

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

**Study of the transformations of *exo*-glycal derivatives:
thiol-ene addition and cycloaddition reactions**

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1. Introduction and objectives

Based on the research in recent decades the function of carbohydrates has been re-evaluated. In addition to their primary functions – to serve as energy sources and as essential structural components in organisms – they play a key role in many physiological and pathological processes, because their conjugates are found in almost all living cells and cell surfaces. Nowadays one of the most important aims of glycobiological research is to map the relationships between the structure and function of carbohydrates. The compounds required for these investigations are predominantly obtained by chemical synthesis, since the glycans are often present in natural sources only in low concentrations and in microheterogeneous form. In addition, their isolation is difficult because of the low stability of glycosidic bonds against chemical and enzymatic hydrolysis. One of the most important goal of synthetic carbohydrate chemistry is the synthesis of such compounds which mimic the structure and biological function of natural derivatives, these are called glycomimetics. The structural modifications are sometimes associated with more favorable metabolic and pharmacological properties, so these compounds can also be used as lead structures in drug design.

Based on this background our aim was the development of selective synthesis methods for new types of carbohydrate mimetics with such favorable properties, starting from *exo*-glycal derivatives possessing reactive double bonds.

The high β -selectivity of the photoinitiated thiol addition reactions of *exo*-glycal derivatives prompted us to investigate this type of transformations of 2-deoxy-*exo*-glycal and *exo*-mannal derivatives, since it was assumed, that this transformation may allow the formation of the corresponding glycosylmethyl sulfides with β configurations whose syntheses are otherwise very challenging tasks.

Furthermore, we also planned to study the [2+2]-cycloaddition reactions of acyl-protected *exo*-glycal derivatives with dichloroketene and chlorosulfonyl isocyanate, which may result in synthetically valuable spirocyclic compounds.

2. Methods

During our 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 by crystallization. New compounds were characterized by their physical property (optical rotation) and their structures were elucidated by 1D- and 2D-, ^1H - and ^{13}C -NMR methods as well as mass spectrometry and IR spectroscopy.

3. New results of the dissertation

3.1. Synthesis of 2-deoxy-*exo*-glycals

Several 2-deoxy-*exo*-glycals **175a-d** were synthesized from per-*O*-acylated 2-deoxy-glycopyranosyl acetates **172a-d**, which were obtained by the addition of acetic acid to *endo*-glycals **171a-d**, via glycopyranosyl cyanides **173a-d** and the corresponding anhydro-aldose tosylhydrazones **174a-d**, according to procedures elaborated in our laboratory (Table 1).

Table 1 Synthesis of 2-deoxy-*exo*-glycals and its precursors

$ \begin{array}{ccccc} \text{(RO)}_n \text{ (171a-d)} & \xrightarrow[\text{dry CH}_2\text{Cl}_2]{\text{AcOH/Ac}_2\text{O, cat. 30\% HBr/AcOH}} & \text{(RO)}_n \text{ (172a-d) OAc} & \xrightarrow[\text{dry CH}_3\text{NO}_2, \text{ r.t.}]{\text{4 equiv. TMSCN, cat. BF}_3\cdot\text{OEt}_2} & \text{(RO)}_n \text{ (173a-d) CN} \\ & & & & \\ & \xrightarrow[\text{py-AcOH-H}_2\text{O/r.t.}]{\text{1.1 equiv. TsNHNH}_2, \text{ 8.4 equiv. NaH}_2\text{PO}_2, \text{ Raney-Ni}} & \text{(RO)}_n \text{ (174a-d) NNHTs} & \xrightarrow[\text{reflux}]{\text{5 equiv. K}_3\text{PO}_4, \text{ dry dioxane}} & \text{(RO)}_n \text{ (175a-d)} \end{array} $				
Configuration, protecting group	Yield (%) (conformation, anomeric/epimeric ratio)			
	172	173	174	175
a	77 ($^4\text{C}_1\text{-}\alpha$: $^4\text{C}_1\text{-}\beta$ = 8:1)	77 ($^4\text{C}_1\text{-}\alpha$: $^4\text{C}_1\text{-}\beta$ = 8:1)	84 ($^5\text{C}_2\text{-}\alpha$: $^5\text{C}_2\text{-}\beta$ = 2:1)	52 ($^5\text{C}_2$)
b	81 ($^4\text{C}_1\text{-}\alpha$: $^4\text{C}_1\text{-}\beta$ = 6:1)	82 ($^4\text{C}_1\text{-}\alpha$: $^4\text{C}_1\text{-}\beta$ = 6:1)	77 ($^5\text{C}_2\text{-}\alpha$: $^5\text{C}_2\text{-}\beta$ = 3:1)	67 ($^5\text{C}_2$)
c	-	90 ($^4\text{C}_1\text{-}\alpha$: $^1\text{C}_4\text{-}\beta$ = 1:6)	81 ($^5\text{C}_2\text{-}\alpha$: $^5\text{C}_2\text{-}\beta$ = 1:5)	76 ($^2\text{C}_5$)
d	53 ($^4\text{C}_1\text{-}\alpha$: $^4\text{C}_1\text{-}\beta$ = 3:1)	73 ($^4\text{C}_1\text{-}\alpha$: $^1\text{C}_4\text{-}\beta$ = 1:4)	73 ($^5\text{C}_2\text{-}\alpha$: $^2\text{C}_5\text{-}\beta$ = 1:4)	68 ($^2\text{C}_5$)

