>
</tbody>
</table>

Scheme 9: Synthesis of 5-aryl-3-(β-D-glucopyranosyl)-1,2,4-triazoles

Applying the same reaction conditions, 3-phenyl-5-β-D-galactopyranosyl-1,2,4-triazole (50a) and several 3-aryl-5-β-D-xylopyranosyl-1,2,4-triazoles 51 were prepared from the corresponding tetrazoles 34 and 35 (Scheme 10).

3.7. Synthesis of 2-(β-D-glucopyranosyl)-5-(1-substituted-1,2,3-triazol-4-yl)-1,3,4-oxadiazoles

In the copper(I) catalysed cycloaddition of aromatic azides and ethynyl-oxadiazole 36h, (1,2,3-triazol-4-yl)-1,3,4-oxadiazoles (52) were prepared (Scheme 11). Azides were prepared and isolated previously (a) or generated from boronic acids (b) and used in the cycloaddition without isolation. These two methods were similarly efficient for the synthesis of 52a. Removal of the ester protecting groups by the Zemplén procedure gave 53.
Scheme 10: Synthesis of 3-aryl-5-β-D-galacto- and -xylopyranosyl-1,2,4-triazoles

\[
\text{Starting material} \quad \begin{array}{c|c|c|c}
\text{Yields (\%)} \\
\hline
\text{Gly} & \text{Ar} & \text{46} & \text{48} & \text{50} \\
\hline
34 & R = \text{Ac} & \text{C}_6\text{H}_5 & \text{Ac} & 65 & 78 & 81 \\
\end{array}
\]

| \text{35} | R = \text{Bz} | \begin{array}{c|c|c|c}
\text{Yields (\%)} \\
\hline
\text{Gly} & \text{Ar} & \text{47} & \text{49} & \text{51} \\
\hline
a & \text{C}_6\text{H}_5 & \text{Bz} & 68 & 91 & 91 \\
e & 4-(\text{CH}_2)_3\text{C}-\text{C}_6\text{H}_4 & \text{Bz} & 42 & 63 & 77 \\
f & 4-\text{NO}_2\text{-C}_6\text{H}_4 & \text{Bz} & 52 & 68 & - \\
j & 2-\text{Naphthyl} & \text{Bz} & - & - & 79 (\text{from 48e}) \\
\end{array}
\]

Scheme 11: Synthesis of 2-(β-D-glucopyranosyl)-5-[1-(substituted)-1,2,3-triazol-4-yl]-1,3,4-oxadiazoles

<table>
<thead>
<tr>
<th>\text{Products (52)}</th>
<th>R</th>
<th>R'</th>
<th>\text{Method}</th>
<th>\text{Yields (%)}</th>
<th>\text{Products (53)}</th>
<th>R</th>
<th>R'</th>
<th>\text{Yields (%)}</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Bz</td>
<td>Ph</td>
<td>\text{a}</td>
<td>73</td>
<td>a</td>
<td>H</td>
<td>Ph</td>
<td>85</td>
</tr>
<tr>
<td>b</td>
<td>Bz</td>
<td>1-Naphthyl</td>
<td>\text{a}</td>
<td>82</td>
<td>b</td>
<td>H</td>
<td>1-Naphthyl</td>
<td>91</td>
</tr>
<tr>
<td>c</td>
<td>Bz</td>
<td>2-Naphthyl</td>
<td>\text{b}</td>
<td>77</td>
<td>c</td>
<td>H</td>
<td>2-Naphthyl</td>
<td>79</td>
</tr>
<tr>
<td>d</td>
<td>Bz</td>
<td>Ac$_4$-β-D-Glc$_p$</td>
<td>\text{a}</td>
<td>91</td>
<td>e</td>
<td>H</td>
<td>β-D-Glc$_p$</td>
<td>93</td>
</tr>
</tbody>
</table>
3.8. Synthesis of 2-aryl-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazoles

Reaction of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-azide (54) and 2-aryl-5-ethynyl-1,3,4-oxadiazoles in the presence of CuSO₄ and L-ascorbic acid yielded (1,2,3-triazol-4-yl)-1,3,4-oxadiazoles 55 (Scheme 12). Acetyl groups of 55 were removed to give unprotected 56.

