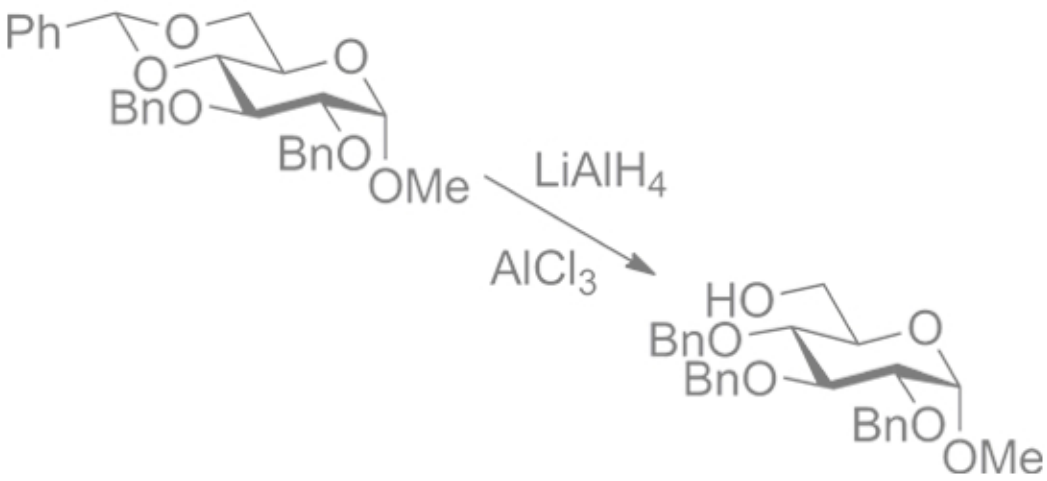
DEBCARB 2015

DEBRECEN COLLOQUIUM ON CARBOHYDRATES 2015

András Lipták Memorial Conference

Nov 6-8, 2015



University of Debrecen
Debreceni Egyetem

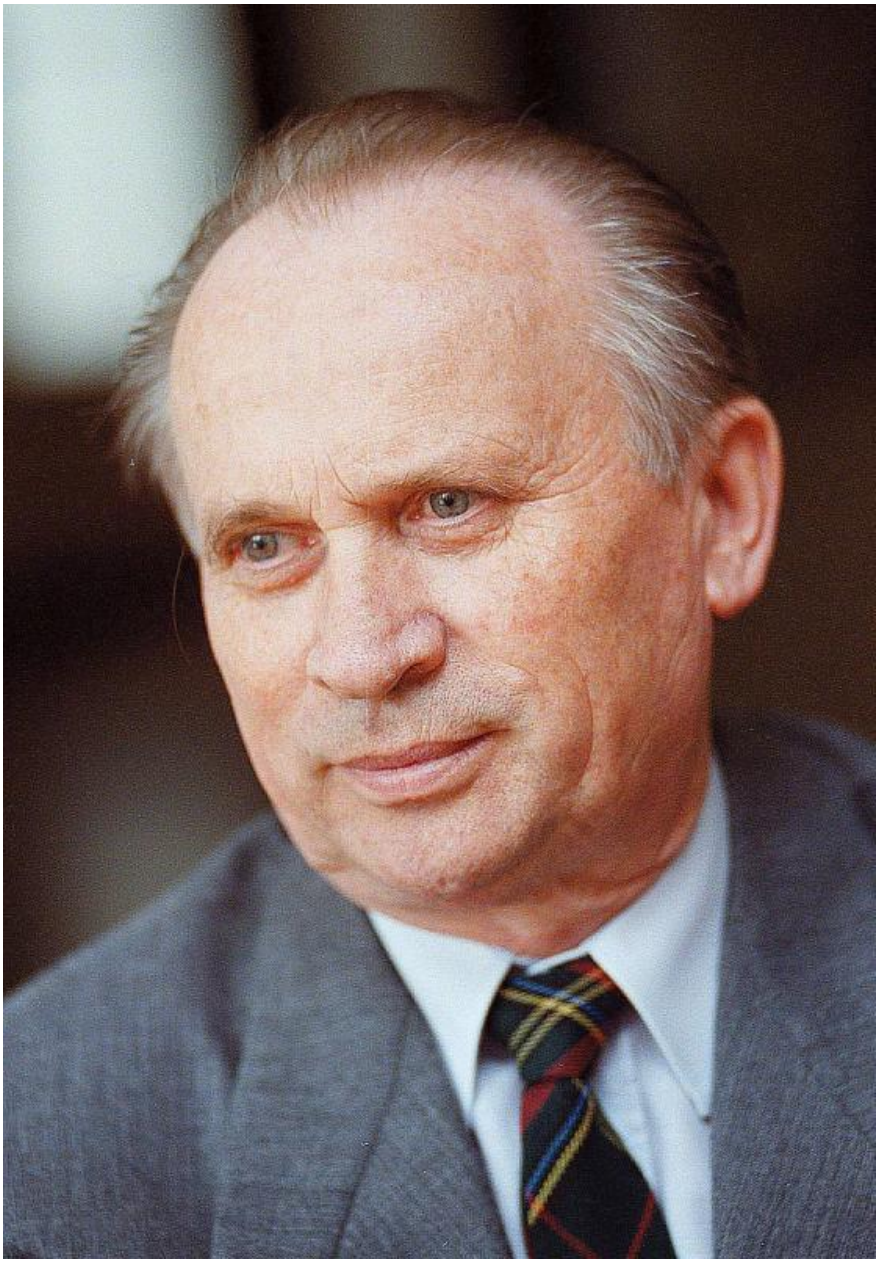
PROGRAM AND ABSTRACTS

Debrecen Colloquium on Carbohydrates 2015

András Lipták Memorial Conference

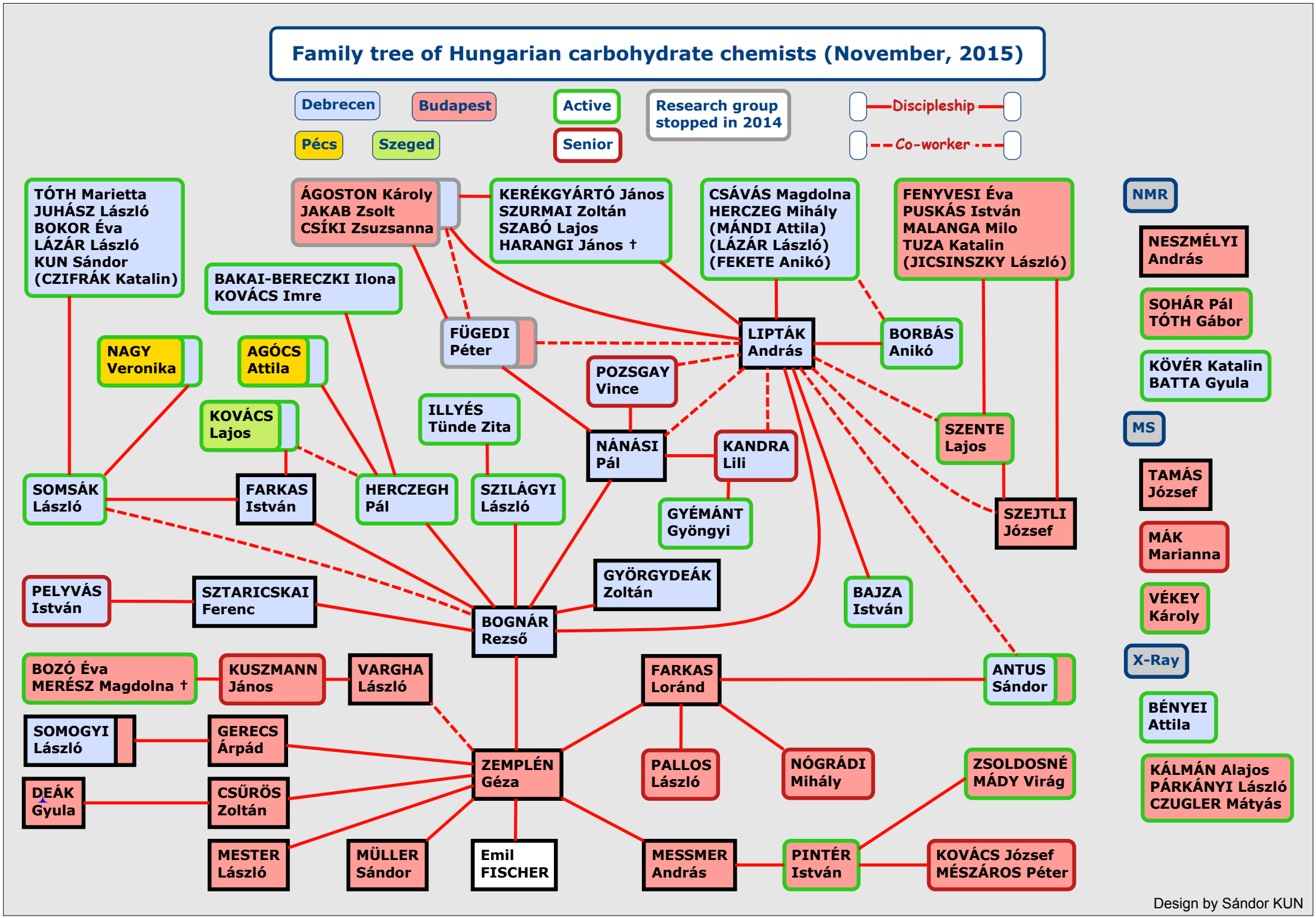
November 6-8, 2015
Debrecen, Hungary

Impressum



András Lipták
(1935-2012)

Family tree of Hungarian carbohydrate chemists (November, 2015)



Design by Sándor KUN

Dear Colleagues,

This conference has been organized to commemorate András Lipták, the well-known carbohydrate chemist, on the occasion of his 80th anniversary. Professor Lipták was an outstanding member of the Debrecen Carbohydrate School, which developed during the past more than half century. The family tree of Hungarian carbohydrate chemists, to be seen in the adjacent page, fairly illustrates his abilities to gather colleagues and youngsters around himself and to hand over his enthusiasm and curiosity as well as mentality and perseverance in cultivating carbohydrate chemistry and science in general.

Besides being an eminent scientist, Professor Lipták was rector of the University of Debrecen, headed the Department of Biochemistry for almost two decades, and served the Hungarian and international scientific communities in several different positions.

Beyond reminiscence, our meeting like any other conference also aims at making aquaintances, exchanging ideas, and visiting new places. We sincerely hope that the blend of almost 50 foreign scientists, the same number of Hungarian participants, and the atmosphere of the University and the City of Debrecen with the aid of our generous sponsors will provide all of you with an enjoyable and memorable stay in Hungary.

Anikó Borbás
conference secretary

László Somsák
conference chair

http://debcarb.unideb.hu/

EDITOR

Magdolna Csávás

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ORGANIZING COMMITTEE

Chair	László Somsák
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	Magdolna Csávás
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DISTINGUISHED SPEAKERS AND PARTICIPANTS

Ulf ELLERVIK, Lund University, Sweden

Jacquelyn GERVAY-HAGUE, University of California at Davis, USA

Narayanaswamy JAYARAMAN, Indian Institute of Science, Bangalore, India

Johannis P. KAMERLING, Universiteit Utrecht, The Netherlands

Paul KOSMA, Universität für Bodenkultur, Vienna, Austria

Frieder W. LICHTENTHALER, Technische Universität Darmstadt, Germany

Thisbe K. LINDHORST, Christiana Albertina University of Kiel, Germany

José Cristóbal LÓPEZ, CSIC, Instituto de Química Orgánica General, Madrid, Spain

Gijs VAN DER MAREL, Universiteit Leiden, The Netherlands

Stefan OSCARSON, University College Dublin, Ireland

Jean-Pierre PRALY, Université Claude Bernard Lyon I, France

Amélia P. RAUTER, Universidade de Lisboa, Lisbon, Portugal

Lajos SZENTE, Cyclolab, Budapest, Hungary

Joachim THIEM, Universität Hamburg, Germany

Igor TVAROŠKA, Slovak Academy of Sciences, Bratislava, Slovakia

Johannes F. G. VLIEGENTHART, Universiteit Utrecht, The Netherlands

PROGRAM

Nov 6, Friday		Nov 7, Saturday		Nov 08, Sunday	
		9:00-9:25	PL-5 Tvaroska	9:00-9:30	Commemoration to András Lipták (laying a wreath at his tomb in the municipal cemetery)
		9:25-9:50	PL-6 Ellervik		
		9:50-10:15	PL-7 Gervay-Hague	10:00-12:00	Guided tour in Debrecen's downtown (optional)
		10:15-10:40	PL-8 Lindhorst		
		10:40-11:30	Break		Departures
			Guided tour at the main campus of the University of Debrecen		
		11:30-11:55	PL-9 Rauter		
		11:55-12:20	PL-10 Lopez		
		12:20-12:45	PL-11 van der Marel		
		12:45-13:00	OL-3 Herczeg		
		13:00- 14:00	Lunch		
		14:00-14:25	PL-12 Jayaraman		
15:00-16:00	Registration	14:25-14:50	PL-13 Thiem		
		14:50-15:05	OL-4 Fenyvesi		
16:00-16:15	Opening ceremony	15:05-15:20	OL-5 McCabe		
16:15-16:35	Lipták memorial lecture M-1 Borbás	15:20-15:35	OL-6 Benkovics		
16:35-16:55	Lipták memorial lecture M-2 Lichtenthaler	15:35-16:30	Poster session		
16:55-17:20	PL-1 Szente	16:30-16:45	OL-7 Malanga		
17:20-17:45	PL-2 Kamerling	16:45-17:00	OL-8 Nagy		
17:45-18:10	Break	17:00-17:15	OL-9 Hayes		
18:10-18:35	PL-3 Oscarson	17:15-17:30	OL-10 Tuza		
18:35-19:00	PL-4 Kosma	17:30-17:45	OL-11 Lázár		
19:00-19:15	OL-1 Batta	17:45-18:00	OL-12 Jicsinszky		
19:15-19:30	OL-2 Bokor		Closing of the conference		
19:30-21:30	Welcome reception	19:00-21:00	Conference dinner		

The Lipták family offered an award to the best poster presented by a student participant of the conference. The poster prize will be handed over at the conference dinner.

PROGRAM

FRIDAY, NOVEMBER 6, 2015

LIFE SCIENCE BUILDING
LECTURE HALL F 008-009

15:00-16:00 REGISTRATION

16:00-16:15 OPENING CEREMONY

WELCOME ADDRESSES
LÁSZLÓ SOMSÁK, CHAIR OF DEBCARB 2015
SÁNDOR KÉKI, VICE DEAN OF THE FACULTY OF SCIENCE AND TECHNOLOGY
FERENC JOÓ, CHAIR OF THE CHEMISTRY SECTION, HUNGARIAN ACADEMY OF SCIENCES

SESSION 1. CHAIRMAN: **LÁSZLÓ SOMSÁK**

16:15-16:35 M-1
ANIKÓ BORBÁS: ANDRÁS LIPTÁK: A SCHOLAR AND A CIVIS DEBRECENIENSIS
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary

16:35-16:55 M-2
FRIEDER W. LICHTENTHALER: IN MEMORIAM ANDRÁS LIPTÁK (VIDEOMESSAGE)
Clemens-Schöpf-Institut für Organische Chemie, Technische Universität Darmstadt, Germany

16:55-17:20 PL-1
LAJOS SZENTE: ANDRÁS LIPTÁK AND THE CYCLODEXTRINS: (FROM A PERSPECTIVE OF AN EYEWITNESS)
CycloLab Cyclodextrin R&D Laboratory, Ltd, Budapest, Hungary

17:20-17:45 PL-2
JOHANNIS P. KAMERLING: GENERATION OF NOVEL GLUCO-PRODUCTS USING MICROBIAL TRANS-GLUCOSYLATING ENZYMES
Groningen Biomolecular Sciences and Biotechnology Institute, University of Groningen, Groningen, The Netherlands
Bijvoet Center for Biomolecular Research, Utrecht University, Utrecht, The Netherlands

17:45-18:10 BREAK

SESSION 2. CHAIRMAN: **JOHANNES F. G. VLIEGENTHART**

18:10-18:35 PL-3
STEFAN OSCARSON: THIOGLYCOSIDES AS GLYCOSYL DONORS IN OLIGOSACCHARIDE SYNTHESIS
Centre for Synthesis and Chemical Biology, University College Dublin, Ireland

18:35-19:00 PL-4
PAUL KOSMA: NEW APPROACHES TOWARDS KDO-OLIGOMERS
University of Natural Resources and Life Sciences, Vienna, Austria

19:00-19:15 OL-1
GYULA BATTA: NMR METHODS FOR DE-NOVO STRUCTURE DETERMINA-TION OF OLIGOSACCHARIDES (THOSE GOOD OLD DAYS WITH ANDRÁS)
Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary

19:15-19:30 OL-2
ÉVA BOKOR: *C*-β-D-GLYCOPYRANOSYL IMIDAZOLES AS NEW NANOMOLAR INHIBITORS OF GLYCOGEN PHOSPHORYLASE
Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary

19:30-21:30 WELCOME RECEPTION
(FOYER, LIFE SCIENCE BUILDING)

SATURDAY, NOVEMBER 7, 2015

LIFE SCIENCE BUILDING
LECTURE HALL F 003-004

SESSION 3. CHAIRMAN: JOACHIM THIEM

9:00-9:25 PL-5
IGOR TVAROŠKA: SWEET/BITTER SECRETS OF GLYCOSYLTRANSFERASES
Institute of Chemistry, Slovak Academy of Sciences, Bratislava, Slovakia

9:25-9:50 PL-6
ULF ELLERVIK: CARBOHYDRATES AS FUTURE DRUGS - DESIGN OF ATYPICAL PHARMACEUTICALS
Center for Analysis and Synthesis, Center for Chemistry and Chemical Engineering, Lund University, Lund, Sweden

9:50-10:15 PL-7
JACQUELYN GERVAY-HAGUE: SYNTHESIS AND BIOLOGICAL ACTIVITY OF GLYCOLIPIDS
Department of Chemistry, University of California at Davis, USA

10:15-10:40 PL-8
THISBE K. LINDHORST: CONTROLLING CARBOHYDRATE-SPECIFIC BACTERIAL ADHESION
Christiana Albertina University of Kiel, Kiel, Germany

10:40-11:30 GUIDED TOUR AT THE MAIN CAMPUS OF THE UNIVERSITY OF DEBRECEN

SESSION 4. CHAIRMAN: IGOR TVAROŠKA

11:30-11:55 PL-9
AMÉLIA P. RAUTER: ANTIBIOTIC GLYCOSIDES WITH A NEW MECHANISM OF ACTION - THE ROLE OF THE GLYCONE STRUCTURE
Universidade de Lisboa, Lisbon, Portugal

11:55-12:20 PL-10
JOSÉ CRISTÓBAL LÓPEZ: 1,2-ORTHOESTERS IN REGIOSELECTIVE GLYCOSYLATION STRATEGIES
Instituto de Química Orgánica General, CSIC, Madrid, Spain

12:20-12:45 PL-11
GIJSBERT A. VAN DER MAREL: A TALE OF PHOSPHATES AND SUGAR: SYNTHESIS OF FRAGMENTS OF BIOPOPLYMERS
Leiden University, Leiden Institute of Chemistry, Leiden, The Netherlands

12:45-13:00 OL-3
MIHÁLY HERCZEG: SYNTHESIS AND ANTICOAGULANT ACTIVITY OF 6-SULFONIC-ACID-CONTAINING ANALOGUES OF IDRAPARINUX
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary

13:00- 14:00 LUNCH
(RESTAURANT NAGYERDEI – UNIVERSITY CANTEEN)

SESSION 5. CHAIRMAN: **JOSÉ CRISTÓBAL LÓPEZ**

14:00-14:25 PL-12
NARAYANASWAMY JAYARAMAN: *ENDO*- AND *EXO*-CYCLIC RING EXPANSIONS OF PYRANOSIDES AND PYRANOSIDE MACROCYCLES
Department of Organic Chemistry, Indian Institute of Science
Bangalore, India

14:25-14:50 PL-13
JOACHIM THIEM: EFFICIENT ROUTES TOWARDS INDOXYL GLYCOSIDES AND APPLICATIONS
Department of Chemistry, Faculty of Science, University of Hamburg,
Hamburg, Germany

14:50-15:05 OL-4
ÉVA FENYVESI: CYCLODEXTRIN POLYMERS CROSSLINKED BY EPICHLOROHYDRIN FOR VARIOUS APPLICATIONS
CycloLab Cyclodextrin R&D Laboratory, Ltd, Budapest, Hungary

15:05-15:20 OL-5
ORLA McCABE: SYNTHESIS OF THE PELLICLE REPEATING UNITS OF *LACTOCOCCUS LACTIS* STRAINS FOR INVESTIGATION OF LACTOCOCCAL PHAGE INFECTION
Centre for Molecular Innovation and Drug Discovery, School of Chemistry, University College Dublin, Belfield, Dublin, Ireland

15:20-15:35 OL-6
GÁBOR BENKOVICS: FLUORESCENT CYCLODEXTRINS AS PHOTO-ACTIVABLE NANOPLATFORMS
CycloLab Cyclodextrin R&D Laboratory, Ltd, Budapest, Hungary

16:35 -17:30 POSTER SESSION

SESSION 6. CHAIRMAN: **JEAN-PIERRE PRALY**

16:30-16:45 OL-7
MILO MALANGA: SYNTHESIS AND CHARACTERIZATION OF CATIONIC CYCLODEXTRINS AND THEIR USE AS SKIN PENETRATION ENHANCER
CycloLab Cyclodextrin R&D Laboratory, Ltd, Budapest, Hungary

16:45-17:00 OL-8
ADRIENN NAGY: NOVEL PEPTIDOGLYCANS SYNTHESIZED FROM FURANOID SUGAR AMINO ACIDS. INTERPRETATION OF THE UNEXPECTED STABILITY OF PHOSPHINIMINO-FURANOSES
ELTE, Institute of Chemistry, Laboratory of Structural Chemistry and Biology, Budapest, Hungary

17:00-17:15 OL-9
JOSEPH M. HAYES: IN SILICO GUIDED DISCOVERY OF NOVEL β-D-GLUCO-PYRANOSE DERIVATIVES AS POTENT INHIBITORS OF GLYCOGEN PHOSPHORYLASE
School of Physical Sciences & Computing, Division of Chemistry, University of Central Lancashire, Preston, U.K.