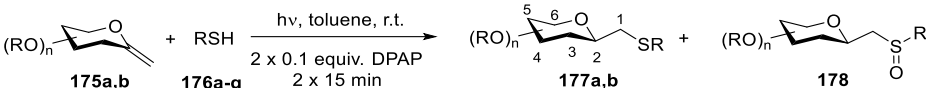
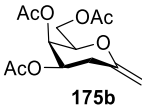
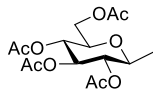
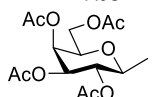
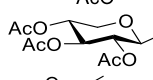
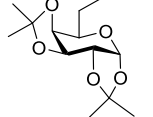
The anomeric configurations and ring conformations of the prepared compounds were determined by NMR methods.

3.2. Study of the photoinitiated thiol addition of 2-deoxy-*exo*-glycals

Thiols **176a-g** were reacted with 2-deoxy-*exo*-glycals **175a-d** in toluene by irradiation at λ_{max} 365 nm in the presence of 2,2-dimethoxy-2-phenylacetophenone (DPAP) as the photoinitiator. The transformations gave the desired 2-deoxy-glycopyranosylmethyl-sulfide type compounds **177a-d**, **179** and **180** in moderate to good yields (35 % – 92 %) with exclusive regio-, and high stereoselectivity. In the case of the 2-deoxy-*exo*-glucal **175a** and 2-deoxy-*exo*-glactal **175b** the β -anomers **177a**, **b** were isolated exclusively in 5C_2 conformations (Table 2).

Table 2 Thioladdition of *exo*-glycals **175a** and **175b**

<i>Exo</i> -glycal		R		Yield (%)	
				177	178
 175a	176a	Bn	aa	75	n.d.
	176b		ab	55	8
	176c		ac	59	7
	176d		ad	53 (65) ^a	3 (n.d) ^a
	176e		ae	49	5
	176f	CH ₃ CH ₂	af	66	n.d.
	176g	Ph	ag	69 (62) ^b	n.d.

					
 175b	176a	Bn	ba	56	n.d.
	176b		bb	42	n.d.
	176c		bc	76	n.d.
	176d		bd	70	n.d.
	176e		be	59	n.d.
	176f	CH ₃ CH ₂	bf	73	n.d.

^aThe reaction was performed under an Ar atmosphere.

^bThe reaction was performed at -78 °C.

Moderate diastereoselectivity was observed in the case of the conformationally flexible pentose derivatives. Both anomers (**177c**, **179**) with ²C₅ conformation were formed from the 2-deoxy-*exo*-arabinal **175c**, and β-⁵C₂-**177d** and α-²C₅ – **180** from **175d** 2-deoxy-*exo*-xylal (Table 3).

The formation of sulfoxides (**178**) as by-products was observed in some cases, when the reactions were performed without Ar atmosphere. We also studied the effect of the cooling (– 78 °C), but no significant changes were observed neither in the yields nor in the products' ratio.