![Reaction diagram]

<table>
<thead>
<tr>
<th>Products (55)</th>
<th>R</th>
<th>R'</th>
<th>Yields (%)</th>
<th>Products (56)</th>
<th>R</th>
<th>R'</th>
<th>Yields (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Ac</td>
<td>Ph</td>
<td>87</td>
<td>a</td>
<td>H</td>
<td>Ph</td>
<td>99</td>
</tr>
<tr>
<td>b</td>
<td>Ac</td>
<td>1-Naphthyl</td>
<td>77</td>
<td>b</td>
<td>H</td>
<td>1-Naphthyl</td>
<td>98</td>
</tr>
<tr>
<td>c</td>
<td>Ac</td>
<td>2-Naphthyl</td>
<td>74</td>
<td>c</td>
<td>H</td>
<td>2-Naphthyl</td>
<td>98</td>
</tr>
</tbody>
</table>

**Scheme 12:** Synthesis of 2-(aryl)-5-[1-(β-D-glucopyranosyl)-1,2,3-triazol-4-yl]-1,3,4-oxadiazoles

3.8. Synthesis of 1-phenyl-3-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-1H-pyrazol-5(4H)-one

Reaction of cyanide 30 with ethyl bromoacetate in the presence of zinc dust followed by an acidic hydrolysis furnished β-ketoester 57. Treatment of 57 with phenylhydrazine yielded pyrazolone 58 which decomposed during the benzoyl deprotection.

![Synthesis diagram]

**Scheme 13:** Synthesis of 1-phenyl-3-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-1H-pyrazol-5(4H)-one
4. Structure-activity relationships

The synthesized derivatives were evaluated as inhibitors of rabbit muscle glycogen phosphorylase b (RMGPb) at the Department of Medical Chemistry of the University of Debrecen.

Table 2: Comparison of the inhibition by the synthesized compounds and known inhibitors (RMGPb, \(K_i\) [\(\mu\text{M}\)])

<table>
<thead>
<tr>
<th>Linker</th>
<th>Ph</th>
<th>2-Naphthyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>81</td>
<td>1c 4</td>
</tr>
<tr>
<td>14a</td>
<td>IC(_{50}) = 700 (\mu\text{M})</td>
<td>14b no inh. at 625 (\mu\text{M})</td>
</tr>
<tr>
<td>17a</td>
<td>no inh. at 625 (\mu\text{M})</td>
<td>17b no inh. at 625 (\mu\text{M})</td>
</tr>
<tr>
<td>25</td>
<td>400 (\mu\text{M})</td>
<td>- -</td>
</tr>
<tr>
<td>27</td>
<td>no inh. at 650 (\mu\text{M})</td>
<td>- -</td>
</tr>
<tr>
<td>5b</td>
<td>64</td>
<td>5c 2,4</td>
</tr>
<tr>
<td>4b</td>
<td>10 % at 625 (\mu\text{M})</td>
<td>4c 10 % at 625 (\mu\text{M})</td>
</tr>
<tr>
<td>3b</td>
<td>151</td>
<td>3c 16</td>
</tr>
<tr>
<td>40b</td>
<td>no inh. at 625 (\mu\text{M})</td>
<td>40c no inh. at 625 (\mu\text{M})</td>
</tr>
<tr>
<td>45a</td>
<td>7</td>
<td>45j 0.41</td>
</tr>
</tbody>
</table>

\(^2\) The cells showing the new compounds are highlighted in grey.
The 2,3-disubstituted pyrroles 17a,b were inactive. This was probably the result of the substitution pattern of the heterocycle which caused unsuitable orientation of the aglycone at the active center. From the 2,5-disubstituted pyrroles 14a,b the phenyl derivative showed weak inhibition.

The isoxazole 27 was inactive against glycogen phosphorylase, the pyrazole 25 displayed weak binding.

Surprisingly the aryl substituted 1,3,4-oxadiazoles 4b-f,i,j did not show any meaningful inhibition. X-Ray studies of RMGPb-methyl 1,3,4-oxadiazole 4a complex indicated that the methyl group did not point to the direction of the β-channel. This orientation seems unfavourable for the bulky aryl-1,3,4-oxadiazoles, thus these compounds can’t bind to the active site.

According to the kinetic results 1-aryl-4-β-D-glucopyranosyl-1,2,3-triazoles 40 proved inactive against GP, it is surprising in the light of good inhibition effect of isomeric 4-aryl-1-β-D-glucopyranosyl-1,2,3-triazoles 3.

The 1,2,4-triazoles 45 were outstandingly efficient GP inhibitors, however their activity was highly affected by the aryl substituent. The 2-naphthyl 45j (K_i = 0.41 μM) and the 4-aminophenyl 45f (K_i = 0.67 μM) derivatives were inhibitors in the submicromolar range, but the 4-βBu-phenyl 45c and the 4-carboxyphenyl 45i derivatives proved entirely inactive.