17:15-17:30 OL-10
KATA TUZA: MODIFIED CYCLIC AND ACYCLIC DEXTRINS: SYNTHESIS AND COMPARISON OF THEIR COMPLEXATION ABILITY
CycloLab Cyclodextrin R&D Laboratory, Ltd, Budapest, Hungary

17:30-17:45 OL-11
LÁSZLÓ LÁZÁR: SYNTHESIS OF CARBON-SULFUR-BRIDGED GLYCOMIMETICS BY THIOL-ENE COUPLING REACTIONS
Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary

17:45-18:00 OL-12
LÁSZLÓ JICSINSZKY: CYCLODEXTRINS IN NON-AQUEOUS COMPLEXATION PROCESSES
Dipartimento di Scienza e Tecnologia del Farmaco, Universitá di Torino, Turin, Italy

CLOSING OF THE CONFERENCE

19:00-21:00 CONFERENCE DINNER
(3rd FLOOR, MAIN BUILDING OF THE UNIVERSITY)

SUNDAY, NOVEMBER 8, 2015

9:00-9:30 COMMEMORATION TO ANDRÁS LIPTÁK (LAYING A WREATH AT HIS TOMB IN THE MUNICIPAL CEMETERY)

10:00-12:00 GUIDED TOUR IN DEBRECEN'S DOWNTOWN (OPTIONAL)

POSTERS

(16:35-17:30 SATURDAY, NOVEMBER 7, 2015)

1. TOWARDS THE SYNTHESIS OF A LIPOPOLYSACCHARIDE BASED GLYCOCONJUGATE VACCINE AGAINST *MORAXELLA CATARRHALIS*

Taigh Anderson, Aisling Ni Cheallaigh, Heather Horan, Stefan Oscarson
University College Dublin, Dublin 4, Republic of Ireland

2. XANTHENE DYE-APPENDED CYCLODEXTRINS: NEW SYNTHETIC STRATEGIES

Mihály Bálint[a], Milo Malanga[a], Tamás Sohajda[a], Gábor Benkovics[a], Szabolcs Béni[b], András Darcsi[b]
[a] *CycloLab Ltd., Budapest, Hungary*
[b] *Department of Pharmacognosy, Semmelweis University, Budapest, Hungary*

3. SYNTHESIS OF SUGAR-CONTAINING GLYCOPEPTIDE ANTIBIOTIC DERIVATIVES POSSESSING ANTI-INFLUENZA VIRUS ACTIVITY

Ilona Bereczki,[a] Máté Kicsák,[a] Ádám Hadházi,[a] Zsolt Szűcs,[a] Bence Molnár,[a] Eszter Lőrincz,[a] Anikó Borbás,[a] Evelien Vanderlinden,[b] Lieve Naesens,[b] Pál Herczegh[a]
[a] *Department of Pharmaceutical Chemistry, University of Debrecen, Hungary*
[b] *Rega Institute for Medical Research, KU Leuven, Belgium*

4. TOWARDS THE SYNTHESIS OF FLUORINATED GALECTIN LIGANDS BASED ON β-GALACTOSIDES

M. Teresa Blazquez-Sanchez, Stefan Oscarson
Centre for Synthesis and Chemical Biology, School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin-4,Ireland

5. DRUG DEVELOPMENT PROGRAMME FOR THIOL-SACCHARIDES AS NOVEL MUCOLYTIC TREATMENT FOR CYSTIC FIBROSIS

Stefan Oscarson, Mairead Boland, Travis Coyle
Centre for Synthesis and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

6. NEW ORGANOCATALYSTS FOR STEREOSELECTIVE SYNTHESIS OF 2-DEOXYGLYCOSIDES

Gary A. Bradshaw, Avene C. Colgan, Nathan P. Allen, Mairead B. Boland and Eoghan M. McGarrigle
Centre for Synthesis and Chemical Biology, UCD School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

7. SYNTHESIS OF GLYCODENDRIMERS CONTAINING 1,2-THIOMANNOBIOSIDE AND INVESTIGATION OF THEIR INTERACTION WITH BC2L-A LECTIN FROM *BURKHOLDERIA CENOCEPACIA*

Magdolna Csávás[a], Lenka Malinovska[b], Milán Gyurkó[a], Michaela Wimmerová[b], Anikó Borbás[a]
[a]*Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary*
[b]*Central European Institute of Technology, Centre for Biomolecular Research, Masaryk University, Brno, Czech Republic*

8. SYNTHESIS OF SULFONIC ACID-CONTAINING MALTOOLIGOMERS WITH POTENTIAL ANTITUMOR AND ANTIMETASTATIC ACTIVITY

Fruzsina Demeter, Mihály Herczeg, and Anikó Borbás
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary

9. SYNTHESIS OF *C-S*-LINKED DISACCHARIDE AND NUCLEOSIDE MIMETICS BY THIOLADDITION REACTIONS

Dániel Eszenyi[a,b], Zita Zsíros[a], Diána Pinke[a], Nóra Debreczeni[a], Miklós Bege[a], Ilona Bereczki[a], Magdolna Csávás[a], Anikó Borbás[a]
[a]*Department of Pharmaceutical Chemistry, Debrecen, Hungary*
[b]*Department of Organic Chemistry, Debrecen, Hungary*

10. A CIRCULAR H-BOND NETWORK ANCHORS THE PYRANOSYL FORM OF COMMON MONOSACCHARIDE ARYLHYDRAZONES

Viktória Goldschmidt-Gőz,[a] István Pintér,[b] Virág Zsoldos-Mády,[b] Antal Csámpai,[c] András Perczel[a,b]
[a]*ELTE, Laboratory of Structural Chemistry and Biology, Budapest, Hungary*
[b]*MTA-ELTE, Protein Modeling Research Group, Budapest, Hungary*
[c]*ELTE, Institute of Chemistry, Department of Inorganic Chemistry, Budapest, Hungary*

11. INTERACTION OF HEPARIN-ANALOGUE PENTASACCHARIDES WITH ANTITHROMBIN-III: NMR AND MOLECULAR DYNAMICS STUDY

Tamás Gyöngyösi[a], István Timári[a], Mihály Herczeg[b], Anikó Borbás[b], István Komáromi[c], Katalin E. Kövér[a]
[a]*Department of Inorganic Chemistry, University of Debrecen, Debrecen, Hungary*
[b]*Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary*
[c]*Division of Clinical Laboratory Science, Department of Laboratory Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*

12. NEW TYPES OF CARBOHYDRATE-BASED *N*-CONTAINING TRICYCLES

Mihály Herczeg, Eszter Szilágyi, Anikó Borbás, Pál Herczegh
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary

13. SYNTHESIS OF SULFATED MONOSACCHARIDES AS SUBSTRATES FOR SULFOTRANSFERASE

Hao Jiang, Stefan Oscarson
Centre for Synthesis and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

14. STUDY OF THE ADDITION REACTIONS OF 1-*C*-SUBSTITUTED GLYCALS

Mária Polyák, László Juhász, László Somsák
Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary

15. 20 YEARS OF STUDIES ON HUMAN SALIVARY α-AMYLASE: AN OVERVIEW OF METHODOLOGY AND RESULTS

Gyöngyi Gyémánt, Gábor Lehoczki, Lóránt Jánossy, Lili Kandra
Department of Inorganic and Analytical Chemistry, Faculty of Sciences and Technology, University of Debrecen, Debrecen, Hungary

16. TRICYCLANOS: A NEW TYPE OF NUCLEOSIDE ANALOGUES

Máté Kicsák,[a] Szabolcs Varga,[a] Erzsébet Rőth,[a] Mihály Herczeg,[a] Gyula Batta,[b] Zoltán Kupihár,[c] Györgyi Ferenc,[d] Anikó Borbás[a] and Pál Herczegh[a]
[a]*Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary*
[b]*Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary*
[c]*Department of Medicinal Chemistry, University of Szeged, Szeged, Hungary* [d]*Institute of Plant Biology, Biological Research Centre, HAS, Szeged, Hungary*

17. PHENYLETHANOID GLYCOSIDE PATTERN IN TISSUE CULTURES OF *PLANTAGO LANCEOLATA* L. BY LC–ESI–MS^n EXPERIMENT

Attila Kiss-Szikszai,[a] Sándor Gonda,[b] Zsolt Szűcs,[b] Csaba Máté,[b] ,Gábor Vasas,[b]
[a]*University of Debrecen, Department of Organic Chemistry, Debrecen, Hungary*
[b]*University of Debrecen, Department of Botany, Division of Pharmacognosy, Debrecen, Hungary*

18. USING DFT METHODS IN COMPUTER-ASSISTED DESIGN OF SELECTIVE INHIBITORS OF HUMAN GOLGI α-MANNOSIDASE II

Adela Bobovská,[a,b] Juraj Kóňa,[a] Igor Tvaroška[a]
[a]*Institute of Chemistry, Center for Glycomics, Slovak Academy of Sciences, Bratislava, Slovakia*
[b]*Department of Physical and Theoretical Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia*

19. A NEW SERIES OF *C*-(β-D-GLUCOPYRANOSYL)-1,2,4-TRIAZOLES FOR THE INHIBITION OF GLYCOGEN PHOSPHORYLASE: VIRTUAL SCREENING, SYNTHESIS AND *IN VITRO* EVALUATION

Sándor Kun,[a] Jaida Begum,[b] Eszter Szennyes,[a] Éva Bokor,[a] László Juhász,[a] Tibor Docsa,[c] Pál Gergely,[c] Joseph M. Hayes,[b] László Somsák[a]
[a]*Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary*
[b]*Centre of Materials Science, Division of Chemistry, University of Central Lancashire, Preston, United Kingdom*
[c]*Department of Medical Chemistry, Faculty of Medicine, University of Debrecen, Debrecen, Hungary*

20. F-18 RADIOLABELLING OF CHITOSAN-BASED NANOPARTICLES AND ITS MODELLING REACTION

Ana Lima[a], Tünde Miklovicz [a], József Varga [a], János Borbély [b], Pál Mikecz [a]
[a]*Department of Nuclear Medicine, University of Debrecen, Debrecen, Hungary*
[b]*BBS NanoTech, Debrecen, Hungary.*

21. DEVELOPMENT OF NOVEL ANTIBIOTICS BASED ON SYNTHETIC GLYCOCONJUGATES

Hanyue Ma, Stefan Oscarson
Centre for Synthesis and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

22. SYNTHESIS OF SIALIC ACID AND β-GALACTOSIDE LIBRARIES: ESSENTIAL TOOLS IN STRUCTURE ACTIVITY RELATIONSHIP INVESTIGATIONS

Austin McCabe, Stefan Oscarson
Centre for Synthesis and Chemical Biology, School of Chemistry and Chemical Biology, University College Dublin, Belfeild, Dublin 4, Ireland

23. SYNTHESIS OF MULTIVALENT RHAMNOBIOSIDES FOR STUDYING THE GLYCAN BINDING ACTIVITY OF RECOMBINANT HORSESHOE CRAB PLASMA LECTIN

Erika Mező, Miháy Herczeg, Tímea Balogh, Nikolett Molnár and Anikó Borbás
Department of Pharmaceutical Chemistry, University of Debrecen, Debrecen, Hungary

24. CLICK-REACTION OF CARBOHYDRATE AZIDES WITH CAROTENOID PENTYNOATES

Miki Hanaura[a], Éva Bokor[b], Attila Agócs[a], József Deli[a], Veronika Nagy[a]
[a]*University of Pécs, Medical School, Department of Biochemistry and Medical Chemistry, Hungary*
[b]*Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary*

25. EFFECTS OF α-CYCLODEXTRINS ON CELL VIABILITY AND SYNTHESIS OF NEW DERIVATIVES

Eszter Róka[a,b], Miklós Vecsernyés[a], Caroline Felix[b], Florent Perret[b], Ildikó Bácskay[a]
[a]*University of Debrecen, Department of Pharmaceutical Technology, Debrecen, Hungary*
[b]*University of Lyon 1, ICBMS Equipe CSAp, 69622, Villeurbanne Cedex, France*

26. SYNTHETIC APPROACHES TOWARDS THE PREPARATION OF FLUORINATED LIGANDS FOR GALECTINS

Cecilia Romanò, Stefan Oscarson
Centre for Molecular Innovation and Drug Discovery, School of Chemistry, University College Dublin, Belfield, Dublin, Ireland

27. STEREOSELECTIVE SYNTHESIS OF 1-*O*-FATTY ACID SUGAR ESTERS

Sahar A. Shehata, Sameh E. Soliman, RafikW. Bassily, Ramadan I. El-Sokkary, Mina A. Nashed
Chemistry Department, Faculty of Science, Alexandria University, Ibrahimia, Alexandria Egypt

28. PREPARATION OF TRISUBSTITUTED *C*-(β-D-GLUCOPYRANOSYL)-1,2,4-TRIAZOLES

Katalin E. Szabó, András Páhi, László Somsák
Department of Organic Chemistry, University of Debrecen, H-4010, PO Box 20 Debrecen, Hungary

29. PREPARATION OF 2-(β-D-GLUCOPYRANOSYL)-PYRIMIDINES

Eszter Szennyes, Éva Bokor, László Somsák
Department of Organic Chemistry, University of Debrecen, Egyetem tér 1, H-4010, PO Box 20, Debrecen, Hungary

30. COUPLING OF ANHYDRO-ALDOSE TOSYLHYDRAZONES WITH THIOLS: A NEW ROUTE FOR THE SYNTHESIS OF *C*-(β-D-GLYCOPYRANOSYL)METHYL-SULFIDES

Marietta Tóth, Tímea Kaszás, László Somsák
Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary

31. SYNTHESIS OF AN IDRAPARINUX ANALOGUE PENTASACCHARIDE MONOSULFONIC ACID

Eszter Varga,[a] Mihály Herczeg,[a] Erika Mező,[a,b] Anikó Borbás[a]
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[b]*Department of Organic Chemistry, University of Debrecen, Debrecen, Hungary*

ABSTRACTS OF PLENARY AND ORAL LECTURES

(LISTED IN THE ORDER OF PRESENTATION)

ANDRÁS LIPTÁK: A SCHOLAR AND A CIVIS DEBRECENIENSIS

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András Lipták was born on Nov 6, 1935 in Székely, Hungary. After maturation at the Debrecen Reformed College in 1955, he studied chemistry and received his diploma from the Lajos Kossuth University of Debrecen in 1961. He completed a Ph.D. in carbohydrate chemistry with Rezső Bognár at the same university in 1966.

One of his greatest scientific contributions was the elaboration of the first, high-yielding, regioselective cleavage of benzylidene acetals of hexopyranosides by using a $LiAlH_4$-$AlCl_3$ reagent combination. In 1975 he published that treatment of 4,6-*O*-benzylidene acetals of gluco- or galactopyranosides with $LiAlH_4$ and $AlCl_3$ resulted in the regioselective clevage of the acetal ring to release the 6-OH derivatives.[1] This achievement was the first breakthrough in the orthogonal protection of carbohydrates, followed by elaboration of numerous similar methodologies. The so-called acetal cleavage strategy, that is the regioselective, reductive opening of dioxane- and dioxolane-type arylmethylene acetals of sugars to the corresponding benzyl-type ethers has been and is being used worldwide in efficient syntheses of oligosaccharides.

As an internationally renowned researcher, András Lipták served the University of Debrecen, as well as the Hungarian and international scientific communities in many different positions. He was the national representative of Hungary in the International Carbohydrate Organization (ICO) and in the International Society of Rare Sugars (ISRS) and also was an editorial board member in high-level international journals like *Carbohydrate Research* and *Journal of Carbohydrate Chemistry*. He served as vice dean of the Faculty of Science and rector of the Lajos Kossuth University, was elected member of the Hungarian Academy of Sciences (HAS). He was president of several scientific institutions e.g. the Hungarian Scientific Research Fund (OTKA) and the Debrecen Committee of HAS.

He believed, that life, especially when dedicated to scientific research, is to be enjoyed. His charming personality, optimism and enthusiasm for scientific exploration fascinated his collegues and students and others who were lucky to know him.

With this lecture, I pay a tribute to the outstanding scholar and my beloved teacher, András Lipták.

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IN MEMORIAM ANDRÁS LIPTÁK

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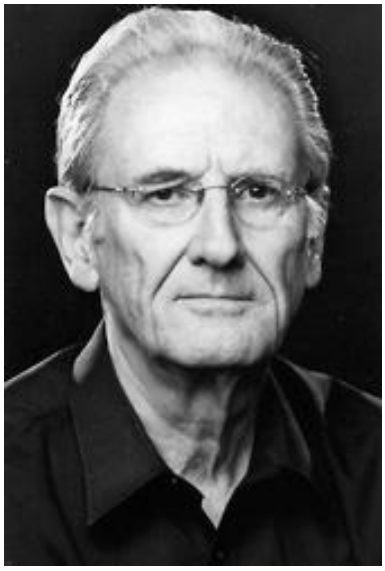

ANDRÁS LIPTÁK AND THE CYCLODEXTRINS: (FROM A PERSPECTIVE OF AN EYEWITNESS)

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The great impact of András Lipták and his group in the early discovery phase of Cyclodextrin Science and Technology will be the subject of this presentation.

Examples will illustrate the way, how the cyclodextrin man, József Szejtli and András Lipták, the carbohydrate chemist collaborated for over 25 years in the topics as follows:

- Marine polysaccharides (purification and characterization of chondroitin sulfate, chitin/ chitosan)
- Selective modifications of oligo- and polysaccharides
- Cyclodextrins: synthesis and characterisation of diverse cyclodextrin derivatives (first systematic mapping in the field)

The short overview of the route on how Lipták's team focused their research from marine polysaccharides to cyclodextrin chemistry, will undoubtedly show why we all consider Lipták's work as the most seminal one in the field of synthetic cyclodextrin chemistry.