The conformation and anomeric configuration of the products were elucidated from their ¹H-NMR spectra using the ³J_{H,H} coupling constants.

In the case of compounds **177a,b,d** the large vicinal coupling constants (~ 11 Hz) between the H-3_{ax} – H-2 and H-3_{ax} – H-4 resonances clearly showed the ⁵C₂ conformation and formally β-anomeric configuration. For compound **177c** the signals of H-3_{ax} and H-3_{eq} overlapped in CDCl₃, but in *d*₆-benzene sufficient resolution was achieved to establish the ²C₅ conformation and α-D-pseudo-anomeric configuration.

Table 3 Thioladdition of *exo*-glycals **175c** and **175d**

<i>Exo</i> -glycal	R		combined yield (%) for 177c + 179 (ratio of 177c and 179)		178
 175c	176a Bn		aa	65 (10 : 1)	n.d.
	176b		ab	67 (10 : 1)	n.d.
	176c		ac	46 (5 : 1)	4
	176d		ad	35 (10 : 1)	n.d.
	176e		ae	50 (10 : 1)	9
combined yield (%) for 177d + 180 (ratio of 177d and 180)					
 175d	176a Bn		da	70 (1 : 1)	n.d. ^a
	176d		dd	86 (1 : 0.6)	n.d. ^a
				79 (1 : 0.5) ^b	n.d. ^a
	176g Ph		dg	90 (1 : 2.5) ^b	n.d. ^a

^aThe reaction was performed under an Ar atmosphere.^bThe reaction was performed at -78 °C.

The multiplets of the minor components **179** significantly overlapped with the signal of the main components **177c**, but we were able to verify the same ring conformation as the main product using some distinct signals. We determined the ²C₅ conformation and α-D configuration for the thiol adducts **180** based on the large vicinal coupling constants ($J = 11.5$ Hz) between H-3_{ax} – H-2 and small ones ($1 \text{ Hz} < J < 6 \text{ Hz}$) between H-3_{ax} – H-4, H-4 – H-5 and H-5 – H-6_{ax} protons (Fig. 1).

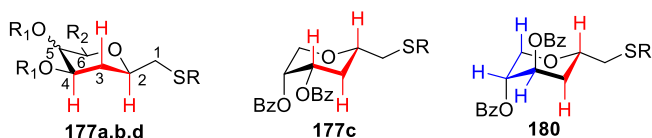


Figure 1 Structure elucidation of thioladducts

3.3. Synthesis of *exo*-mannal derivatives and examination of their thioladdition

Per-*O*-acylated *exo*-mannals **184a,b** were synthesized from the corresponding glycosyl-cyanides (Fig. 2A) according to our proven method, while the isopropylenated furanoid *exo*-mannal **17a** was prepared by a modified Julia-Kocienski reaction using the literature procedure (Fig. 2B).