The xylosyl-1,2,4-triazoles 51 showed no or very weak inhibition. This points to the fact that the presence of the CH_2OH group in the pyranose ring is essential, an aglycone with high affinity towards the β-channel is not enough for strong binding.

The acyl-urea analogue 2-(1,2,3-triazol-4-yl)-1,3,4-oxadiazoles 53 and 56 proved practically inefficient. The double replacement of NHCONHCO moieties by 1,3,4-oxadiazole and 1,2,3-triazole caused the complete loss of inhibition compared to the parent compounds.
5. Possible application of the results

In the course of my research potential glycogen phosphorylase inhibitors of C-glycosyl heterocyclic structure were prepared. The enzyme kinetic parameters of the synthesized compounds were determined against rabbit muscle glycogen phosphorylase \( b \). After further biological studies the most efficient inhibitors may be applicable for the treatment of type two diabetes mellitus as well as other diseases connected to disorders of glycogen metabolism (e. g. myocardial and cerebral ischemias or tumourous growth).
Documented scientific results

*Scientific articles published in peer reviewed international journals*

Papers related to the theses

   Synthesis and structure–activity relationships of C-glycosylated oxadiazoles as inhibitors of glycogen phosphorylase
   IF: 2.903 Independent citation: 15

2. Somsák L., Bokor É., Czifrák K., Kónya B., **Kun S.**, Tóth M.
   A glikogén foszforiláz glükózanalog gátlószerei, mint potenciális antidiabetikumok (Glucose analogue inhibitors of glycogen phosphorylase as potential antidiabetic agents)
   IF: - Independent citation: 1

   Synthesis of variously coupled conjugates of D-glucose, 1,3,4-oxadiazole, and 1,2,3-triazole for inhibition of glycogen phosphorylase
   IF: 2.044 Independent citation: 3

   Glikogén foszforiláz inhibitorok
   *PCT/HU 2012/000116 international patent application.*

New synthesis of 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles, nanomolar inhibitors of glycogen phosphorylase


**Other publications**

1. **M. Tóth, S. Kun, L. Somsák, D. Goyard**

Preparation of exo-Glycals from 2,6-Anhydro-aldose-tosylhydrazones


**Conference participations**

Oral presentations

1. **É. Bokor, S. Kun, L. Somsák**

Heterocyclic derivatives of D-glucose for glycogen phosphorylase inhibition


Nitrogen-heterocyclic derivatives of D-glucose as inhibitors of glycogen phosphorylase

3. É. Bokor, S. Kun, M. Tóth, L. Czecze, L. Somsák
New heterocyclic derivatives of D-glucose as inhibitors of glycogen phosphorylase
*MTA Szénhidrátkémiai Munkabizottsága éves előadóülése, Mátrafüred, 2008. május 29.-30.*

C- And N-glucopyranosyl heterocycles as inhibitors of glycogen phosphorylase

5. S. Kun, É. Bokor, M. Tóth, L. Somsák
Further steps towards a general synthesis of C-glycosyl-1,2,4-triazoles
*MTA Szénhidrátkémiai Munkabizottsága éves előadóülése, Mátrafüred, 2009. május 28.-29.*

New C-β-D-glucopyranosyl heterocycles for glycogen phosphorylase inhibition

Heterociklusos glükózszármazékok, mint potenciális antidiabetikumok

8. S. Kun, É. Bokor, L. Somsák
C-Glycosyl azole derivatives for glycogen phosphorylase inhibition
*MTA Szénhidrátkémiai Munkabizottsága éves előadóülése, Mátrafüred, 2010. május. 27.-28.*

*N- és C-glükopiranozil heterociklusok, mint potenciális glikogén foszforiláz inhibítorok*


Synthesis of 3-glucopyranosyl-5-substituted-1,2,4-triazoles and their evaluation as glycogen phosphorylase inhibitors


3-(β-D-Glükopiranozil)-5-szubsztituált-1,2,4-triazolok, a glikogén foszforiláz enzim új nanomólos inhibítorai

Posters

12. Bokor É., Kun S., Tóth M., Czecze L., Somsák L.
   2-(β-D-Glúkopiranosil)-1,3,4-oxadiazol származékok, mint glikogén foszforiláz
   inhibítorok előállítása

13. S. Kun, L. Somsák
   Synthesis of C-glucosyl pyrroles for inhibition of glycogen phosphorylase

   Synthesis and evaluation of 2-β-D-glucopyranosyl-4- and -5-aryl pyrroles for
   inhibition of glycogen phosphorylase
   4th German-Hungarian Workshop, Synthesis, Isolation and Biological Activity of
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