The decades-long collaboration between Lipták and Szejtli has resulted in a number of significant publications and valuable patents. Case studies serve in this talk as illustrations of Lipták's significant achievements from the perspective of a cyclodextrin chemist.

Case No.1: Heptakis-2,6-(di-O-methyl)–beta-cyclodextrin: synthesis, purification, discovery of some unique properties of one of the most controversial cyclodextrin derivative to date. Role of this compound in making safe Daptacel™ vaccine (Sanofi Pasteur)

Case No. 2. **From cyclodextrins toward crown ether mimics**: Application of the Smith degradation to create unique macrocyclic compounds with special complexation properties.

Case No. 3. From cyclodextrin to maltooligomers: Lipták and Szejtli elaborated a patented process for gentle opening cyclodextrin ring and making malto-oligosaccharides for diagnostic purposes (as amylase substrates).

The multiyear fruitful collaboration between Lipták's team and Szejtli's team has resulted in numerous highly cited common publications and in more than 100 scientific technical reports with many so far unpublished valuable observations and unexplored technical opportunities.

The collaboration and the personal relationship between the two great scientists - besides being a touching experience for all of us - is a real example on how academic and applied research can be coupled in a mutually rewarding manner.

I feel really lucky and honoured that I had the opportunity to be mentored by both Lipták and Szejtli enabling me to be productive on the subject that has made my entire life-work.

GENERATION OF NOVEL GLUCO-PRODUCTS USING MICROBIAL TRANS-GLUCOSYLATING ENZYMES

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In the field of food and pharmacy technologies synthesis and hydrolysis of glycans with (trans-)glycosidases play important roles. Besides the focus on applications of the generated products, also enzyme crystal structures and binding modes of substrates at the enzymes get much attention. In this context, especially α-amylases and cyclodextrin glycosyltransferases have been investigated widely. Here, we will discuss the enzymatic synthesis of glucan chains using microbial α-glucosidases and β-glucosidases.

Incubation of sucrose (donor/acceptor) with the GTFA glucansucrase enzyme from *Lactobacillus reuteri* 121/35-5 yielded a high-molecular-mass branched (1→4,1→6)-α-D-glucan with prebiotic properties. Short-time sucrose incubation with GTFA gave insight into the structures of the initially formed reaction products.

When incubated with malto-type glucans, including starch, another enzyme from *Lactobacillus reuteri* 121, i.e. GTFB which turned out to be a 4,6-α-glucanotransferase, cleft terminal α1→4 linkages, and catalyzed the elongation with new α1→6 linkages in linear sequence, yielding isomalto-/malto-oligosaccharide or polysaccharide products. The modified starch derivatives have dietary fiber properties.

Incubation of (β1→3)-gluco-oligosaccharides with the Glt20 β-glucosidase from *Bradyrhizobium japonicum* yielded an array of novel multiple branched (via β1→6) gluco-oligosaccharides (DP5 → DP8 + DP11 + DP14; DP6 → DP10 + DP14 + DP18; etc.).

When incubated with sucrose as donor/acceptor substrate, the enzyme GTF180 glucansucrase from *Lactobacillus reuteri* 180 yielded a high-molecular-mass branched (1→3,1→6)-α-D-glucan with anti-corrosive properties. Incubation of the enzyme with sucrose and rebaudioside A (additional acceptor molecule; 13-[(2-*O*-β-D-Glc*p*-3-*O*-β-D-Glc*p*-β-D-Glc*p*)oxy]*ent*-kaur-16-en-19-oic acid β-D-Glc*p* ester), one of the major steviol glycoside components of the Stevia plant, yielded short C-19-α-glucosylated extensions of rebaudioside A in an α1→6/α1→3 sequential order. The major mono-(α1→6)-glucosylated rebaudioside A tasted sweeter and less bitter than rebaudioside A itself.

THIOGLYCOSIDES AS GLYCOSYL DONORS IN OLIGOSACCHARIDE SYNTHESIS

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Thioglycosides and other 1-thio sugars have for a long time been an important part of carbohydrate chemistry research.[1,2] The last 30 years have seen the development of their use as efficient glycosyl donors.[3] A review of this development will be given, with examples taken mainly from our own research, on the use of thioglycoside donors in the syntheses of human, plant, and microbe oligosaccharide structures.

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NEW APPROACHES TOWARDS KDO-OLIGOMERS

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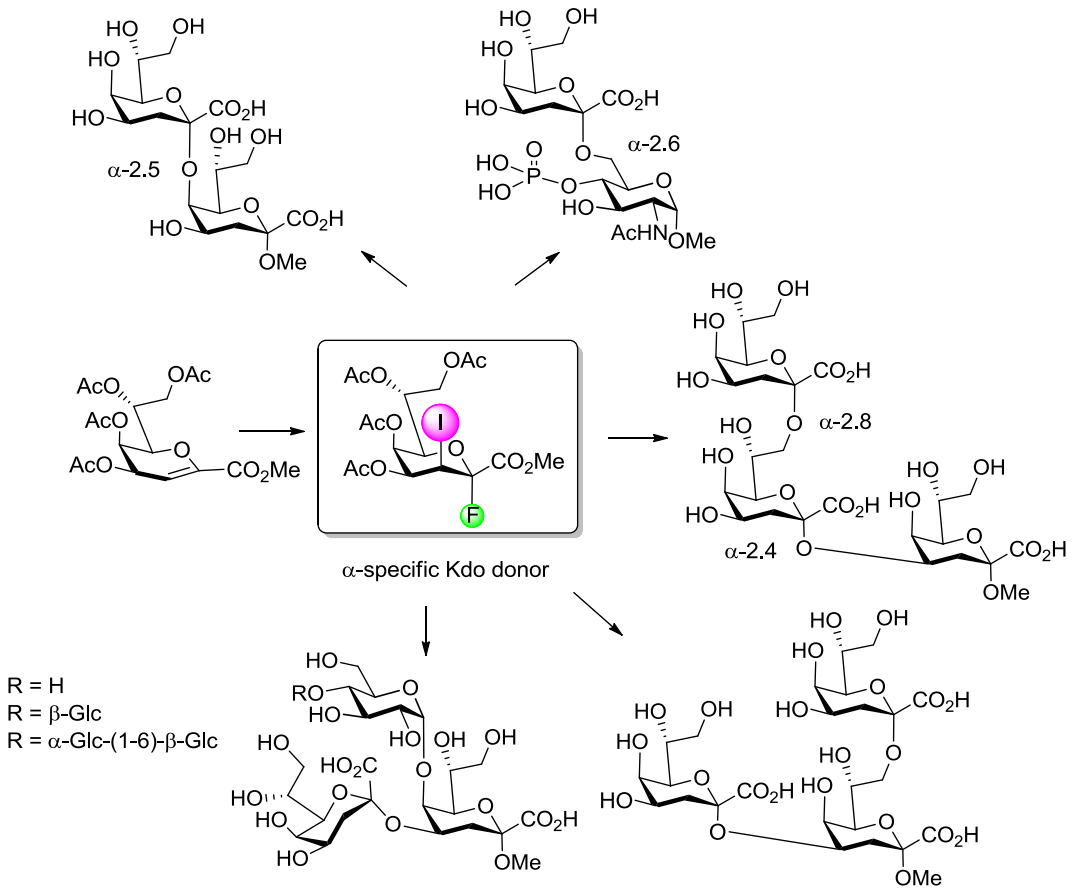
Glycosides of 3-deoxy-D-*manno*-oct-2-ulosonic acid (Kdo) represent a biomedically important group of bacterial saccharides as constituents of capsular polysaccharides and the inner-core region of lipopolysaccharides.[1] Glycosylation reactions of Kdo donors are challenging due to the absence of neighboring group participation, deactivation of the anomeric center via the adjacent carboxyl group and facile elimination reactions resulting in glycal ester formation. Recently, however, easily accessible glycal esters have been utilized as precursors of respective 3-iodo-Kdo fluoride donors with remarkable glycosylating properties.[2-4] The lecture will cover recent applications to efficiently synthesize oligomers of *Chlamydia* and *Acinetobacter* LPS fragments as ligands for binding and crystallographic studies.



Financial support by FWF (grant P 24921) is gratefully acknowledged.

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NMR METHODS FOR DE-NOVO STRUCTURE DETERMINATION OF OLIGOSACCHARIDES (THOSE GOOD OLD DAYS WITH ANDRÁS)

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Detection and determination of through-bond spin-spin couplings (J), and through-space dipolar interactions (NOE, ROE) are essential for all biomolecular structure determination. In addition, NMR relaxation is an invaluable tool to disclose molecular dynamics in between the 10^{-10} - 10 s time range. Magnetisation transfer experiments are useful to discover relatively weak carbohydrate-protein interactions. Among the myriads of NMR methods, a few early ones will be reiterated for sequencing, glycosidic bond-type / conformation determination and H-bond hunting by observing OH groups in aqueous solution.

The power of the Lipari-Szabó model-free relaxation analysis will be demonstrated on the example of trehalose, famous for it's cryoprotective and chaperoning nature.

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C-β-D-GLYCOPYRANOSYL IMIDAZOLES AS NEW NANOMOLAR INHIBITORS OF GLYCOGEN PHOSPHORYLASE

Éva Bokor,[a] Csenge Koppány,[a] Andrea Szakács,[a] Anastasia L. Kantsadi,[b] George Stravodimos,[b] Demetra S.M.Chatzileontiadou,[b] Demetres D. Leonidas,[b] Tibor Docsa,[c] Pál Gergely,[c] László Somsák[a]

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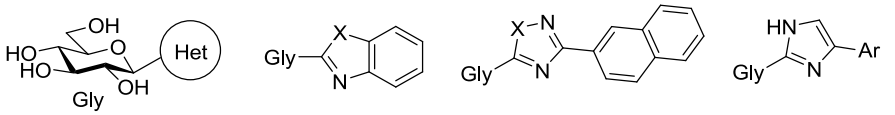
The continuing efforts to find effective glycogen phosphorylase inhibitors (GPIs) have been primarily based on the possible application of such molecules as hypoglycaemic agents for type II diabetes.[1]

Among the diverse compound types of GPIs[2] the most widely investigated group is that of glucose derivatives which bind mostly to the catalytic site of the enzyme.[3] The *C*-β-D-glucopyranosyl heterocycles (e.g. **1-4**) with low micromolar inhibitory constants belong to the most potent representatives of this inhibitor class.[3,4] The protein crystallographic analysis of the binding peculiarities of some of these compounds (**1-3**) indicated that the H-bonding capacities of the heteroaromatic rings as well as the extensive interactions of the aromatic appendage in the so-called β-channel of the enzyme were important contributors to the strong bindings.[2,5]



1 X = S K_i = 76 μM
2 X = NH K_i = 9 μM
3 X = O K_i = 2.4 μM
4 X = NH K_i = 0.4 μM
5 Target compounds

Based on these preliminaries, synthesis and study of 4(5)-aryl-substituted *C*-glycosyl imidazole derivatives were envisaged anticipating that compounds **5** possessing the beneficial structural features of **2** or **4** would also be potent inhibitors of GP. Furthermore, some alterations of the glucose moiety of this type of heterocycles were also carried out to investigate the effect of such modifications on the inhibition.

In the presentation the syntheses of the new compounds along with their enzyme kinetic and protein crystallographic evaluations will be summarized to disclose the *most potent glucose analog GPIs* to date.

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SWEET/BITTER SECRETS OF GLYCOSYLTRANSFERASES

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N- and *O*-linked oligosaccharide chains of glycoproteins play a crucial role in some biological processes. These compounds are found throughout biological systems and have been implicated in molecular recognition events such as bacterial, viral, and cell-cell adhesion, inflammation, and tumor invasion. Numerous glycosyltransferases that catalyze the addition of a specific glycosyl residue from sugar nucleotide to an acceptor substrate were validated as prime targets for therapeutic intervention in human diseases. Though transition state analogs are valued tools for drug discovery as potent and specific inhibitors of enzymes, up to date, the ability to generate transition state analogs of glycosyltransferases has lagged behind. It is obvious that design of transition state analog inhibitors of an enzyme requires knowledge of the mechanism of the enzymatic reaction and the structure of transition state. Although structural and kinetics data have provided insight into mechanistic strategies employed by these enzymes, molecular modeling studies are essential for the understanding of glycosyltransferase-catalyzed reactions at the atomistic level. For such modeling, combined quantum mechanics/molecular mechanics (QM/MM) methods have emerged as crucial. These methods allow the modeling of enzymatic reactions by using quantum mechanical methods for the calculation of the electronic structure of the active site models and treating the remaining enzyme environment by faster molecular mechanics methods. These results provided detailed insight into the mechanism of the monosaccharide transfer catalyzed by glycosyltransferases and revealed the main structural features of the transition states. In the talk, the application of QM/MM methods to glycosyltransferase-catalyzed reactions is reviewed, and the insight from modeling of glycosyl transfer into the mechanisms and transition states structures of both inverting and retaining glycosyltransferases are discussed.

Acknowledgments. This work was supported by the Slovak Research and Development Agency (Contract No. APVV-0484-12) and the project VEGA- 2/0064/15.

CARBOHYDRATES AS FUTURE DRUGS - DESIGN OF ATYPICAL PHARMACEUTICALS

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For long, carbohydrates have been neglected as lead compounds in the pharmaceutical industry. One reason is that carbohydrates have not been considered drug-like, as defined by Lipinski's rule of five. Furthermore, carbohydrates are synthetically challenging, due to several stereocenters and hydroxyl groups of similar reactivity. Unfortunately, the trend in the pharmaceutical industry is moving towards even more unpolar compounds - a tendency that will result in less selective compounds. Accordingly, we see a decrease in drugs that reach the market and the number of successful clinical trials is rapidly declining. In Sweden, new clinical studies have decreased by 50% - in the last 7 years. This trend must be reversed and carbohydrates are important lead compounds for future drugs. The role of carbohydrates in biological systems is complex and carbohydrates are vital in highly sophisticated signaling and transportation systems and are thus important drug targets. All cells are dependent on carbohydrate structures to function and they have specific transportation systems to fulfill their need for sugars. This means that drugs based on carbohydrates may be very efficient, and certainly specific, even if they are not drug - according to the Lipinski's rules. In this lecture I will discuss how carbohydrates may be used as pharmaceuticals with examples of anti-tumor drugs, and anti-viral drugs.

SYNTHESIS AND BIOLOGICAL ACTIVITY OF GLYCOLIPIDS

Jacquelyn Gervay-Hague

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Glycolipids represent a global molecular ecology shared among microbial, plant, and mammalian life. The amphiphilic properties of these molecules and their structural complexity make isolation from natural sources a tedious process that presents roadblocks to scientific discovery. Research in the Gervay-Hague laboratory is dedicated to developing efficient and sustainable methods for the synthesis of glycolipid glycans. The chemistry exploits the unique reactivity of glycosyl iodides in combination with Regioselective Silyl Exchange Technology (ReSET) providing step economical processes to prepare biologically relevant glycoconjugates.

Exquisite stereocontrol is an important feature of the synthetic platform that has led to the synthesis of bacterial derived immunostimulatory glycolipids that modulate host recognition processes. Structurally, the carbohydrate headgroup and the lipid anchor are polar opposites joined by a stereogenic acetal and remarkably the positioning of a single bond or diastereoisomer has profound biological consequences. Recent studies relating glycolipid structure to immune function will be presented.

CONTROLLING CARBOHYDRATE-SPECIFIC BACTERIAL ADHESION

Thisbe K. Lindhorst

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The first contact of cells is mediated through their glycosylated surfaces. Therefore, in order to understand the fundamental principles of cell adhesion, it is necessary to investigate details of carbohydrate recognition and binding. While many aspects of carbohydrate-protein interactions, in particular carbohydrate specificities and multivalency effects have been studied in great detail, we are just beginning to appreciate the importance of the orientation of carbohydrates projecting from a surface.

We have recently commenced a programme in which azobenzene glycosides (ABG) were chosen to serve as photosensitive probes for the photochemical control of cell adhesion.[1] We have shown that ABG can be immobilised on gold to form self-assembled monolayers (SAM),[2] and that reversible *E*/*Z* isomerisation of the azobenzene N=N double bond can be reliably effected on that surface. Furthermore, biological testing of the carbohydrate-specific adhesion of *E. coli* bacterial cells to such photosensitive glyco-SAMs has revealed that the *E*-oriented SAM is more adhesive than the respective *Z*-oriented one (Figure 1).[3] It will be shown in this account that this new principle is also relevant in the much more complex context of cell-cell adhesion.

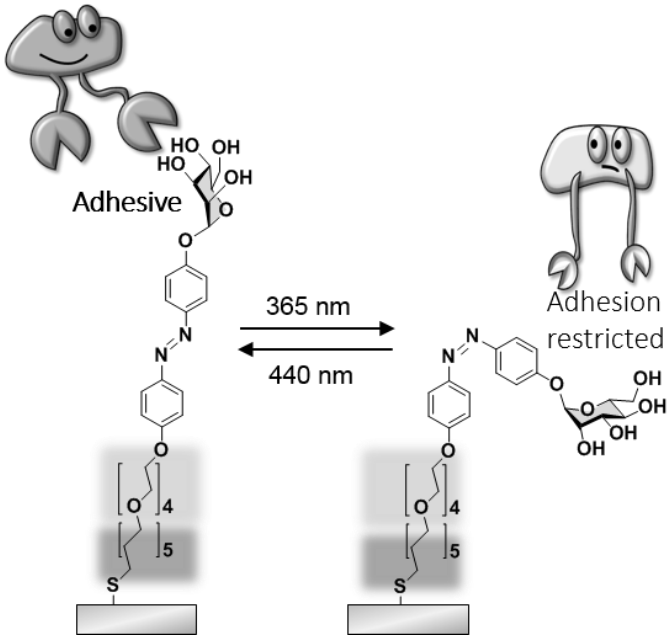

Figure 1. Photoswitchable ABG-SAM for control of bacterial adhesion

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ANTIBIOTIC GLYCOSIDES WITH A NEW MECHANISM OF ACTION - THE ROLE OF THE GLYCONE STRUCTURE

Amélia P. Rauter

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Anthrax is an acute infectious disease caused by *Bacillus anthracis*, a Gram-positive bacterium that has been used as a biological weapon since World War II. The disease also affects herbivorous mammals, it is contagious and can be transmitted through contact or consumption of infected meat. Early antibiotic treatment is essential, and the drug is taken for 60 days by people that has been exposed to anthrax. However, it is known that *B. anthracis* strains have developed resistance against the antibiotics approved for anthrax treatment. These findings justify the need for new antibiotics with a new mechanism of action.

We disclose now a family of antibiotic glycosides active against *B. anthracis*. Generation of a small library of compounds varying in glycone and aglycone structure allowed identification of the key structural features for bioactivity. Synthetic approaches for glycosides varying in glycone deoxygenation pattern, synthesis of alkyl glycosides with linear, substituted and branched chains, and of S-glycosides and analogues with the chain C-C linked to the glycosyl residue will be presented and discussed. Antimicrobial activity, cytotoxicity and surface activity data and the study of the mechanism of action demonstrate the potential of this family of compounds for the generation of new antibiotics with a new mechanism of action against anthrax.

Acknowledgements:

QREN – COMPETE program is gratefully acknowledged for the support of FACIB project (QREN – SI I&DT Co-Promotion Project nr 21547).

1,2-ORTHOESTERS IN REGIOSELECTIVE GLYCOSYLATION STRATEGIES

J. Cristóbal López,[a] Juan Ventura,[a] Clara Uriel, [a] Ana M. Gómez,[a] Bert Fraser-Reid[b]

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[b] *Natural Products Glycotechnology, Research Institute, NC 27312, Pittsboro, USA*
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n-Pentenyl 1,2-orthoesters (NPOEs) are well-established glycosyl donors, which display good regioselectivity in glycosyl couplings.[1,2] Recent studies have shown that methyl 1,2-orthoesters can also be used in regioselective glycosylation strategies.[3,4,5]

The use of both types of 1,2-orthoesters in regioselective glycosylation strategies leading to mannose oligosaccharides will be presented.