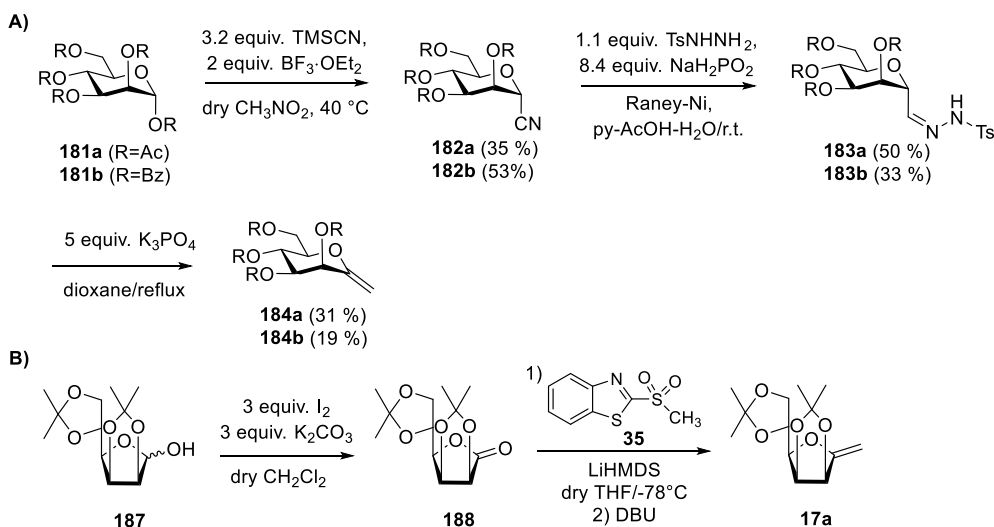


Figure 2 Synthesis of *exo*-mannal derivatives

The addition of thiols **176a-g** to the *exo*-mannal derivatives **17a**, **33b**, **184a,b** was carried out under the same conditions as described above. In the case of the addition of thiols **176a-e** to *exo*-mannals **184a,b** at room temperature the desired D-mannosylmethyl-sulfides **185** were isolated in good to excellent yields (51% – 79%) with exclusive regio- and complete stereoselectivity. When benzenethiol was used as thiol no transformation was detected at room temperature, however at – 78 °C the sulfides **185ag** and **185bg** were isolated in good yields.

Table 4 Thioladdition of *exo*-mannals **184a,b** and **33b**

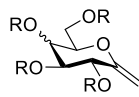
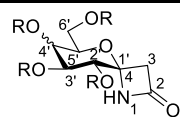
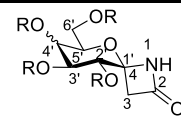
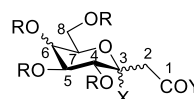
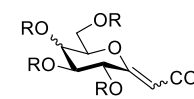
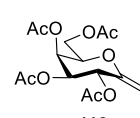
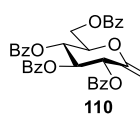
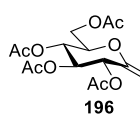
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^aThe reaction was performed at -78 °C.^bLow conversion and decomposition of glycal were observed.

The reaction of the per-*O*-benzylated *exo*-mannal **33b** with thiols **176a** and **176g** gave only low conversion and decomposition of the starting glycal were observed both at -78 °C and room temperature. If the addition of thiol **176d** to both *exo*-mannals **184a** and **184b** were performed under air, sulfoxides **186ad** and **186bd** were also isolated as minor components (Table 4).

The β-configuration of the anomeric carbon-atom could be determined by NOE measurements, based on the correlations between H-2_{ax}, H-4_{ax} and H-6_{ax}, which also confirmed the ⁵C₂ ring conformation of the products.

Table 5 Reaction of *exo*-glycals and chlorosulfonyl isocyanate

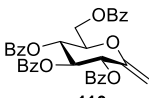
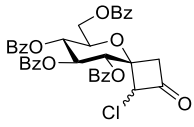
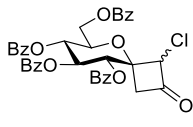
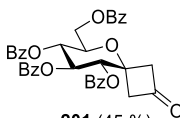
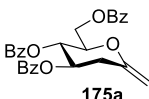
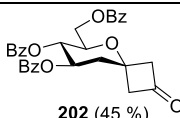
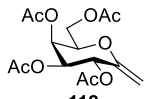
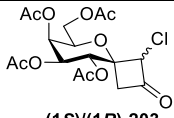
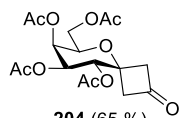
	1) 4 equiv. CSI 2 equiv. K ₂ CO ₃ dry toluene 2) 5 equiv. Lil Et ₂ O -78 °C → 0 °C	 (1'S)-190 (D-Gal, R=Ac) (1'S)-193 (D-Glc, R=Bz) (1'S)-197 (D-Gal, R=Ac)	 (1'R)-190 (D-Gal, R=Ac) (1'R)-193 (D-Glc, R=Bz) (1'R)-197 (D-Gal, R=Ac)				
112 (D-Gal, R=Ac) 110 (D-Glc, R=Bz) 196 (D-Glc, R=Ac)		 191a (D-Gal, R=Ac; X=OH, Y=NH ₂) 191b (D-Gal, R=Ac; X=NH ₂ , Y=OH) 194 (D-Glc, R=Bz; X=OH, Y=NH ₂) 198 (D-Glc, R=Ac; X=OH, Y=NH ₂)	 192 (D-Gal, R=Ac) 195 (D-Glc, R=Bz)				
<i>Exo</i> -glycal	T (°C)	Yield (%)					
		(1'S)-190	(1'R)-190	191a,b	192		
 112	0	12	n.d.	8	30		
	-20	19	n.d.	8	25		
	-40	16	4	3	17		
	-78	32	16	15	8		
 110		(1'S)-193	(1'R)-193	194	195		
	r.t.	21	n.d.	20	24		
	0	42	n.d.	n.d.	15		
	-20	20	n.d.	8	8		
	-40	14	n.d.	n.d.	13		
	-78	low conversion					
 196		(1'S)-197	(1'R)-197	198			
	-40	10	7	7			

3.4.2. Addition of dichloroketene to the *exo*-glycals

We also investigated the reaction of *exo*-glycals **110**, **112** and **175a** with dichloroketene, which was generated *in situ* from 2,2,2-trichloroacetyl chloride under reductive conditions. In the case of the *exo*-glucal **110** and *exo*-galactal **112** the monochloro spiro-cyclobutanone derivatives **199**, **200** and **203** were isolated after a second reduction step, only 2-deoxy-glycal derivative **175a** gave the desired spiro-

cyclobutanone derivative. Compounds **199**, **200** and **203** were converted to the target compounds **201** and **204** with a new portion of activated zinc powder in the presence of acetic acid (Table 6). The structure of the regioisomers **199-204** was established by HMBC measurements by the identification of the cross peak between H-2' proton and C-1 or C-3 atom of the monochloro-cyclobutanone ring. In the case of the diastereomers **199**, **200**, **203** the spatial correlation between the hydrogens in the monochloro-cyclobutanone ring and the certain hydrogen atoms in the sugar ring allowed us to determine the anomeric configuration and the absolute configuration of the C-1 atom, too.

Table 6 Reaction of *exo*-glycals and dichloroketene

$ \begin{array}{c} \text{(RO)}_n \text{---} \text{C} \equiv \text{C} \text{---} \text{O} \\ \xrightarrow[0^\circ\text{C} \rightarrow \text{r. t.}]{\begin{array}{l} 1) 4 \text{ equiv. CCl}_3\text{COCl} \\ 6 \text{ equiv. Zn(Cu)} \\ \text{dry THF} \end{array}} \\ \xrightarrow[0^\circ\text{C} \rightarrow \text{r. t.}]{2) \text{ Zn/AcOH}} \end{array} $			
$ \begin{array}{c} \text{(RO)}_n \text{---} \text{C} \equiv \text{C} \text{---} \text{O} \xrightarrow{\text{Zn/AcOH}} \text{(RO)}_n \text{---} \text{C} \equiv \text{C} \text{---} \text{O} \text{---} \text{Cyclobutanone} \\ \text{r. t.} \rightarrow 70^\circ\text{C} \end{array} $			
<i>Exo</i> -glycal	Products		
 110	 (1S)/(1R)-199 (18 %, 1S:1R=4:1)	 (1S)/(1R)-200 (35 %, 1S:1R=5:1)	 201 (45 %)
 175a	n.d.		
			 202 (45 %)
 112	 (1S)/(1R)-203 (20 %, 1S:1R=1:5)		 204 (65 %)

Baeyer-Villiger oxidation of spiro-cyclobutanone **201** to lactones (**1'S**)/(**1'R**)-**205** was also performed. The mixture of the anomeric lactones could be separated by preparative HPLC and the structures were determined by NMR measurements (Fig. 4).

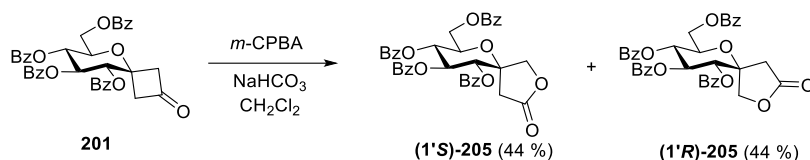


Figure 4 Baeyer-Villiger oxidation of **201** spiro-cyclobutanone

In the future, we plan to extend these cycloaddition reactions to other sugar configurations (e.g. *D-xyl**o*, *D-manno*), and we also wish to study the Beckmann-rearrangement reaction of oximes, which can be prepared from the corresponding spiro-cyclobutanones.