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A TALE OF PHOSPHATES AND SUGAR: SYNTHESIS OF FRAGMENTS OF BIOPOPLYMERS

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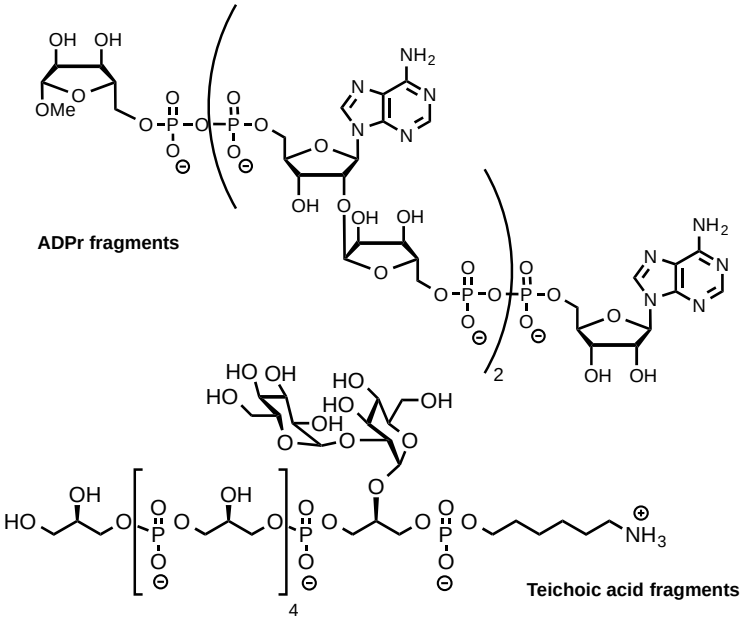
Many biological molecules contain characteristic phosphodiester and carbohydrate motifs. A major focus of our laboratory is the development of synthetic strategies and procedures to allow for the effective preparation of fragments of biopolymers containing these structural elements. To this end we have developed novel glycosylation procedures and strategies, protecting group chemistry, pyrophosphate construction methodology and innovative automated solid phase assembly techniques.

This lecture will describe some of these efforts and highlight our recent work in the area of teichoic acid synthesis to deliver suitable synthetic antigens for vaccine modalities against Gram-positive bacteria.[1] Attention will also be paid to the solid phase assembly of poly(adenosine diphosphate ribose) (poly-ADPr) oligomers, featuring synthetically challenging pyrophosphate and α-ribosyl linkages.[2]



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SYNTHESIS AND ANTICOAGULANT ACTIVITY OF 6-SULFONIC-ACID-CONTAINING ANALOGUES OF IDRAPARINUX

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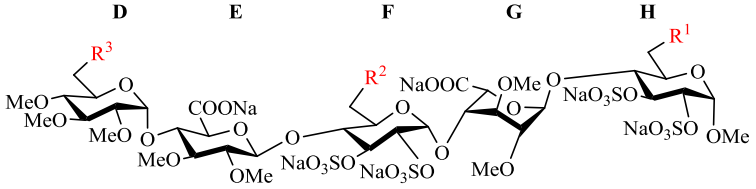
Heparin is a linear sulfated polysaccharide that plays a crucial role in maintaining the haemostatic state of blood. Heparin interacts with antithrombin, a serine protease inhibitor that blocks thrombin and factor Xa in the coagulation cascade. The active pentasaccharide fragment of heparin and many simplified analogues possessing selective factor Xa inhibitory activity were prepared, including the synthetic antithrombotic drug Arixtra. Our research group has been dealing with the synthesis of sulfonic acid analogues of the anticoagulant pentasaccharide domain of heparin. Higher stability and an increased activity of the molecules are expected by exchanging the sulfate esters to bioisosteric sulfonic acid moieties.

In the frame of this work, we have found that the pentasaccharide sulfonic acids **2** and **3** inhibited the blood coagulation factor Xa, however, in a substantially different rate depending on the number and position of the sulfonatomethyl groups[1]. To acquire further information on the effect of the sulfonic acid moieties on the antithrombotic action and to develop novel anticoagulants we decided to prepare heparinoid pentasaccharides by systematic replacement of the sulfate esters with sulfonatomethyl moiety.



1 $R^1 = R^2 = R^3 = -OSO_3Na$ (Idraparinux)
2 $R^1 = R^2 = -CH_2SO_3Na$, $R^3 = -OSO_3Na$
3 $R^1 = R^2 = R^3 = -CH_2SO_3Na$
4 $R^1 = R^3 = -CH_2SO_3Na$, $R^2 = -OSO_3Na$
5 $R^1 = -OSO_3Na$, $R^2 = R^3 = -CH_2SO_3Na$
6 $R^1 = R^2 = -OSO_3Na$, $R^3 = -CH_2SO_3Na$
7 $R^1 = -CH_2SO_3Na$, $R^2 = R^3 = -OSO_3Na$

Figure 1. Structure of the planned pentasaccharides

Here, we present efficient routes to the synthesis of the sulfonatomethyl-containing pentasaccharides **4-7** by applying orthogonal protecting group strategy, carbanion chemistry, and chemo- and stereoselective glycosylations.

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Acknowledgement: This research was supported by the Hungarian Research Found (OTKA PD 115645, K 105459) and the Mizutani Foundation for Glycoscience (150091).

ENDO- AND *EXO*-CYCLIC RING EXPANSIONS OF PYRANOSIDES AND PYRANOSIDE MACROCYCLES

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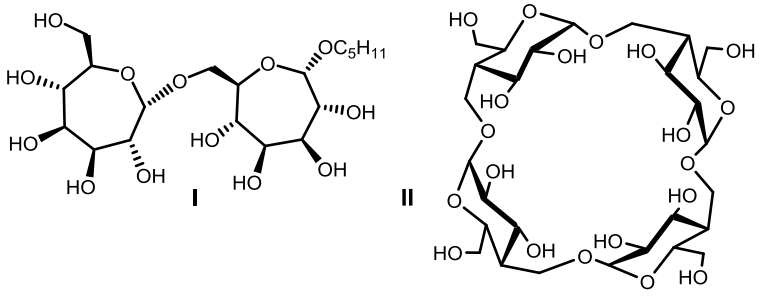
Endo- and *exo*-cyclic ring expansions herein correspond to one-carbon homologation of pyranosides and pyranosidic macrocycles. One carbon homologation within a pyranoside is facilitated under an acid or base-catalyzed condition through installation of a quarternary carbon center within the ring, in a [4.1.0] bicyclic system. Hydroxyglycal ether is a suitable synthon to install a quarternary carbon center, which in a subsequent synthetic step, leads to the bicyclic system. Ring expansion is then facilitated in the presence of a nucleophile, which could be a glycan or an aglycan. Synthetic method developed in this effort permits synthesis of a range of septanoside mono-, di- (**I)** and trisaccharides. Relative glycosidic bond stabilities of septanosides are influenced by electronic nature of neighboring groups, as seen in the case of pyranosides, under acid-catalyzed hydrolytic conditions.[1-3]

On the other hand, *exo*-cyclic one-carbon homologation pertained to the incorporation of methylene moieties in between the glycosidic bonds in the pyranosidic macrocycle, namely, cyclodextrin. 4-*C*-Hydroxymethyl pyranose acted as the monomer moiety, which upon cyclo-oligomerization, leads to glycosidic bond expanded cyclic oligosaccharides. These new types of cyclic oligosaccharides were constituted with 2, 4 and 6 pyranosidic moieties. The free hydroxyl group containing cyclic tetrasaccharide (**II**) is amphiphilic, namely, it is freely soluble in both organic solvents and aqueous solutions. Due to this property, the encapsulation properties could be evaluated under both the solution conditions.

The talk shall provide salient features of synthesis and studies of ring expanded pyranosides and pyranoside macrocyles.[4,5]



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EFFICIENT ROUTES TOWARDS INDOXYL GLYCOSIDES AND APPLICATIONS

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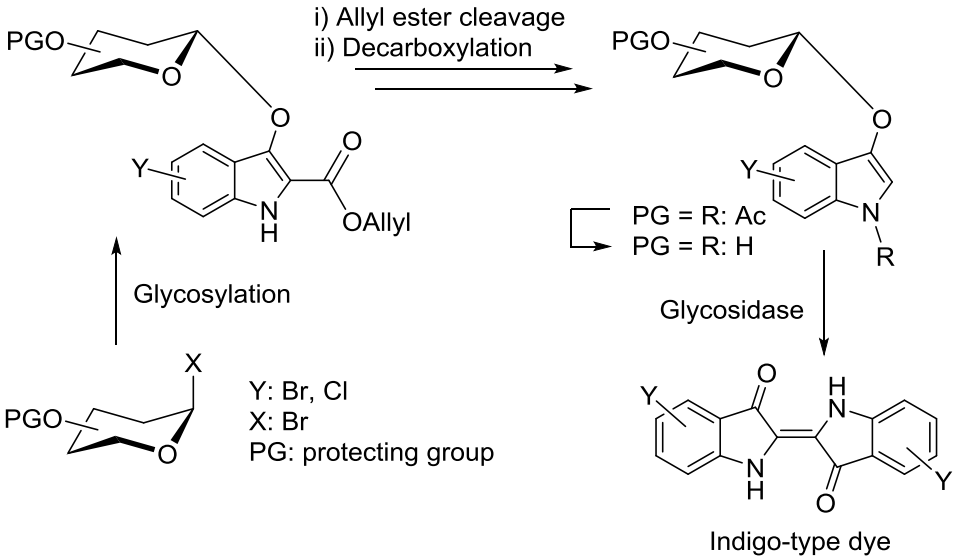
Phase transfer glycosylation with halogenated indoxylic acid allyl esters, selective allyl ester deprotection and subsequent mild silver-mediated decarboxylation enables access to a variety of the corresponding indoxyl glycosides in convincing overall yields.



This methodology could be applied for various glycosyl halides and indoxylic acid esters with the most important substitution patterns to give mono- (Glc, Gal, GlcUA, L-Fuc, Neu5Ac), di- (Lac, LacNAc, LNB), and trisaccharide (Neu5Ac-Lac) indoxylic glycosides, which are ideally suited for detection as well as monitoring of (trans)glycosidase activities.[1-5]

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CYCLODEXTRIN POLYMERS CROSSLINKED BY EPICHLOROHYDRIN FOR VARIOUS APPLICATIONS

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The benefits of inclusion complex formation can be preserved or even multiplied by coupling several cyclodextrins (CDs) together. The most often used coupling agent is epichlorohydrin. The polymers with lower degree of crosslinking are water soluble and can be used as solubilizers of drugs and food preservatives. The polymers with higher degree of polymerization are not water soluble, but because of their high swelling in water, they are proper sorbents useful in acceleration of wound healing, as chromatographic column packings and for removal of various organic contaminants from waste water.

Cyclodextrins keep their inclusion complex forming ability within the polymer structures. A synergism between the carbohydrate cavities of well defined dimensions and the interstitial cavities in the cross-linked structure can be observed.

Our group developed both soluble and insoluble polymers by using epichlorohydrin as cross-linking agent. Recently fluorescent labeling has been worked out to help tracking the drug delivery systems containing soluble cyclodextrin polymers. Several examples will be shown from scientific aspects to applications in various fields.

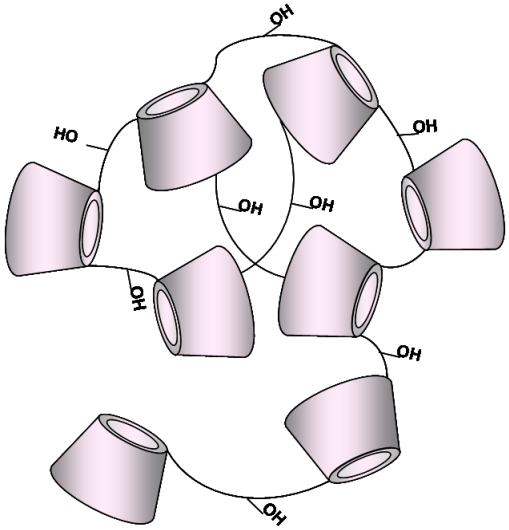

Figure 1. Scheme of cyclodextrin-epichlorohydrin copolymers

Acknowledgement

The research was supported by the following projects: EU FP5 (Biopack, Quality of life QLRT-2000-00799), EU Marie Curie Programme (CYCLON ITN-2008-237962, CYCLONHit ITN-2013-608704), National Competitiveness Programme of Hungary (Fólia, GVOP-3.0-0217-04), Hungarian Research & Development Program (CDFILTER, TECH_08-A4/2-2008-0161)

SYNTHESIS OF THE PELLICLE REPEATING UNITS OF *LACTOCOCCUS LACTIS* STRAINS FOR INVESTIGATION OF LACTOCOCCAL PHAGE INFECTION

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Lactococcus lactis, a Gram-positive bacteria, is widely used by the dairy industry due to its innate ability to produce lactic acid *via* lactose fermentation. The bacteria is encased in a strain specific polysaccharide pellicle, typically composed of hexasaccharide repeating units bridged by phosphodiester bonds.[1] These pellicles function as protective barriers against host phagocytosis, however lactococcal bacteriophages have been found to bind to these carbohydrate moieties. Infection can lead to delayed fermentation, alteration of product quality and, in severe cases, loss of product; all resulting in considerable economic loss. Understanding the recognition and binding processes involved in lactococcal bacteriophage infection is key to the prevention and control of its occurrence.

A common core trisaccharide, derived from the repeating units of *L. lactis* pellicles, was chemically synthesised. The trisaccharide was complexed with a receptor binding protein (RBP) of lactococcal phage 1358, and the crystal structure was determined by X-ray diffraction. Unprecedented structural information of the RBP/receptor site-specific binding was acquired.[2]

The chemical synthesis of a core trisaccharide, and its role in investigating the adsorption process of lactococcal phages to their host strains, will be discussed. Larger strain-specific pellicle fragments are necessary to verify this adsorption mechanism. Therefore, the block synthesis of the pellicle repeating units corresponding to *L. lactis* strains SMQ-388, MG1363 and 3107 will also be presented.

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FLUORESCENT CYCLODEXTRINS AS PHOTOACTIVABLE NANOPLATFORMS

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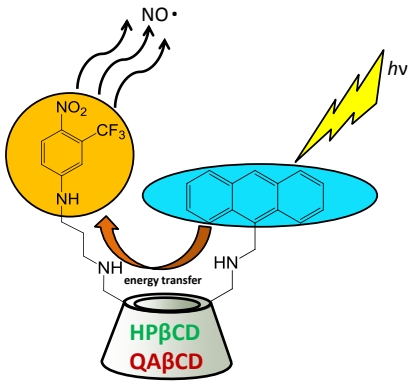
New water soluble bichromophoric and monochromophoric *β*-cyclodextrin derivatives were synthesized integrating a commercial nitroaniline derivative as a suitable nitric oxide (NO) photodonor and an anthracene moiety as a fluorescent label in their structure.The key intermediate which allowed the selective disubstitution was the 6-monodeoxy-6-monoazido-6'-monotosyl-β-cyclodextrin which was synthesized in multi-gram scale. The water solubility of the prepared derivatives was ensured by covalently appended quaternary ammonium (QA) groups to the cyclodextrin scaffold. The intermediates and the final compounds bearing two different chromophores were characterized by NMR, UV-Vis and mass spectrometry.



The prepared conjugates represent photoactivable nanoplatforms which exhibit simultaneous release of NO under visible light irradiation and allow localization in cells due to the fluorescent tagging. Furthermore the anthracene unit in the structure allows the effective delivery of the NO donor to the close proximity of the DNA and amplifies the NO release *via* effective photoinduced energy transfer mechanism[1]. Due to the high bioavailability and cell penetration ability of cyclodextrin derivatives the prepared structures are expected to be useful research tools for NO stimulated therapy and for studies of the biological roles of NO.

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Acknowledgements
The financial support of CyclonHit project (FP7-PEOPLE-ITN-2013-608407) is greatly acknowledged.

SYNTHESIS AND CHARACTERIZATION OF CATIONIC CYCLODEXTRINS AND THEIR USE AS SKIN PENETRATION ENHANCER

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Cationic cyclodextrins can act as cell penetrating systems and DNA delivery agents,[1] can be utilized as efficient drug delivery systems[2] and can be used as transdermal penetration enhancers.[3]

The versatility of these molecules is due to the simultaneous presence of a cavity for molecular complexation and a positively charged cloud that can increase the stability of the inclusion and/or facilitate the interaction with biological membrane via electrostatic forces.

In this work we report the synthesis and the characterization of a library of 6-monosubstituted, per-6-substituted cationic cyclodextrins bearing *N*-hetetocycles such as piperazine, piperidine, pyrrolidine or morpholine. The permanently charged, *N*-methylated analogues were also prepared and characterized.

The 6-monosubstituted derivatives were prepared starting from 6-monotosyl-β-cyclodextrin and 6-monotosyl-permethyl-β-cyclodextrin; the per-6-substituted derivatives were obtained starting from per-6-halogenated β-cyclodextrin and per-6-halogen-2,3-permethyl-β-cyclodextrin.

In order to evaluate and visualize their *in-vitro* skin penetration ability, the cationic derivatives were additionally modified with a fluorescent probe by reacting the *N*-heterocyclic moiety with rhodamine B or fluorescein.

The complexing capacity and the drug delivery efficiency through skin of these novel cyclodextrin derivatives were tested towards a fluorescent model compound, namely acridine orange. The extent of the interactions between the cationic compounds and acridine orange was determined by capillary electrophoresis, while the movements of the model compound through skin was visualized by two photon confocal microscopy.

All the derivatives were characterized by spectroscopic techniques (NMR, IR, UV-Vis), mass spectrometry, capillary electrophoresis and the purity was established by HPLC.

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Acknowledgements
The financial support of CyclonHit project (FP7-PEOPLE-ITN-2013-608407) is greatly acknowledged.

NOVEL PEPTIDOGLYCANS SYNTHESIZED FROM FURANOID SUGAR AMINO ACIDS. INTERPRETATION OF THE UNEXPECTED STABILITY OF PHOSPHINIMINO-FURANOSES

Adrienn Nagy, Barbara Csordás, Dóra Karancsiné M., Veronika Harmat, Virág Zsoldos-Mády, Viktor Farkas, István Pintér, András Perczel

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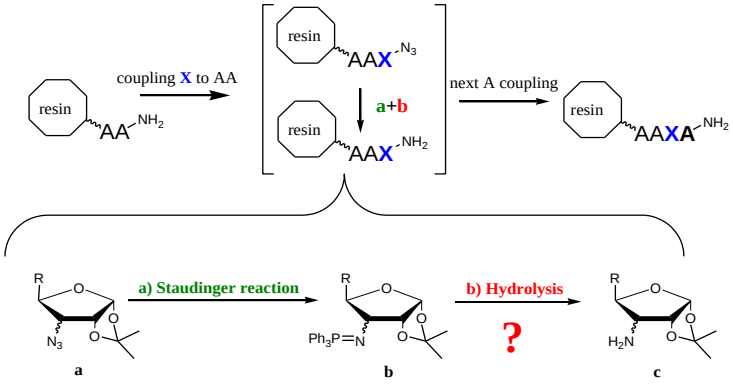
There is a growing interest and demand of non-natural, biocompatible and biodegradable polymers, such as foldamers. Various foldamers were constructed from different cyclic and/or acyclic amino acids of modified side-chains to obtain peptide- or protein-mimetics. Recently, sugar amino acids (SAA), particularly, five- or six-membered cyclic aminosugar carboxylic acids have appeared as appropriate building blocks for peptido-glycan foldamers.[1,2]

Herein we present the synthesis of new peptidoglycans containing *cis*-/*trans*-3-amino-3-deoxy-α-D-furanuronic acids as building blocks obtained by the Staudinger reaction of the corresponding 3-azido-3-deoxy-sugars. The furanoid *β*-sugar amino acids were treated and coupled on solid phase support with *N*-protected α-amino acids to deliver α/β-heterooligomers.