4. Possible application of the results

During our research, we have developed new synthetic methods for the preparation of glycomimetics possessing *C*-(2-deoxy- β -D-glycopyranosyl)methyl-, *C*- β -D-mannosylmethylsulfanyl, spirocyclic azetidin-2-one, cyclobutanone and γ -lactone moieties. The applied synthetic methods and the synthesized compounds may provide novel, alternative possibilities for the synthesis of biologically active compounds.



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Registry number: DEENK/249/2021.PL
Subject: PhD Publication List

Candidate: János József
Doctoral School: Doctoral School of Chemistry
MTMT ID: 10062013

List of publications related to the dissertation

Foreign language scientific articles in international journals (2)

1. **József, J.**, Debreczeni, N., Eszenyi, D., Borbás, A., Juhász, L., Somsák, L.: Synthesis and photoinitiated thiol-ene reactions of exo-mannals - a new route to C- β -d-mannosyl derivatives.
RSC Adv. 10 (57), 34825-34836, 2020. ISSN: 2046-2069.
DOI: <http://dx.doi.org/10.1039/D0RA07115C>
IF: 3.119 (2019)
2. **József, J.**, Juhász, L., Somsák, L.: Thio-click reaction of 2-deoxy-exo-glycals towards new glycomimetics: stereoselective synthesis of C-2-deoxy-D-glycopyranosyl compounds.
New J. Chem. 43 (15), 5670-5686, 2019. ISSN: 1144-0546.
DOI: <http://dx.doi.org/10.1039/C8NJ06138F>
IF: 3.288





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List of other publications

Foreign language scientific articles in international journals (1)

3. **József, J.**, Juhász, L., Illyés, T. Z., Csávás, M., Borbás, A., Somsák, L.: Photoinitiated hydrothiolation of pyranoid exo-glycols: the d-galacto and d-xylo cases.
Carbohydr. Res. 413, 63-69, 2015. ISSN: 0008-6215.
DOI: <http://dx.doi.org/10.1016/j.carres.2015.05.008>
IF: 1.817

Total IF of journals (all publications): 8,224

Total IF of journals (publications related to the dissertation): 6,407

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on the basis of the Journal Citation Report (Impact Factor) database.

05 May, 2021



Conference participation

Lectures and posters in the subject of the Ph.D. thesis

Lectures:

1. L. Juhász, **J. József**, D. Eszenyi, N. Debreczeni, A. Borbás, L. Somsák; Study Of The Photoinduced Hydrothiolation Of *O*-Peracetylated *Exo*-Glycols. 18th European Carbohydrate Symposium, Moscow, Russia, August 2 -6, 2015
2. L. Juhász, **J. József**, D. Eszenyi, N. Debreczeni, A. Borbás, L. Somsák; Acetilezett *exo*-glikál származékok fotokatalitikus tiol addíciójának tanulmányozása; 2.NKK, Hajdúszoboszló, 2015. augusztus 31. – szeptember 02.
3. L. Lázár, **J. József**, M. Csávás, M. Tóth, L. Juhász, A. Borbás, L. Somsák; Synthesis Of Carbon-Sulfur-Bridged Glycomimetics By Thiol-Ene Coupling Reactions, Debrecen Colloquium on Carbohydrate – András Lipták Memorial Conference, 06 – 08 of November, 2015
4. **János József**, Ferenc Béke, László Juhász, László Somsák: Photochemical thiol-ene additions onto *O*-peracylated 2-deoxy-*exo*-glycols and *exo*-mannal. Annual meeting of the Working Committee for Carbohydrates, Nucleic Acids and Antibiotics of the Hungarian Academy of Sciences, Mátraháza, May 25–27, 2016
5. **János József**, Tünde Zita Illyés, Katalin E. Kövér, László Juhász, László Somsák: Study of [2+2] type cycloadditions of *exo*-glycal derivatives. Annual meeting of the Working Committee for Carbohydrates, Nucleic Acids and Antibiotics of the Hungarian Academy of Sciences, Mátrafüred, May 23–25, 2018
6. **János József**, Nóra Debreczeni, Dániel Eszenyi, László Juhász, Anikó Borbás, László Somsák: *Exo*-Mannal Derivatives As Substrates Of Thiol-Ene Reactions; International Workshop on Chemistry and Chemical Biology of Carbohydrates, Nucleic Acids and Antibiotics, 2019. május 22-24, Mátrafüred, Hungary
7. László Juhász, **János József**, Nóra Debreczeni, Dániel Eszenyi, Anikó Borbás, László Somsák: Synthesis and photoinitiated thiol-ene reaction of *exo*-mannal derivatives; 20th EUROCARB, 2019. június 30 – július 04., Leiden Hollandia

Posters:

8. **József János**, Fekete Attila, Juhász László, Somsák László; *O*-Peracilezett 2-dezoxi-*exo*-glikálok fotoiniciált tiol-én reakciója, Vegyészkonferencia, Hajdúszoboszló, 2017. június 19-21.
9. **József János**, Illyés Tünde Zita, E. Kövér Katalin, Juhász László, Marietta Tóth, Somsák László: *Exo*-Glikál Származékok [2+2] Típusú Cikloaddíciós Reakciói. MKE Vegyészkonferencia, 2019, július 24 – 26, Eger, Magyarország
10. **József János**, Debreczeni Nóra, Eszenyi Dániel, Juhász László, Borbás Anikó, Somsák László: *Exo*-mannál származékok szintézise és fényiniciált tioladdícióinak vizsgálata; MKE Vegyészkonferencia, 2019, július 24 – 26, Eger, Magyarország
11. László Juhász, **János József**, Tünde Zita Illyés, Katalin E. Kövér, Marietta Tóth, László Somsák: [2+2] Types cycloaddition reactions of *exo*-glycal derivatives; 20th EUROCARB, 2019. június 30 – július 04., Leiden Hollandia

12. László Juhász, **János József**, Nóra Debreczeni, Dániel Eszenyi, Anikó Borbás, László Somsák: Synthesis and photoinitiated thiol-ene reaction of *exo*-mannal derivatives. 20th EUROCARB, 2019. június 30 – július 04., Leiden Hollandia
13. **József János**, Eszenyi Dániel, Debreczeni Nóra, Juhász László, Borbás Anikó, Somsák László: Per-*O*-Acilezett *exo*-mannálok fotoiniciált tiol-én reakciója FKF Szimpózium, 2019. április 3 – 5, Debrecen

Lectures and posters in other subject:

Lectures:

1. D. Eszenyi, Z. Zsíros, N. Debreceni, L. Lázár, M. Csávas, **J. József**, F. Béke, L. Juhász, M. Tóth, L. Somsák, A. Borbás; Synthesis of C-S-linked disaccharide mimetics by thioladdition reactions. Annual meeting of the Working Committee for Carbohydrates, Nucleic Acids and Antibiotics of the Hungarian Academy of Sciences, Mátraháza, May 27–29, 2015

Posters:

2. Gergely Varga, Andrea Sztankovics, **János József**, László Juhász, Tibor Docsa, Pál Gergely, László Somsák; Synthesis and Kinetic Study of the Analogues of A Natural Glycogen Phosphorylase Inhibitor; 4th German – Hungarian Workshop – Debrecen, 2011
3. Varga Gergely, Sztankovics Andrea, **József János**, Juhász László, Docsa Tibor, Gergely Pál, Somsák László; Természetes eredetű glikogén foszforiláz gátló analogoinjainak szintézise és kinetikai vizsgálata. 1 NKK, Sopron, 2011, május 22 – 25.
4. Gergely Varga, Andrea Sztankovics, **János József**, László Juhász, Tibor Docsa, Pál Gergely, László Somsák; Synthesis and Kinetic Study of the Analogues of A Naturally Glycogen Phosphorylase Inhibitor; 17th ESOC; Crete, Greece; 10 – 15 of July, 2011.
5. Gergely Varga, Andrea Sztankovics, **János József**, László Juhász, Tibor Docsa, Pál Gergely, László Somsák; Synthesis and Kinetic Study of the Analogues of A Natural Glycogen Phosphorylase Inhibitor 4th ECCLS, Hungary, Budapest, 31 of Augustus – 03 of September (2011)