The unexpected stability of the *cis*-furanoid iminophosphorane intermediate was observed when Ph_3P was used. A stability unseen for the *trans* stereoisomer is attributed to the vicinity of the phosphinimino group at C^3 and substituent of C^4, respectively. Steric and electronic repulsions hindered the transformation into the targeted aminosugar derivatives. The 3D-structure of the key intermediate was fully characterized by NMR and X-ray diffraction methods, furthermore, they were corroborated by DFT calculations.

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IN SILICO GUIDED DISCOVERY OF NOVEL β-D-GLUCOPYRANOSE DERIVATIVES AS POTENT INHIBITORS OF GLYCOGEN PHOSPHORYLASE

Joseph M. Hayes,[a*] Jaida Begum,[a] Vicky T. Skamnaki,[b] Anastasia L. Kantsadi,[b] Dimitris Komiotis,[b] Demetres D. Leonidas,[b] Gergely Varga,[c] Tibor Docsa,[d] Sándor Kun,[c] Eszter Szennyes,[c] Pál Gergely,[d] Éva Bokor,[c] László Juhász,[c] László Somsák[c]

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[b] *Department of Biochemistry and Biotechnology, University of Thessaly, 26 Ploutonos Str., 41221 Larissa, Greece.*
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Regulation of the glycogen metabolism is a therapeutic strategy for blood glucose control in type 2 diabetes. Glycogen phosphorylase (GP) plays a key role in the glycogenolysis pathway, hence GP has been widely used as a target for compounds that might prevent glycogen breakdown under high glucose conditions.[1,2] GP is an allosteric enzyme with six different binding sites discovered to date. The majority of inhibitor design efforts to date have focused on the catalytic site and in particular the design of glucose analogue inhibitors.[2,3] Computation has played a key role in many of these discoveries.[4] Recent examples of *in silico* guided discovery of GP catalytic site inhibitors will be presented, where docking and post-docking methods have led to some of the most potent GP inhibitors discovered to date.[5-7]

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MODIFIED CYCLIC AND ACYCLIC DEXTRINS: SYNTHESIS AND COMPARISON OF THEIR COMPLEXATION ABILITY

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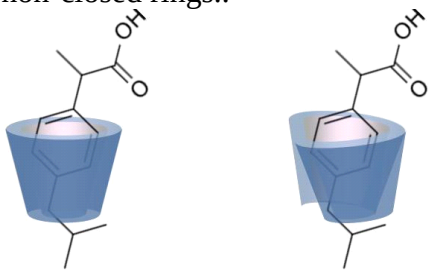
In a previous study[1] we compared the complex forming ability of native and 2-hydroxypropyl (HP)-α-, β- and γ-cyclodextrins with their open-ring analogues (acyclodextrins). A new synthetic route was developed to obtain the modified maltooligomer counterparts via subsequent bromination,[2] benzylation,[3] deacetylation[4] and debenzylation.[5]

Similarly to the HP-derivatives, a new set of modified cyclodextrins and the corresponding maltooligomers – functionalized with neutral (methyl), negatively and positively charged (sulfobutyl, carboxymethyl and quaternary ammonium) moieties – were synthesized this time in order to investigate their complexing ability.

The interactions between model guest compounds and the cyclodextrin-acyclodextrin pairs were studied with capillary electrophoresis (CE) and photon correlation spectroscopy (PCS). In CE the change in the mobility of a guest in the electric field in the presence of a host indicates molecular interaction,[6-8] while in PCS the diminished aggregation of the guest drug in the presence of the hosts indicates the interaction.[9]

In some cases cyclodextrins and their open-ring analogs show similar complexation abilities, while with other guests considerably different behavior was observed depending on the molecular dimensions and chemical characteristics of the guests. This was explained by the enhanced flexibility of the non-closed rings..



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SYNTHESIS OF CARBON-SULFUR-BRIDGED GLYCOMIMETICS BY THIOL-ENE COUPLING REACTIONS

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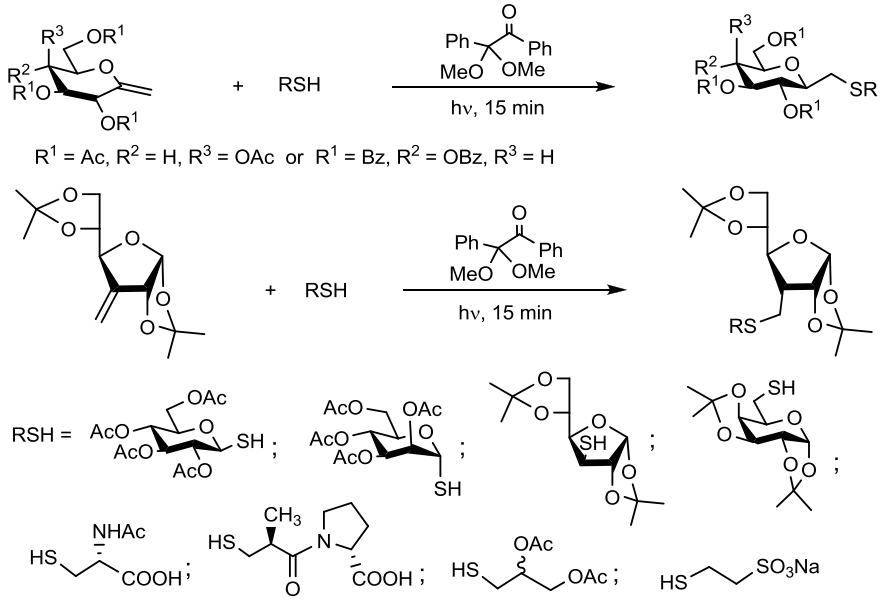
Over the last few years, photoinduced free-radical addition of thiols to alkenes, termed thiol–ene coupling or thiol–ene click reaction, has emerged in the field of carbohydrate chemistry as a robust ligation tool providing an easy access to S-linked glycoconjugates.[1] Interestingly, there are very few examples for the application of unsaturated carbohydrates bearing an exo- or endocyclic double bond within the thiol–ene coupling strategy.[2-4] Thus, the inherent potential of this mild and efficient synthetic methodology to incorporate a sugar unit into another bioactive compound through a carbon-sulfur linker has remained unexploited until now.

Here, we demonstrate the benefits of free-radical hydrothiolation of alkenyl sugars bearing an exocyclic double bond providing stable carbon-sulfur-bridged glycomimetics.



This work was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences.

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CYCLODEXTRINS IN NON-AQUEOUS COMPLEXATION PROCESSES

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For pharmaceutical purposes, aqueous cyclodextrin complexes are prepared and studied routinely. In analytical applications, particularly in capillary electrophoresis, the organic solvents play important role and the utilization of non-aqueous complexation of chiral molecules with cyclodextrins is common.

The formation cyclodextrin complexes in aqueous medium theoretically well established: the apolar guests easily displace the water molecules in the macrocycle cavity *via* complexation resulting in a thermodynamically more favorable state. The inclusion complexes and the sandwich-like molecular associations are often stabilized by hydrogen bonds. Changing the water to an organic solvent can dramatically change the driving forces of the host-guest complexation, particularly in aprotic or apolar solvents.

It is known that water and alcohols are able to form three-component complexes with peracetylated cyclodextrins. The distorted structure of peracylated cyclodextrins, as compared to the unsubstituted or partially substituted versions, usually does not allow the formation of real inclusion complexes. When an apolar ester interacts with peracetylated cyclodextrins in an apolar solvent, like chloroform, the water exclusion is not expected from the complex because of the reversed polarity profile of the persubstituted cyclodextrin. Studying the complexation of an aromatic ester with peracetylated cyclodextrins by NMR spectroscopy in deuterochloroform revealed that water plays important role in these complexations. Determination of the chemical shifts of substituents was influenced by the low water content of the deuterochloroform and/or the host molecules. The higher cyclodextrin concentration in all the cases of the studied cyclodextrins resulted in the full disappearance of the water signal. In the case of peracetyl γ-cyclodextrin completely dry sample could not be obtained by the usual methods, 1 mol of water remained and the water signal showed reversed movement, with respect to the other two CD analogs, upon increasing host concentration. The estimated 1:1 stability constants for the water:peracetyl CD complexes are in the 50-150 M^{-1} range in $CDCl_3$, but show a relatively large calculation error. The calculated 1:1 stability constants for the peracetyl CD:ester complexes are also in this range, but 1:2 and 2:1 complex compositions are also possible. These results highlight dynamic aspects of water nanoconfined in a highly hydrophobic environment, thus mimicking biological recognition where a few water molecules often play a pivotal role.

Preparation of cyclodextrin-derived maltooligosaccharides is a demonstrative example for the practical utilization of the non-aqueous complexation, which allows their synthesis even on kg-scale. Splitting of the macrocycle with an appropriate Lewis acid is an effective method for the preparation of linear maltodextrins but the product is readily fragmented in the reaction mixture and so the crude product is contaminated with shorter maltodextrins and the intact peracetyl cyclodextrin, as well. Their removal requires multiple crystallizations and chromatography. Using toluene to remove the unsplitted cyclodextrin derivatives simplifies the purification process. The water content of the otherwise very lipophilic peracetyl cyclodextrins has also crucial importance in the purification steps.

ABSTRACTS OF POSTER PRESENTATIONS

TOWARDS THE SYNTHESIS OF A LIPOPOLYSACCHARIDE BASED GLYCOCONJUGATE VACCINE AGAINST *MORAXELLA CATARRHALIS*

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Moraxella catarrhalis is a Gram-negative bacteria that causes acute otitis media in children and lower respiratory tract infections in adults.[1] It has the ability to produce β-lactamase and is therefore resistant to almost all first line β-lactam antibiotics. Currently there is no licensed vaccine to prevent *M. catarrhalis* infection.[2]

A synthetic vaccine based on the lipopolysaccharide (Figure 1) of *M. catarrhalis* is possible due to the highly conserved inner core, and could potentially induce a protective immune response to all three serotypes.[3] Synthesis of the core tetrasaccharide and subsequent strategy for glycosylation with the Kdo unit will be presented.

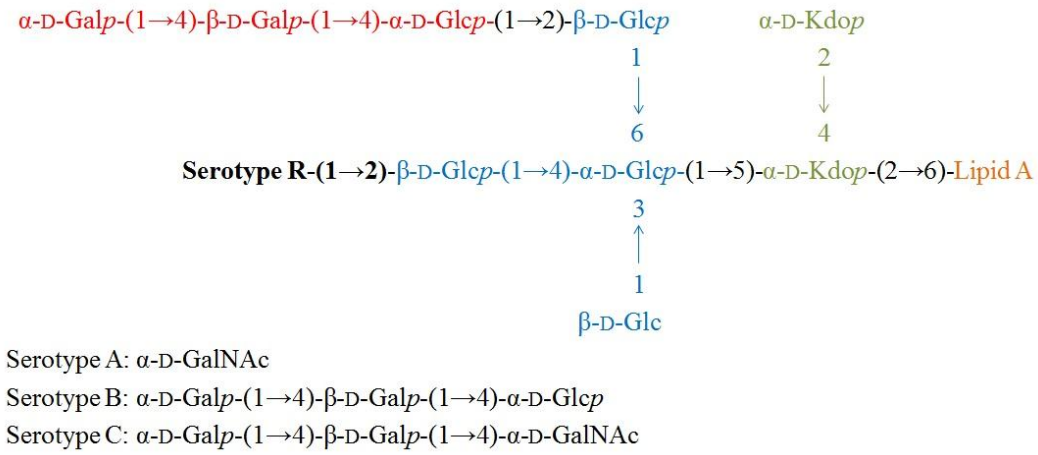

Figure 1: The lipopolysaccharide of *Moraxella catarrhalis.*

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XANTHENE DYE-APPENDED CYCLODEXTRINS: NEW SYNTHETIC STRATEGIES

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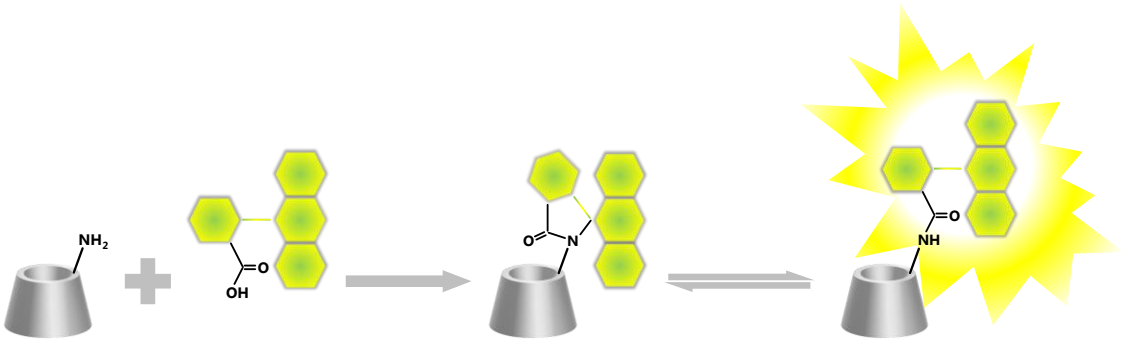
Xanthene dye-appended cyclodextrins are well known from the literature.[1,2] The fluorophore can be introduced into the cyclodextrin scaffold, for example, via a stable thioureido moiety thus rendering the molecules fluorescent in a wide range of pH[3]: this type of fluorescent conjugate can be well utilized in cases when the fluorescent reporting is continuously required regardless of the environment. There are some examples where the fluorophore is connected to the cyclodextrin rim through an ester or amide bridge allowing cyclization to form nonfluorescent lactones or lactams, making the fluorescence of the molecule possible to be switched on or off. This phenomenon can be utilized for detecting the changes of the environment, e.g. change of the pH, temperature, presence of a specific analyte.[4]

In this context we report a green approach for the synthesis of xanthene dye-appended cyclodextrins based on the coupling agent 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium (DMTMM). By using 6-monoamino-β-cyclodextrin (NH_2-BCD) as starting material, we prepared Rhodamine-, Fluorescein- and two kinds of Eosine-appended derivatives, a small library of xanthene dye-appended cyclodextrins. The compounds were fully characterized by NMR spectroscopy with a particular focus on the 2D techniques. The UV-Vis spectra of the compounds were recorded at different pH and compared with the spectra of the unfunctionalized dyes.



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SYNTHESIS OF SUGAR-CONTAINING GLYCOPEPTIDE ANTIBIOTIC DERIVATIVES POSSESSING ANTI-INFLUENZA VIRUS ACTIVITY

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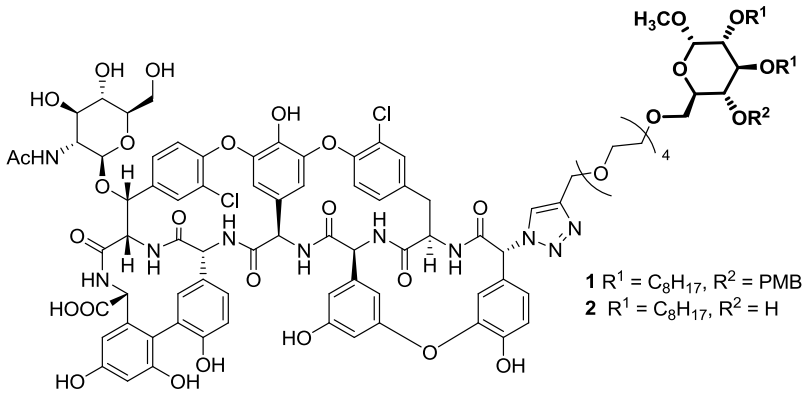
The flare-up influenza epidemics are highly pathogenic, and the seasonal epidemics also cause several deaths in high risk populations. The influenza virus has two important glycoproteins on its surface: the hemagglutinin (HA) and the neuraminidase (NA). In the virus replication process HA helps the initial attachment of the virus on the host cell and NA performs the release of the newly formed virions at the end of the viral life cycle. Currently just NA inhibitors are in use for the treatment of influenza virus infections. The increasing resistance even against these inhibitors urges the researchers to find new types of antiviral agents. At present, no hemagglutinin inhibitor is in use, although the application of these inhibitors to prevent virus entry into the host cell can be a highly attractive antiviral strategy.

Recently, we have found that a special lipophilic modification of the glycopeptide antibiotic teicoplanin resulted in derivatives **1** and **2** showing surprisingly high activity against influenza A strains.[1] These derivatives contain a sugar carrier molecule equipped with two lipophilic side chains, and the sugar molecule was connected to teicoplanin pseudoaglycone through a tetraethylene glycol chain and a triazol ring. The mode of action of **1** and **2** has not been exactly known yet, however it was shown that in the presence of **1** and **2** influenza virus-induced hemagglutination was inhibited and they hinder the attachment of the virus on the host cell's surface, in this way they hinder the HA in its function. This mode of action can be highly advantageous in the therapy of a viral infection.

On the basis of these results new derivatives were designed and prepared.



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TOWARDS THE SYNTHESIS OF FLUORINATED GALECTIN LIGANDS BASED ON B-GALACTOSIDES

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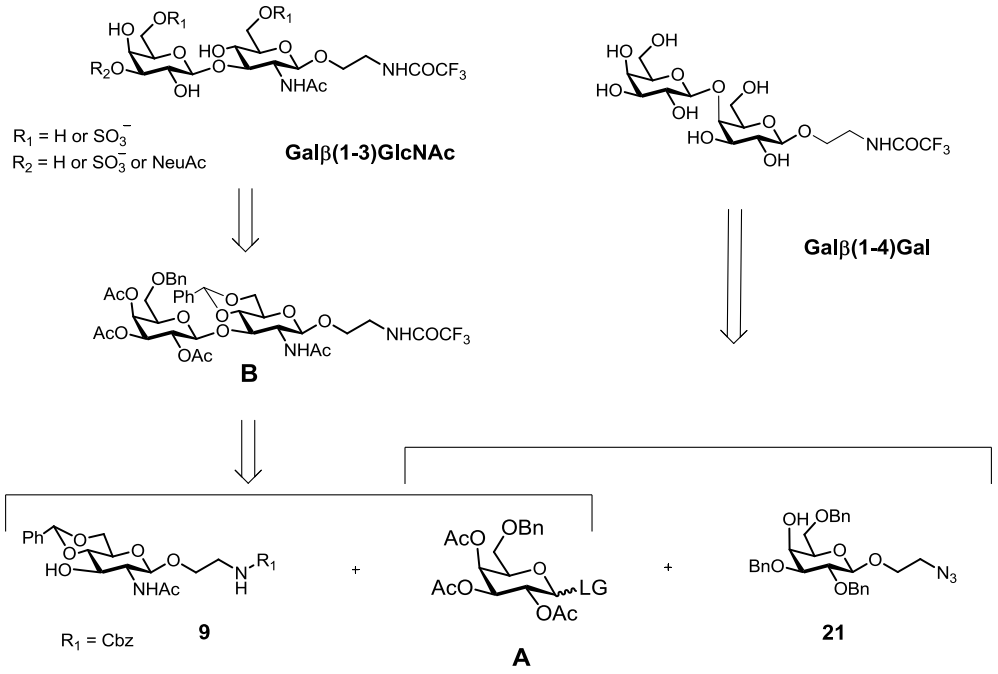
Galectins are lectins that bind β-galactoside-containing glycans and are defined by a conserved carbohydrate recognition domain and a common structural fold.[1] Several strategies on the use of fluorine-tagged molecules as a screening method for ligand binding using NMR techniques have recently been reviewed[2], so we have taken advantage of ^{19}F properties as a reporter atom for carbohydrate recognition using NMR spectroscopy.

The synthesis of the target molecules, Galβ(1-3)GlcNAc and Galβ(1-4)Gal, (see figure below), is presented in this work with the aim of getting information about their binding with certain galectins and galectin-like lectins. A linker to allow conjugation and the formation of multivalent systems has also been included in the saccharide structures.



The synthetic route that we employ make use of the same donor structure (**A**) as a common building block in order to obtain both saccharides. A common building block precursor **B** for getting LacNAc derivates has also been chosen.

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DRUG DEVELOPMENT PROGRAMME FOR THIOL-SACCHARIDES AS NOVEL MUCOLYTIC TREATMENT FOR CYSTIC FIBROSIS

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Airway obstruction can occur due to pathological mucous accumulation in patients with cystic fibrosis, asthma and chronic obstructive pulmonary disease.[1] Pathological mucous in the lungs restricts normal clearance of mucous in the airways, causing blockages. Treating pathological mucous in the lungs is not only helpful for relief from coughing and congestion but also in decreasing other measures of lung morbidity.

Previously it has been found that an oxidative process causes the formation of intermolecular disulfide cross-links between mucin molecules. This causes abnormal elastic mucous in cystic fibrosis patients. A recent collaborative effort between the Oscarson and Fahy groups has shown that thiol-modified carbohydrate compounds can act as reducing agents of pathological mucous by acting to break disulfide bonds, this work is also subject of a patent (WO 2014/153009 A2).[2]

This project aims to modify carbohydrate structures with the aim of producing a pharmacological effect in the treatment of mucous pathology, with an initial emphasis on cystic fibrosis. Analogues of these compounds are also currently being synthesised, which will be used as molecular probes. Synthesis of selected target compounds will be discussed.

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NEW ORGANOCATALYSTS FOR STEREOSELECTIVE SYNTHESIS OF 2-DEOXYGLYCOSIDES

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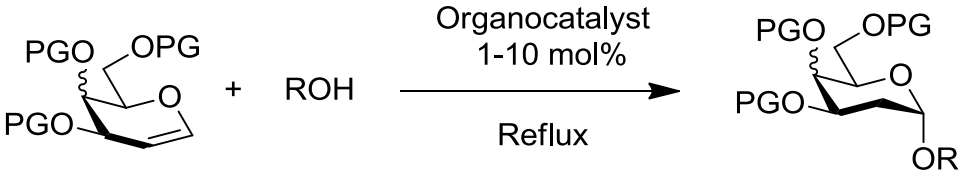
Following previous work in the McGarrigle group involving a thiourea organocatalyst for the synthesis of 2-deoxygalactosides,[1] new cheaper organocatalysts have since been discovered within our group to catalyse this process. This organocatalytic method is a simple way to form disaccharides of which one moiety is a 2-deoxymonosaccharide. The standard method uses mild conditions and very low catalyst loadings (1-10 mol%) to obtain high yields. The process is tolerant of many common protecting groups and is selective for α-glycosidic linkages. The catalytic system works with monosaccharide acceptors bearing free primary/secondary alcohols and for the first time acceptors bearing an amine functional group are tolerated. This is also the first time that D-Glucal can be used as a donor in our catalytic system.



The new organocatalysts, which will be outlined in this poster, show that the previously proposed mechanism involving double hydrogen-bonding by a thiourea catalyst is not operative and a new mechanistic hypothesis is shown.[1]

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SYNTHESIS OF GLYCODENDRIMERS CONTAINING 1,2-THIOMANNOBIOSIDE AND INVESTIGATION OF THEIR INTERACTION WITH BC2L-A LECTIN FROM *BURKHOLDERIA CENOCEPACIA*

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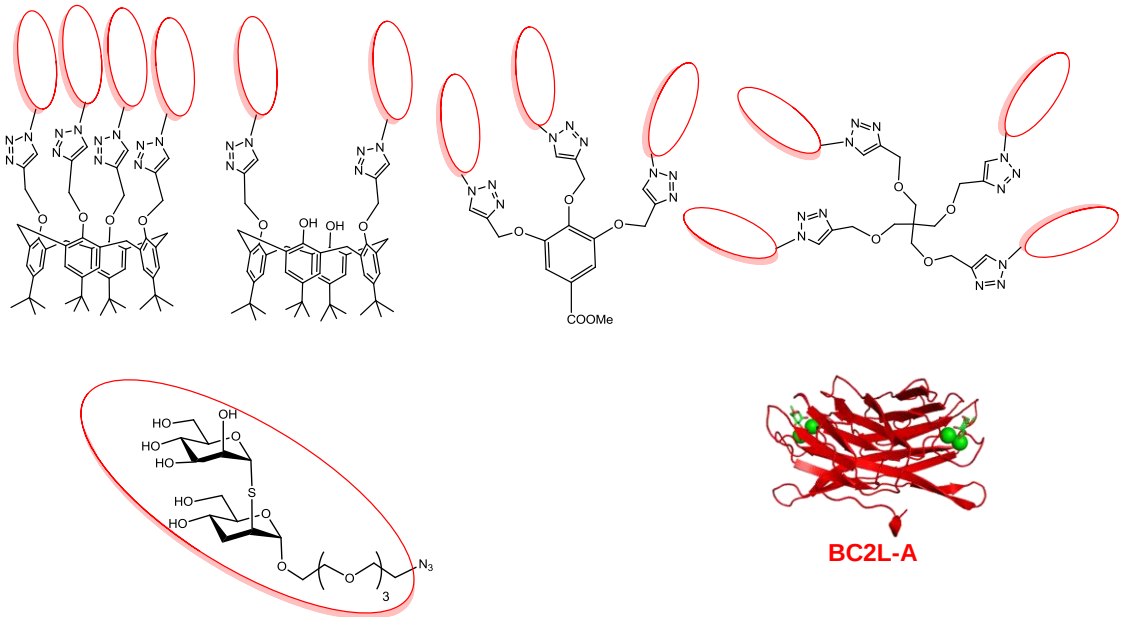
Highly mannosylated glycodendrimers might be useful agents in anti-adhesion therapy because they are considered as potential ligands of mannose-binding lectins. Herein, we report on the synthesis of α–(1→2)-thio-linked mannobioside[1]-containing dendrimers by azide-alkyne 1,3-dipolar cycloaddition, using different multivalent scaffolds like propargylated calix[4]arenes, gallic acid and pentaerythritol. Their interaction with mannose binding BC2L-A lectin[2] isolated from *Burkholderia cenocepacia* was studied by isothermal microcalorimetry, surface plasmon resonance and yeast agglutination inhibition assay.



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SYNTHESIS OF SULFONIC ACID-CONTAINING MALTOOLIGOMERS WITH POTENTIAL ANTITUMOR AND ANTIMETASTATIC ACTIVITY

Fruzsina Demeter, Mihály Herczeg, and Anikó Borbás

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Angiogenesis, the growth of new blood vessels from the preexisting vasculature, is a critical process in tumor development, and its inhibition is now a well-established strategy for the treatment of cancer. Sulfated cyclodextrin and maltohexaose derivatives exhibits anticancer activity, presumably through an anti-angiogenic mechanism. Recently, a fully sulfated maltotetraose glycoside displaying improved antitumor and antimetastatic activity was evaluated in a phase I clinical trial in cancer patients.[1]

Because of the great therapeutic potential of the sulfated malto-oligosaccharides we decided the synthesis of their isosteric sulfonic acid analogues in which the primary sulfate esters are replaced with a sodium sulfonatomethyl moiety. We assume that resistance of the sulfonate moiety to hydrolases could be advantageous from a therapeutic point of view.

Preparation of di-, tri-, tetra- and pentasaccharides with α(1→4)-interglycosidic linkages and containing a sulfonatomethyl moiety at position C-6 of each glucose unit was planned. The synthesis of the 6-sulfonatomethyl-containig glycosyl donor and acceptor building blocks (Figure 1.) was accomplished *via* reaction of the corresponding primary triflate derivative with the lithiated ethyl methanesulfonate.[2,3] To get access to the planned ologosaccharides, stepwise synthesis, block synthesis and polymerization reactions were studied. Here, our synthetic results will be presented.

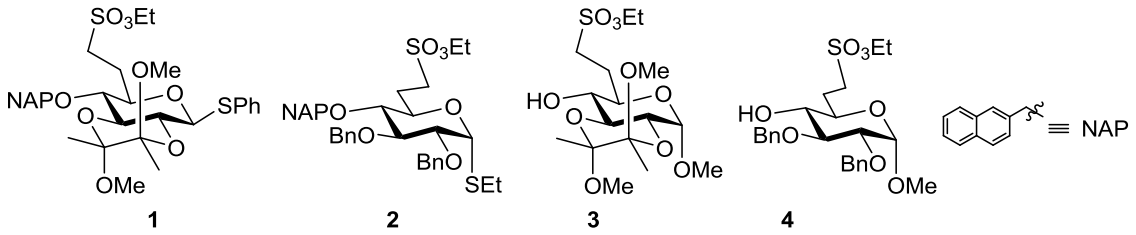

Figure 1. Glycosyl donor and acceptor building blocks

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This research was supported by the Hungarian Research Found (OTKA PD 115645) and the Mizutani Foundation for Glycoscience (150091).

SYNTHESIS OF *C*-*S*-LINKED DISACCHARIDE AND NUCLEOSIDE MIMETICS BY THIOLADDITION REACTIONS

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Glycomimetics play an important role in discovering the biological function of carbohydrates. Since their structure is similar to the natural carbohydrates, they can be used as probes in biological studies.

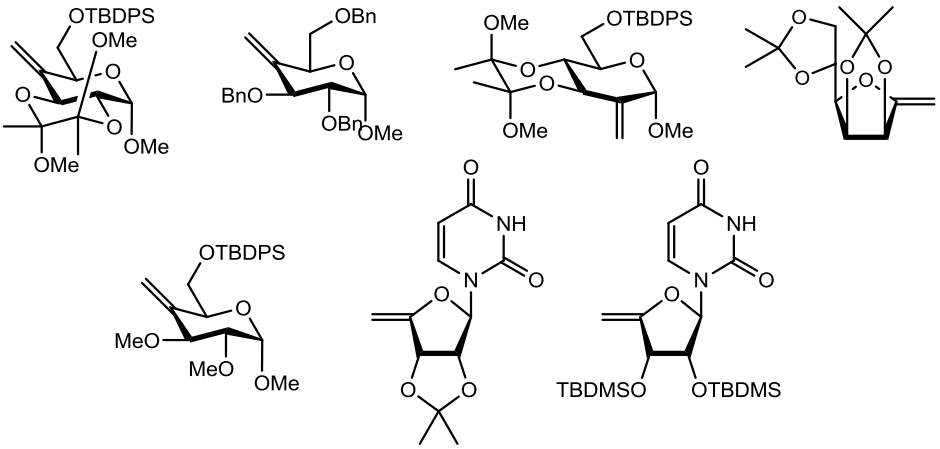
The most widely used stable glycomimetics are *C*- and *S*-glycosides. In these molecules, the glycosidic oxygen is replaced with a methylene group or a sulfur atom which results in an increased hydrolytic and enzymatic stability.

Researches are also in progress with glycomimetics containing two or more bridge atoms.

There are numerous ways to form a C-S bond between two saccharides. One of them is the free radical addition of a thiol to an alkene.

Our research group synthesizes C-S linked disaccharides with free radical thioladdtiton. We perform these reactions on saccharides containing endo-[1] and exocyclic[2,3] C=C bond.

Photoinduced thiol-ene reactions of exo-glycals (Scheme 1.) were performed with thiosugars. Systematic studies were carried out on sugars with *exo*-methylene moiety on different positions. We also investigated the effect of different protecting groups on the *exo*-glycal.



Scheme 1.

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A CIRCULAR H-BOND NETWORK ANCHORS THE PYRANOSYL FORM OF COMMON MONOSACCHARIDE ARYLHYDRAZONES

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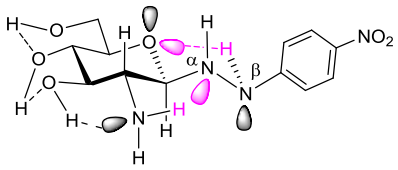
Chemistry of sugar arylhydrazones initiated by Emil Fischer classical experiments,[1] is an ongoing and still challenging topic, as both arylhydrazones and their derivatives (*e.g.* formazans) are key intermediates. Surprisingly, however, the fine solution state structure of arylhydrazones was never studied in details. Although Fischer had spelled out three isomers of D-glucose phenylhydrazones, namely α-, β-pyranosyl, beside the acyclic form isolated later,[2] their conformational ratios on general has not yet been rationalized. Several aldose arylhydrazones and their derivatives were studied by IR, NMR and X-ray methods, only those of D-glucose were found to form a pyranosyl ring.[3] This feature was attributed to all equatorial hydroxyl groups in D-glucopyranosyl derivatives. Most literature data focuses on establishing whether cyclic or acyclic form of the saccharides moiety is present but no comprehensive synthetic and theoretical approaches were conducted on the driving force determining 3D-structure propensities.

We will present our comprehensive analysis on arylhydrazones of different hexoses and hexosamines (*e.g.* D-*gluco*, D-*galacto*, D-*manno*, D-*talo*) based on their structural investigation (IR, MS, 2D-NMR, etc.). We have determined the steric influence of the monosaccharide moieties and the different intramolecular interaction triggering and determining their 3D-structures. We have found that only D-glucosamine 4-nitrophenylhydrazone is the sole molecule that presents exclusively a cyclic structure, but any other configuration exists as a conformational weighted ensemble of cyclic and acyclic forms. By using *ab initio* stability measures we are able to explain the above conformational preference. Theoretical modelling revealed a Δ*G* (kcal/mol) driven circular H-bond network, anchoring the pyranosyl form of D-glucose.



Schematic 3D-structure of D-glucosamine 4-nitrophenylhydrazone and the operative circular H-bond network

In addition, we have found that if the latter H-bond network is weakened or "damaged" by axial substituent(s) (D-*manno*- or D-*galacto* configuration), then the acyclic isomers starts to dominate the solution state structural ensemble.

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INTERACTION OF HEPARIN-ANALOGUE PENTASACCHARIDES WITH ANTITHROMBIN-III: NMR AND MOLECULAR DYNAMICS STUDY

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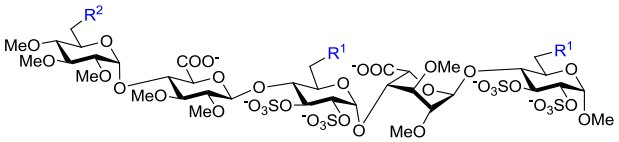
Heparin, isolated from natural sources, has been used as an antithrombotic agent in clinical practice since 1937. Since its administration is associated with rare serious side effects, several research groups are making efforts to synthesize heparin-analogue oligosaccharides displaying better pharmacological properties than heparin.

During our research we studied the structure and dynamics of novel heparin-analogue pentasaccharides containing two or three sulfonatomethyl groups at specific positions and their interaction with antithrombin III (AT-III) using a combined NMR experimental – MD computational approach.



1 $R^1 = R^2 = OSO_3^-$
2 $R^1 = CH_2SO_3^-$, $R^2 = OSO_3^-$
3 $R^1 = R^2 = CH_2SO_3^-$

Although the chemical composition of these analogues is almost the same, the in vitro anticoagulation studies revealed significant differences in their biological activities. Specifically, the trisulfonate analogue exhibited markedly lower activity than the two other ones. In order to identify the structural and/or dynamic factors behind the biological profile, the conformation along with the conformational flexibility have been investigated in both the free and the antithrombin-bound forms of the three pentasaccharides. Gratifyingly, the conformationally relevant proton-proton distances and torsion angles assessed by the NMR and MD approaches were generally in good agreement. Noticeably, the three analogues in complex with AT-III displayed conformations alike, on the contrary, the free forms exhibited significant variations in their conformations and conformational flexibility, which can explain their different biological activities.

To characterize the stoichiometry of pentasaccharide-AT-III complex and the thermodynamics of interaction, ITC measurements have been also performed.

This research was supported by the Hungarian Research Found (OTKA K 105459).

NEW TYPES OF CARBOHYDRATE-BASED *N*-CONTAINING TRICYCLES

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The glycosidase enzymes are involved in the regulation of carbohydrate metabolism, the processes of cell-cell and cell-virus recognition and the degradation of *N*-glycoproteins. Inhibitors of these enzymes are researched extensively, and a number of imino- and carbasugar-like glycosidase inhibitors have been found which can be used for the treatment of diabetes, various viral infections and tumor metastases. Some important glycosidase inhibitors are also available as a medicine: acarbose, miglitol and voglibose are excellent α-glucosidase inhibitor medicines of type II diabetes and neuraminidase inhibitors are available as anti-influenza agents. Bicyclic nitrogen-containing molecules, such as pyrrolizidine, indolizidine and quinolizidine are also good inhibitors of glycosidases[1]. Among the indolizidine and pyrrolizidine derivatives several very promising anti-cancer compounds can be found.

The aim of our research is the synthesis of carbohydrate-based tricyclic derivatives of potential glycosidase inhibitory activity. The starting materials of the synthesis were partially protected glucoside derivatives which were subjected to oxidation by metaperiodate. Stereoselective cyclizations of the resulting dialdehydes with tris(hydroxymethyl)aminomethane (Tris) led to the formation of various five-, six- or seven-membered ring-containing tricyclic systems with oxygen and nitrogen heteroatoms (**1**-**5**).

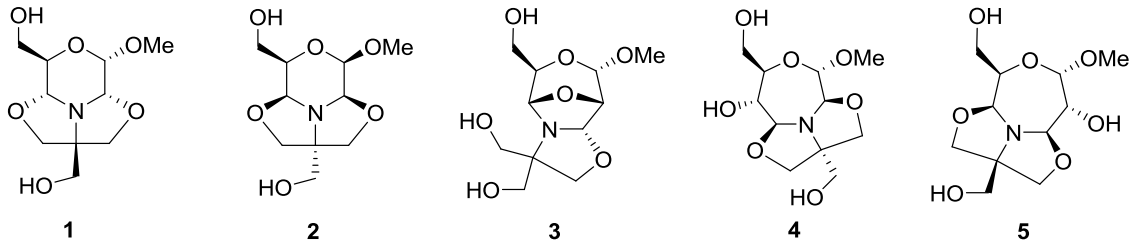

Figure 1. Structures of the new tricycles

Here, the synthesis and the structure-determination of these compounds will be presented.

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SYNTHESIS OF SULFATED MONOSACCHARIDES AS SUBSTRATES FOR SULFOTRANSFERASE

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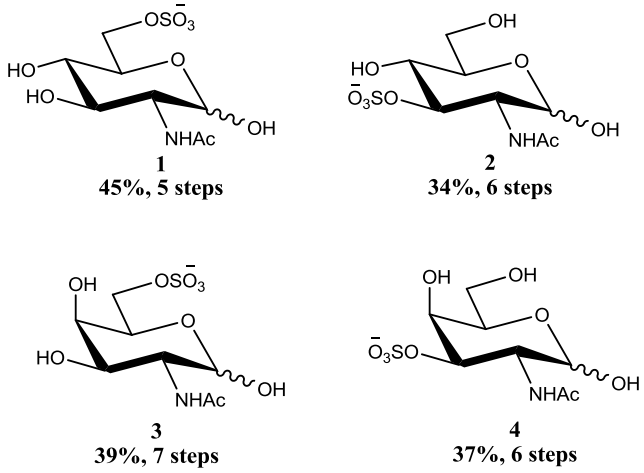
Sulfated molecules are used in metabolic and biosynthetic processes for enhancing elimination to avoid potential toxicity and induction of specific cellular or acellular responses. To determine the specificity of sulfotransferase in bacteria, we have designed four sulfated monosaccharides, *6-sulfonate*-D-*GlcNAc* ***1***, *3-sulfonate*-D-*GlcNAc* ***2***, *6-sulfonate*-D-*GalNAc* ***3*** *and 3-sulfonate*- D-*GalNAc* ***4***. Here we report the high yielding chemical synthesis of these sulfated glycans.



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STUDY OF THE ADDITION REACTIONS OF 1-*C*-SUBSTITUTED GLYCALS

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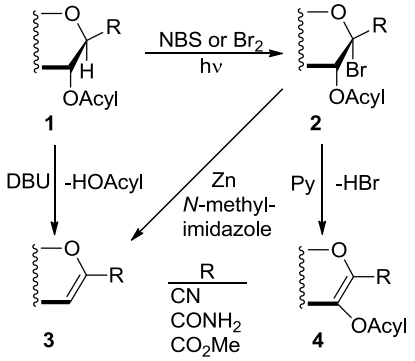
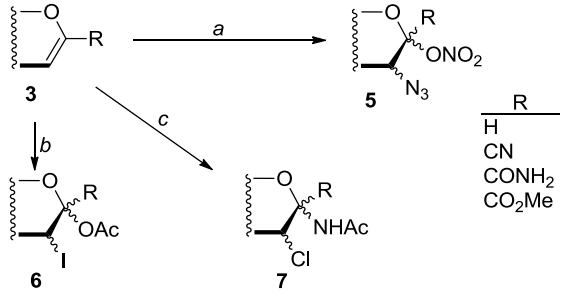
Glycals and 2-hydroxyglycals [**3** (R = H) and **4** (R = H), Scheme 1] are saccharide derivatives having a double bond between the C-1 and C-2 carbons. The reactivity of these compounds is characterized by electrophilic ionic and radical additions to the electron rich double bond.

Some known chemical transformations of unsubstituted glycals **3** are summarized in Scheme 2: among CAN-mediated reactions[1] azidonitration[2] (*a* to **5**, R = H) is a well studied and widely applied transformation; iodoacetoxylation[3] (*b* to **6**, R = H) is analogous to azidonitration and chloroamidation (*c* to **7**, R = H).[5]

Reactivity of 1-*C*-substituted glycals (**3**, **4**) is much less studied in part due to the not easy accessibility of such compounds.[6, 7]



Scheme 1.



Scheme 2.

We have elaborated synthetic methods for 1-*C*-acceptor-substituted glycals (**3** and **4**) from **1** or **2**,[8-10] and studied their reactivity under azidonitration, iodoacetoxylation and chloroamidation conditions.

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20 YEARS OF STUDIES ON HUMAN SALIVARY α-AMYLASE: AN OVERVIEW OF METHODOLOGY AND RESULTS

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Our research interest is focused on human amylases. We would like to understand their physiological functions, in order to design and synthesize new substrates and efficient inhibitors. Human amylases of both salivary (HSA) and pancreatic origins (HPA) have been extensively studied from the viewpoint of clinical chemistry because they are important as indicators in evaluating diseases of pancreas and salivary glands. Furthermore, they are used as targets for drug design in attempts to treat diabetes, obesity and other carbohydrate metabolism disorders.

The widening interest in the treatment of sugar metabolic diseases and in the prevention of caries has stimulated our work to test new natural[1-3] and synthetic compounds[4] as amylase inhibitors. Among them, there are carbohydrate type[1.4], protein type, and small, drug-like inhibitors without sugar moieties5.

Formerly measurements were carried out on two different substrates, a synthetic one, 2-chloro-4-nitrophenyl-4-O-β-D-galactopyranosyl-α-maltoside (GalG2CNP) and the natural one, amylose. The amount of liberated CNP or reducing sugar units (after reaction with dinitrosalycilic acid), was measured by spectrophotometry. Surface plasmon resonance (SPR) and saturation transfer difference-NMR methods[2] were used for detecting molecular interactions between enzyme and inhibitor. New substrates (maltooligomers and its CNP glycosides[6]) and new methods (HPLC and ITC) were introduced for inhibitor activity measurements.

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TRICYCLANOS: A NEW TYPE OF NUCLEOSIDE ANALOGUES

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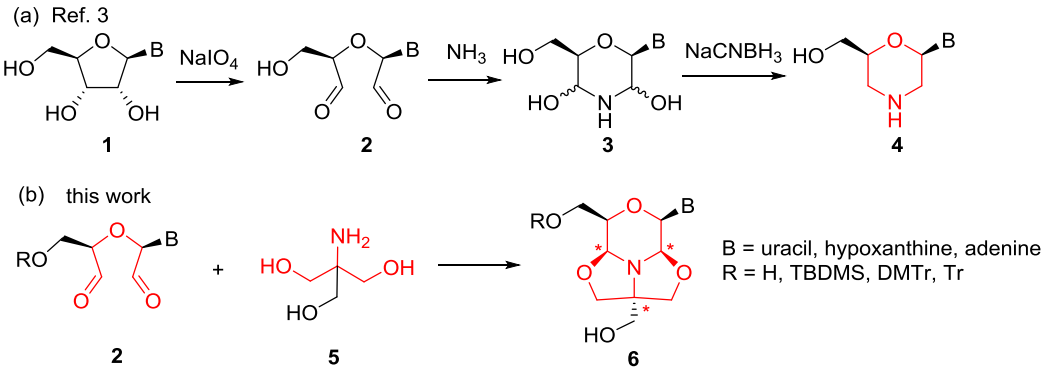
E-mail: emperormate@hotmail.com

There is an exponential progress in the field of oligonucleotide-based therapeutics and, in particular, gene silencing agents such as antisense therapeutics[1] and small interfering RNAs.[2] In the first stage of antisense research phosphorothioate linked DNA oligonucleotides were the dominant analogues. In 1990s Summerton developed morpholinos which are built up of dimethylamino phosphinylideneoxy-linked nucleoside analogues having morpholine ring in the place of ribose moieties.[3] The nucleoside analogue monomers **4** can be prepared from simple ribonucleosides **1** by periodate oxidation and a subsequent reductive amination (Scheme 1a). In these compounds the morpholine ring is connected to heterocyclic base recognition moieties of DNA (adenine, cytosine, thymine and guanine).

Inspired by Summerton's work we envisioned the synthesis of a new type of nucleoside analogues having structure **6** in which the ribose unit is substituted with a morpholine-containing tricyclic ring system (Scheme 1b).

Herein, we present the synthesis of uridine-, inosine- and adenosine-derived members of the new nucleoside family which we call tricyclanos, by analogy of Summerton's morpholinos. In these nucleoside analogues the sugar part is replaced by a new tricycle: 3,7,10-trioxa-11-azatricyclo[5.3.1.$0^{5,11}$]. 1,5-Dialdehydes obtained from uridine, inosine and adenosine reacted readily with tris(hydroxymethyl)aminomethane to provide the corresponding tricyclic derivatives with full stereoselectivity.



Scheme 1. Synthesis of morpholinos (a) and morpholine-containing tricyclanos (b)

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PHENYLETHANOID GLYCOSIDE PATTERN IN TISSUE CULTURES OF *PLANTAGO LANCEOLATA* L. BY LC–ESI–MS^n EXPERIMENT

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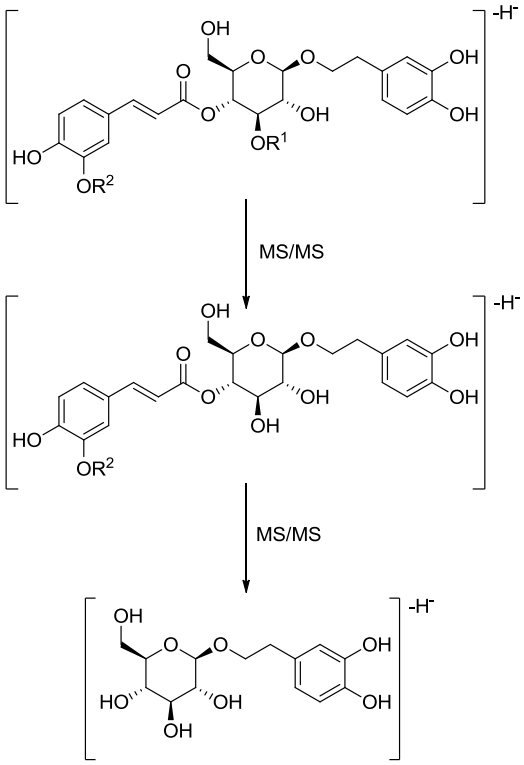
[b] *University of Debrecen, Department of Botany, Division of Pharmacognosy, H-4010, Debrecen, Hungary*
E-mail:kiss.attila@science.unideb.hu

Tissue cultures of a medicinal plant, *Plantago lanceolata* L. were screened for phenylethanoid glycosides (PGs) and other natural products (NPs) with LC–ESI–MS^3. The effects of N source concentration and NH_4^+/NO_3^- ratio were evaluated in a full-factorial (FF) experiment. N concentrations of 10, 20, 40 and 60 mM, and NH_4^+/NO_3^- ratios of 0, 0.11, 0.20 and 0.33 (ratio of NH_4^+ in total N source) were tested.

Several peaks could be identified as PGs, of which, 16 could be putatively identified from the MS/MS/MS spectra. N source concentration and NH_4^+/NO_3^- ratio had significant effects on the metabolome, their effects on individual PGs were different despite these metabolites were of the same biosynthetic class.



Chief PGs were plantamajoside and acteoside (verbascoside), their highest concentrations were 3.54 ± 0.83% and 1.30 ± 0.40% of dry weight. NH_4^+/NO_3^- ratio and N source concentration effects were examined on a set of 89 NPs. For most NPs, high increases in abundance were observed compared to Murashige–Skoog medium.

USING DFT METHODS IN COMPUTER-ASSISTED DESIGN OF SELECTIVE INHIBITORS OF HUMAN GOLGI α-MANNOSIDASE II

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[b]*Department of Physical and Theoretical Chemistry, Faculty of Natural Sciences, Comenius University, Mlynska dolina CH-1, Ilkovičová 6, 842 15 Bratislava, Slovakia*
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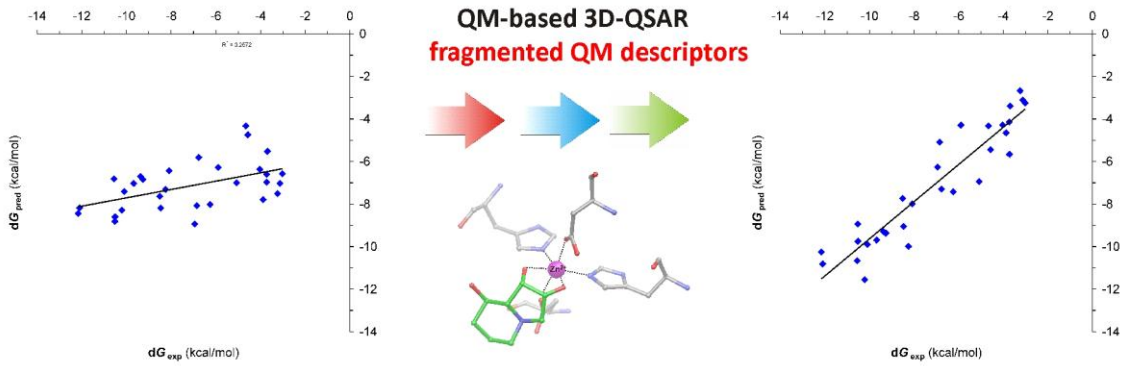
Human Golgi α-mannosidase II (hGM) is a zinc ion co-factor dependent glycoside hydrolase (the GH family 38) included in the biosynthesis of complex N-glycan structures. It is a target for inhibition of metastasis and growth of cancer cells. Up to now many known potent inhibitors of hGM are not sufficiently selective to be interesting for a pharmaceutical industry. We used several computational procedures to build QSAR models and design selective inhibitors of hGM. Fragment docking techniques and 3D-QSAR models with interaction energy quantum mechanics-based descriptors were employed. The predictive models were built and validated with a library of 55 structurally diverse hGM inhibitors and 25 non-active hGM compounds. A Schrödinger library of small fragments, derived from molecules in the medicinal chemistry literature, was used to design a selective linker of an inhibitor.



Acknowledgement: This work was supported by the the Slovak Research and Development Agency (Contract No. APVV-0484-12) and the project VEGA- 2/0064/15.

A NEW SERIES OF *C*-(β-D-GLUCOPYRANOSYL)-1,2,4-TRIAZOLES FOR THE INHIBITION OF GLYCOGEN PHOSPHORYLASE: VIRTUAL SCREENING, SYNTHESIS AND IN VITRO EVALUATION

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[b]*Centre of Materials Science, Division of Chemistry, University of Central Lancashire, Preston, United Kingdom*
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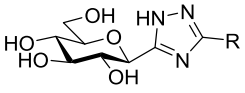
Type two diabetes mellitus is a severe metabolic disease of carbohydrate metabolism with economic and social consequences. Since this disease is incurable, the primary goal of the treatment is to keep the blood sugar concentration at a desirable level. Current antihyperglycaemic drugs are often inefficient and/or have undesirable side effects,[1] therefore, search of new therapeutic possibilities is required. Suppression of hepatic glucose output by the inhibition glycogen phosphorylase (GP) may result in new antidiabetic drugs.

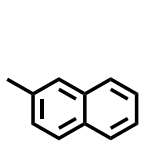
3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles (**1**) are among the best glucose analog inhibitors of GP (K_i = 0.41 μM for **1a**).[2] Virtual screening calculations exploiting the ZINC database with CombiGlide and quantum-mechanics polarized ligand docking (QM-PLD) predicted 150 compounds with docking scores significantly better than **1a**. From these structures eight (**1b-i**) were chosen for synthesis and *in vitro* evaluation.

Details of the dockings, syntheses and inhibition properties of the target compounds will be described in the presentation.

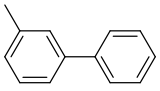


1

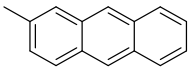
R (docking score)



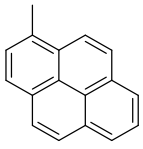
a (-12.46)



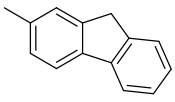
b (-13.85)



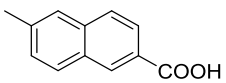
c (-13.71)



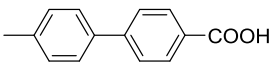
d (-13.92)



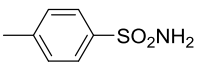
e (-13.49)



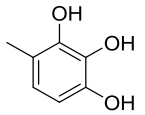
f (-13.61)



g (-14.16)



h (-14.51)



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F-18 RADIOLABELLING OF CHITOSAN-BASED NANOPARTICLES AND ITS MODELLING REACTION

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AIM: The aim of this work was to label chitosan-based nanoparticles via [F-18]-4-fluorobenzaldehyde ([^{18}F] -FBA) on one of its amine groups. The reaction was modelled on one of its components, Glucosamine (GlcN), instead of the use of the whole polymer. Subsequently, the developed procedure was applied to chitosan radiolabeling.

MATERIALS AND METHODS: [^{18}F]-FBA was synthesized from 3 mg 4-Formyl-N,N,N-Trimethylanilinium triflate , in a 5 minutes reaction at 80°C, using SCX cartridge to remove side products. To model chitosan labelling, direct and indirect reductive amination were used, between the carbonyl group of [18F]-FBA with the amine group of GlcN and 1,3,4,6-Tetra-O-Acetyl-2-amino-GlcN (TAGlcN), at different temperatures: 110°C, 70°C, 50°C and room temperature, during 30 minutes. $NaBH_3CN$ was employed as reducing agent. To study the possible aldol side products, we performed the same experiments with N-Acetyl-GlcN and glucose. The modelling reaction concluded to use direct reductive amination at elevated temperatures (70ºC and 50ºC) for the labelling of the polymer. The reaction was followed by TLC analysis with samples taken at 5, 10, 20 and 30 minutes.

RESULTS: [18F]-FBA radiochemical yield was 56±10%, with >95% radiochemical purity. For the reaction between FBA and TAGlcN via direct reductive amination, the HPLC-determined conversion yields were: 110° C: 7±1%, 70°C: 42±0.7%, 50°C: 41±4%, room temperature: 20±8% In case of indirect reductive amination, (with TA-GlcN), at 110 C the results are similar, 8±1%, as with direct reductive amination at the same temperature. Room temperature yield was 41±12%, but it took longer time (1h). The reactions with N-Acetyl-GlcN and glucose gave significantly different compounds of less than 5 % of activity. When radiolabeling chitosan via [18F]-FBA, using direct reductive amination, radiochemical conversion was at 50 ºC: 33±3%, 46±2%, 60±2%, 68±1%; and at 70ºC: 54±4%, 65±2%, 71±1%, 72±1% after 5, 10, 20 and 30 min, respectively.

CONCLUSIONS: Modelling reaction of direct and indirect reductive amination showed that [18F]-FBA reacts mainly with the NH_2 group of GlcN or TA-GlcN, with high yields at 70°C and lower temperatures. In case of absence or blocked amine group, we observed low yield aldol side reactions. These results were successfully applied to chitosan radiolabeling. Both at 50ºC and 70ºC, after 30 minutes approximately 70% of FBA was built in, but the reaction was faster at higher temperature. This method may be employed for radiolabeling chitosan, or other nanoparticles based on a polymer rich in amine groups.

ACKNOWLEDGEMENTS: This work was supported by FP7-PEOPLE-2012-ITN (316882 RADIOMI project).

DEVELOPMENT OF NOVEL ANTIBIOTICS BASED ON SYNTHETIC GLYCOCONJUGATES

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Helicobacter pylori is a spiral-shaped Gram negative bacterium that is present in the human gastric tissue and infects the stomachs of approximately half the human population. In most individuals, patients who are infected with *H. pylori* remain asymptomatic, but in some cases chronic inflammation may lead to development of gastric ulcers and even gastric cancers.

The mechanism of adhesion occurs through binding of protein receptors expressed in the outer membrane of *H. pylori*, to fucosylated carbohydrate ligands of the mucous layer. One of these protein receptors is called the "blood group antigen binding adhesion" (BabA).

It was reported that *H. pylori* barely colonizes gland mucous cell-derived mucin where α-1,4-GlcNAc-capped O-glycans exist. In vitro experiments show that α-1,4-GlcNAc-capped O-glycans function as a natural antibiotic to inhibit *H. pylori* growth.

In this study, a new carbohydrate molecule and its derivatives, which include the Lac-di-NAc structure, were synthesized for interaction studies with microbial and human lectin. It is hoped that this molecule can prevent bacterial infection by blocking binding sites that the bacteria would use. It could promote and develop a new method to cure gastric ulcers and even gastric cancers caused by the infection with *H. pylori*.

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SYNTHESIS OF SIALIC ACID AND β-GALACTOSIDE LIBRARIES: ESSENTIAL TOOLS IN STRUCTURE ACTIVITY RELATIONSHIP INVESTIGATIONS

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Sialic acid is a general term for *N*- or *O*- substituted neuraminic acid, which encompasses a family of sugars containing nine carbons. They are abundant in mammalian tissues and microbes, and specific families of proteins are involved in their recognition.[1] Such interactions are important for regulating immune responses to bacterial proteins, viral/bacterial pathogenicity, and the inflammatory response. It has also been documented that a particular form of sialic acid, *N*-Glycolylneuraminic acid (Neu5Gc), promotes the malignancy of some carcinomas.[2] Indeed, it has been shown that some tumour suppressor genes act by modulating glycosylation and lectin expression.

A class of lectins known to play a role in cancer development are the galectins.[3] Galactose, in particular β-galactosides, are the natural ligands of galectins. Galectins are sugar binding proteins that are abundant within all organisms and have roles in autoimmune and inflammatory responses as well as being linked to tumour development and progression. They regulate mRNA processing, apoptosis, cell-cell and cell-matrix interactions. Their role in such essential cellular functions highlights the biological and potential therapeutic importance of protein/carbohydrate interactions.

We are interested in synthesising well defined libraries of sialic acid and galactose derivatives that will be utilised for structure-activity relationship investigations. The libraries will consist of collections of monomeric and polymeric compounds that will be used to enable fundamental advances in several biological research areas. These structures represent not only tools for scientific discovery, but also potential therapeutic agents. The synthesis of an *N*-acetylneuraminic acid (modified at C-5) derivative for conjugation to lactose moieties has been completed. Neu5Gc (*N*-glycolylneuraminic acid) containing trisaccharides are also of particular interest. Investigations into galactose containing trisaccharides to target galectins are on-going.

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SYNTHESIS OF MULTIVALENT RHAMNOBIOSIDES FOR STUDYING THE GLYCAN BINDING ACTIVITY OF RECOMBINANT HORSESHOE CRAB PLASMA LECTIN

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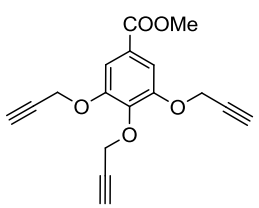
The emergence of pathogenic bacterial strains that are resistant to existing antibiotics is a major public health concern worldwide. The antibiotic-resistant organisms are capable of causing serious, life-threatening infection that difficult to manage in the absence of variety of treatments.

Lectins are carbohydrate-binding proteins with high specificity for special sugar moieties. Because of that property, these macromolecules are able to recognize of bacterial cell-wall carbohydrates, and this specific recognition may provide an alternative way for pathogen detection and inhibition.

Recently, Taiwanese researchers has expressed a soluble and functional recombinant horseshoe crab plasma lectin (rHPL) in an *Escherichia coli* system.[1] It was shown that rHPL bound to selective medically important pathogens isolated from clinical specimens, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Streptococcus pneumoniae* serotypes. The binding was demonstrated to occur through a specific molecular interaction with rhamnose in pathogen-associated molecular patterns on the bacterial surface. Additionally, rHPL inhibited the growth of *P. aeruginosa* PAO1 in a concentration-dependent manner. The results suggest that a specific protein-glycan interaction between rHPL and rhamnosyl residue may further facilitate development of novel diagnostic and therapeutic strategies for microbial pathogens.

To assist this work our research group accomplished the synthesis of several multivalent rhamnobioside derivatives as potential ligands of rHPL. For the preparation of the multivalent derivatives the following building blocks were used:



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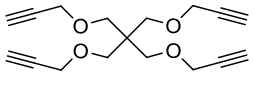

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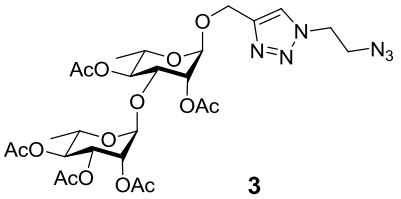

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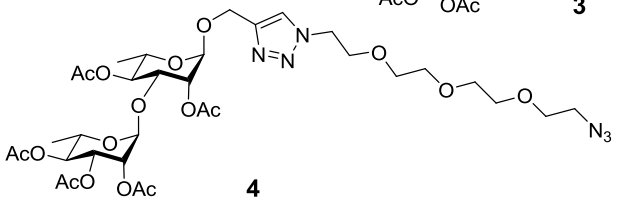

4

Here, synthesis and preliminary results of lectin binding assays will be presented.

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CLICK-REACTION OF CARBOHYDRATE AZIDES WITH CAROTENOID PENTYNOATES

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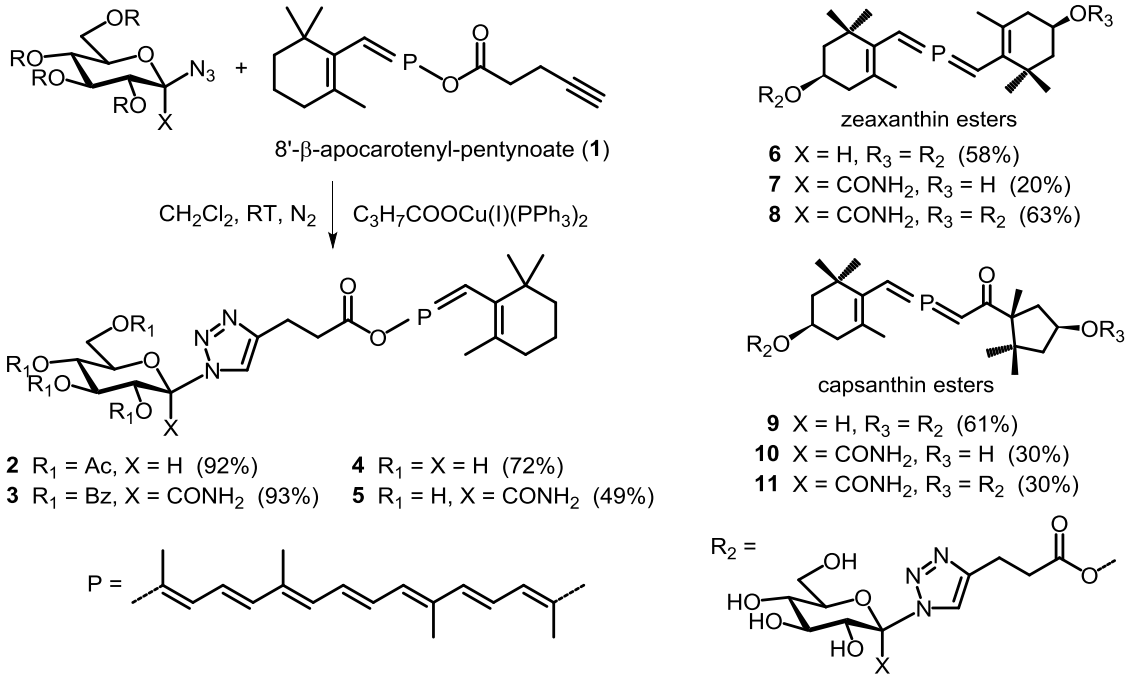
Pentynoate esters of various carotenoids were previously synthesized, and were used in [3+2] azide-alkyne cycloaddition (click) reactions.[1] Performing the reactions with protected or deprotected glycosyl azides the corresponding triazoles formed in reasonable yields.



Coupling carotenoid pentynoates to glycosyl azides via click reaction

The deprotected triazol products have amphipatic structures, which may make them be able to form self-aggregates and/or incorporate into lipid bilayers.

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EFFECTS OF α-CYCLODEXTRINS ON CELL VIABILITY AND SYNTHESIS OF NEW DERIVATIVES

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Cyclodextrins (CDs) have been in the focus of pharmaceutical and industrial research from decades.[1] β-CDs are more popular in use, considering the preferable size of their cavity for the common used active pharmaceutical ingredients (APIs).[2] Nevertheless, evaluating the opportunities of α-CD usage in the pharmaceutical practice is worth, because for certain APIs their smaller cavity could be more convenient. On the other hand, in future drug delivery systems, their amphiphilic derivatives could be used, as they form more stable nanoparticles than other CD families.[3]

CDs, as pharmaceutical excipients, are always in higher concentration in the products than stoichiometrically required. Thus evaluation of their effects on living organisms is indispensable. One aim of our study was to investigate the cytotoxic properties of different α-CD derivatives. Toxicological studies were performed on Caco-2 cell line and human red blood cells (RBC). By MTT cell viability assay, Real Time Cell Electronic Sensing (RT-CES) and hemolysis test, the IC50 and HC50 concentration values were determined. Based on these values, comparison of the effect of chemical changes can be made, and it drives to the selection of those products which are the most safe to use in further developments. However, CDs which are available on market mostly possess only approximate degree of substitution (DS), considering the difficulties and high price of complete separation. However, for reaching the clear conclusion of structure-toxicity correlations, separated derivatives should be examined. The aims of our research is to synthesize and separate different alkylated CDs and their further modified 2nd generation derivatives.[4,5]

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SYNTHETIC APPROACHES TOWARDS THE PREPARATION OF FLUORINATED LIGANDS FOR GALECTINS

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Galectins are a large class of proteins that selectively target substituted β-galactosyl-containing glycoconjugates and share a primary structural homology in their carbohydrate recognition domain. They have broad specificity and multiple subcellular localizations and are involved in the modulation of a variety of biological functions, e.g. cell-cell adhesion and signalling, immune and inflammatory responses, tumour development and metastasis.[1,2]

Galectins contribute to different steps of tumour formation and progression by modulating different biological events including adhesion, metastasis, angiogenesis and tumour immune escape. Consequently, the inhibition of the interaction between galectins and tumour cell surface glycans could represent a novel method of combating certain types of cancer, with galectin targeted inhibitors as novel therapeutic agents.[3]

Given the importance of glycan-galectin interactions, the development of novel tools to thoroughly investigate the binding process is essential for the design of suitable inhibitors.

In this context, ^{19}F NMR spectroscopy has proven to be a novel and powerful technique, providing a way to monitor the binding event and to evaluate its characteristics, i.e. affinity, binding exchange, binding modes and binding epitope.[4,5]

Herein we present the synthetic work towards the preparation of fluorinated LacNAc-type ligands for ^{19}F NMR spectroscopy studies.

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STEREOSELECTIVE SYNTHESIS OF 1-*O*-FATTY ACID SUGAR ESTERS

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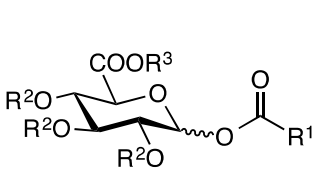
Sugar fatty acid esters are non-ionic biodegradable surfactants with broad applications in food, cosmetic and pharmaceutical industries. We have developed a convenient and high yielding strategy for the stereoselective synthesis for a series of α- and β-1-*O*-fatty acid sugar esters (saturated and unsaturated fatty acyl derivatives). The successful preparation based on finding suitable hydroxyl and carboxylic protecting groups, which can be easily removed under mild and non-hydrolytic conditions. The choice of protecting groups for preparing the 1-*O*-fattyacyl glucuronides was crucial. In our synthesis, we have chosen the chloroacetyl protecting group for the hydroxyl groups (at C-2, 3, and 4) and the allyl, benzyl, or methyl esters for protecting the carboxylic acid group.



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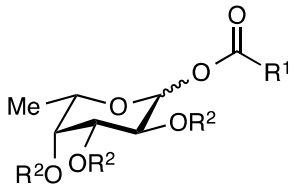
R^3 = All or Bn or Me



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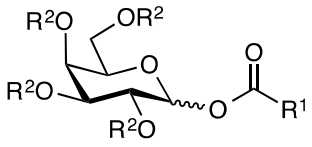

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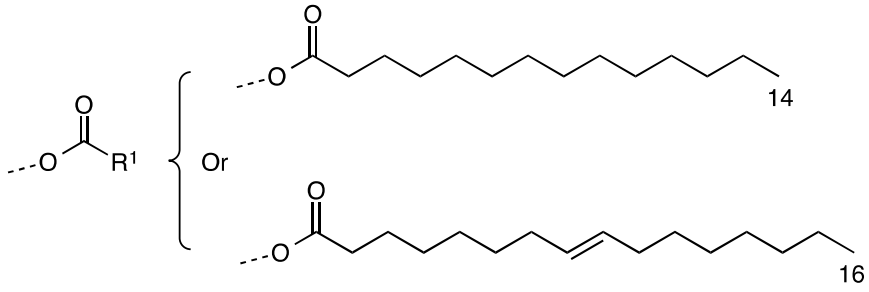

PREPARATION OF TRISUBSTITUTED *C*-(β-D-GLUCOPYRANOSYL)-1,2,4-TRIAZOLES

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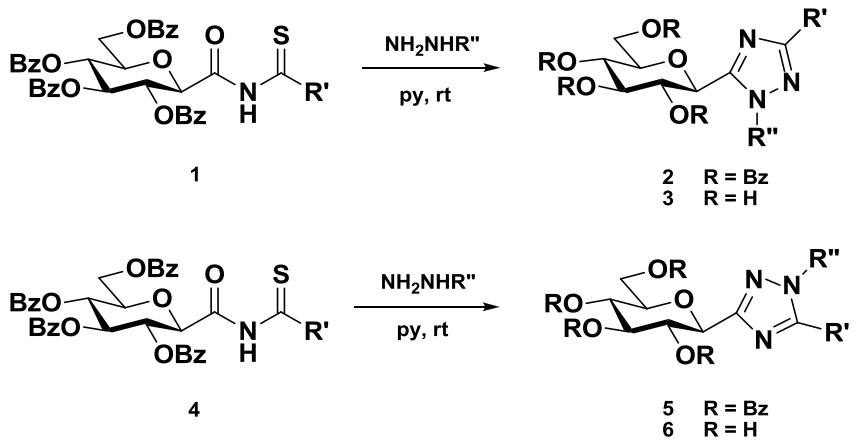
Recently, 3-(β-D-glucopyranosyl)-5-substituted-1,2,4-triazoles have been shown to be very efficient glucose analog inhibitors of glycogen phosphorylase.[1] Trisubstituted *C*-glycosyl-1,2,4-triazoles are scarcely known, only a few examples can be found in the literature.[2]

Given the interest in compounds containing the 1,2,4-triazole ring in general and *C*-glycosyl 1,2,4-triazoles in particular,[3] we have started a program to study the synthetic possibilities towards the latter types of compounds. First, the preparation of 5-(β-D-glucopyranosyl)-1,3-disubstituted- (**2**) and 3-(β-D-glucopyranosyl)-1,5-disubstituted-1,2,4-triazoles (**5**) were investigated as to the variability of the R' and R" substituents. Compounds **2** and **5** were obtained by the reactions of acyl-thioamides **1** and **4** with hydrazine derivatives, respectively. The key for the regioselectivity is the different reactivity of the carbonyl and the thiocarbonyl groups. Removal of the *O*-benzoyl protecting groups by base catalysed transesterification provided series of 1,2,4-triazoles **3** and **6** with aliphatic and aromatic substituents in the 1,3 and 1,5 positions. In the presentation the scope and limitations of the synthesis will be shown.



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PREPARATION OF 2-(β-D-GLUCOPYRANOSYL)-PYRIMIDINES

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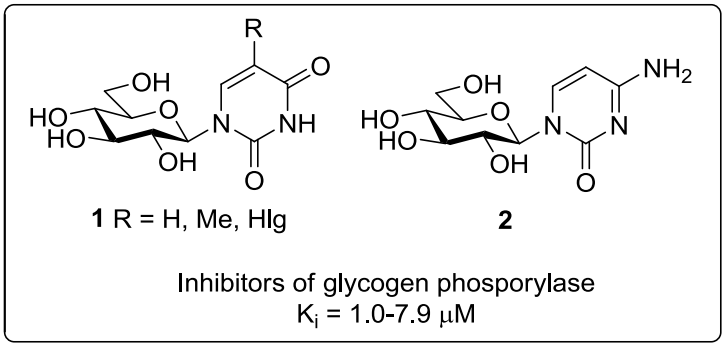
C-Glycosylated variants of nucleosides and their analogues have become a widely studied class of glycomimetics due to their increased resistance to metabolic degradation as compared to that of their *N*-glycosyl counterparts.[1]

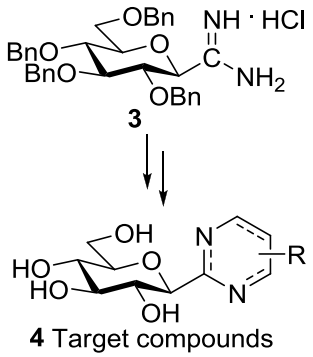
Recently, several *N*-β-D-glucopyranosyl derivatives of nucleobases were assayed against glycogen phosphorylase enzyme (a validated target for the treatment of type 2 diabetes), and among them several pyrimidine based compounds (e. g. **1** and **2**) proved micromolar inhibitors.[2] To study the inhibitory effect of analogue *C*-glucosyl heterocycles, syntheses and tests of 2-(β-D-glucopyranosyl)-pyrimidines (**4**), a scarcely known class of compounds was envisaged.

For the construction of pyrimidines the base-induced ring closing reaction of carboxamidines with 1,3-dielectrophiles is a generally applied method[3] which was successfully employed earlier in syntheses of *C*-glycofuranosyl-pyrimidines,[4] as well.

Following this convenient route the preparation of the target *C*-glucopyranosyl heterocycles was planned by using *O*-perbenzylated *C*-(β-D-glucopyranosyl)formami-dine hydrochloride (**3**) as starting material.

In the presentation the synthesis of the amidine precursor and its cyclisation with a set of 1,3-dielectrophiles will be reported.





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COUPLING OF ANHYDRO-ALDOSE TOSYLHYDRAZONES WITH THIOLS: A NEW ROUTE FOR THE SYNTHESIS OF *C*-(β-D-GLYCOPYRANOSYL)METHYL-SULFIDES

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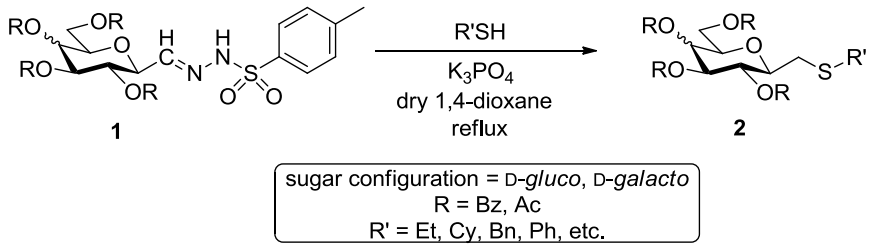
Metal-catalyzed and metal-free cross-coupling reactions have profoundly changed the way how complex organic molecules are assembled nowadays.[1] In the past ~10 years tosylhydrazones (as equivalents of the less readily handled diazo compounds) emerged as partners in metal-catalyzed and also in metal-free transformations in a variety of coupling reactions[2] for example with thiols.[3]

Tosylhydrazones can easily be prepared from aldehydes or ketones, and this is feasible on carbohydrate scaffolds as well. However, anhydro-aldose tosylhydrazones **1** are not readily available, and their preparation needs special methods. We have elaborated synthetic procedures for these types of compounds: reduction of glycosyl cyanides and *in situ* trapping of the intermediate imine by tosylhydrazine.[4] With these compounds in hand we have started a program to study their coupling reactions.

In this presentation we disclose our first results to couple the above tosylhydrazones with thiols to give *C*-(β-D-glycopyranosyl)methyl-sulfides **2** which can be regarded as new glycomimetic compounds.



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SYNTHESIS OF AN IDRAPARINUX ANALOGUE PENTASACCHARIDE MONOSULFONIC ACID

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Heparin is a linear sulfated polysaccharide that has numerous biological functions. It plays a crucial role in maintaining the haemostatic state of blood. For its anticoagulant effect a pentasaccharide fragment (DEFGH pentasaccharide) is responsible. Heparin interacts with antithrombin, a serine protease inhibitor that blocks thrombin and factor Xa in the coagulation cascade. The active DEFGH pentasaccharide fragment of heparin and many simplified analogues possessing selective factor Xa inhibitory activity were prepared. Our research group has been dealing with the synthesis of sulfonic acid analogues of the anticoagulant pentasaccharide domain of heparin. Longer duration of action and increased activity of the molecules are expected by exchanging the sulfate esters to bioisosteric sulfonic acid moieties.

According to our previous results, the Xa factor inhibitory activity of the pentasaccharide depends on the number and the position of the sulfonatomethyl groups[1]. To acquire further information on the effect of the sulfonic acid moieties on the antithrombotic action and to develop novel anticoagulants we decided to prepare heparinoid pentasaccharides by systematic replacement of the sulfate esters with a sulfonatomethyl moiety. Synthesis of the protected pentasaccharides with primary sulfonatomethyl groups has been published, but further eight more synthetic steps are required for each unprotected derivatives

In this work we present the synthesis of a pentasaccharide monosulfonic acid bearing a primary sulfonatomethyl moiety at the unit F.

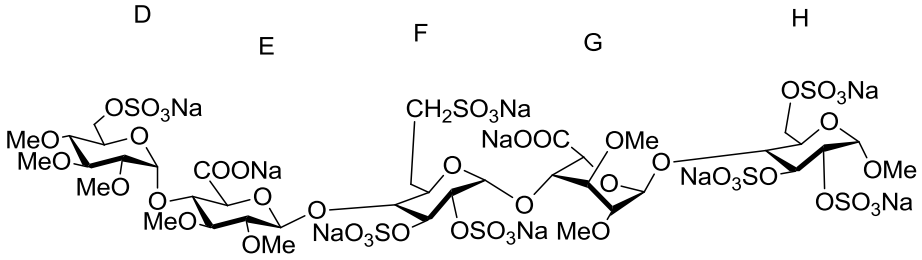

Figure 1: The synthesized pentasaccharide

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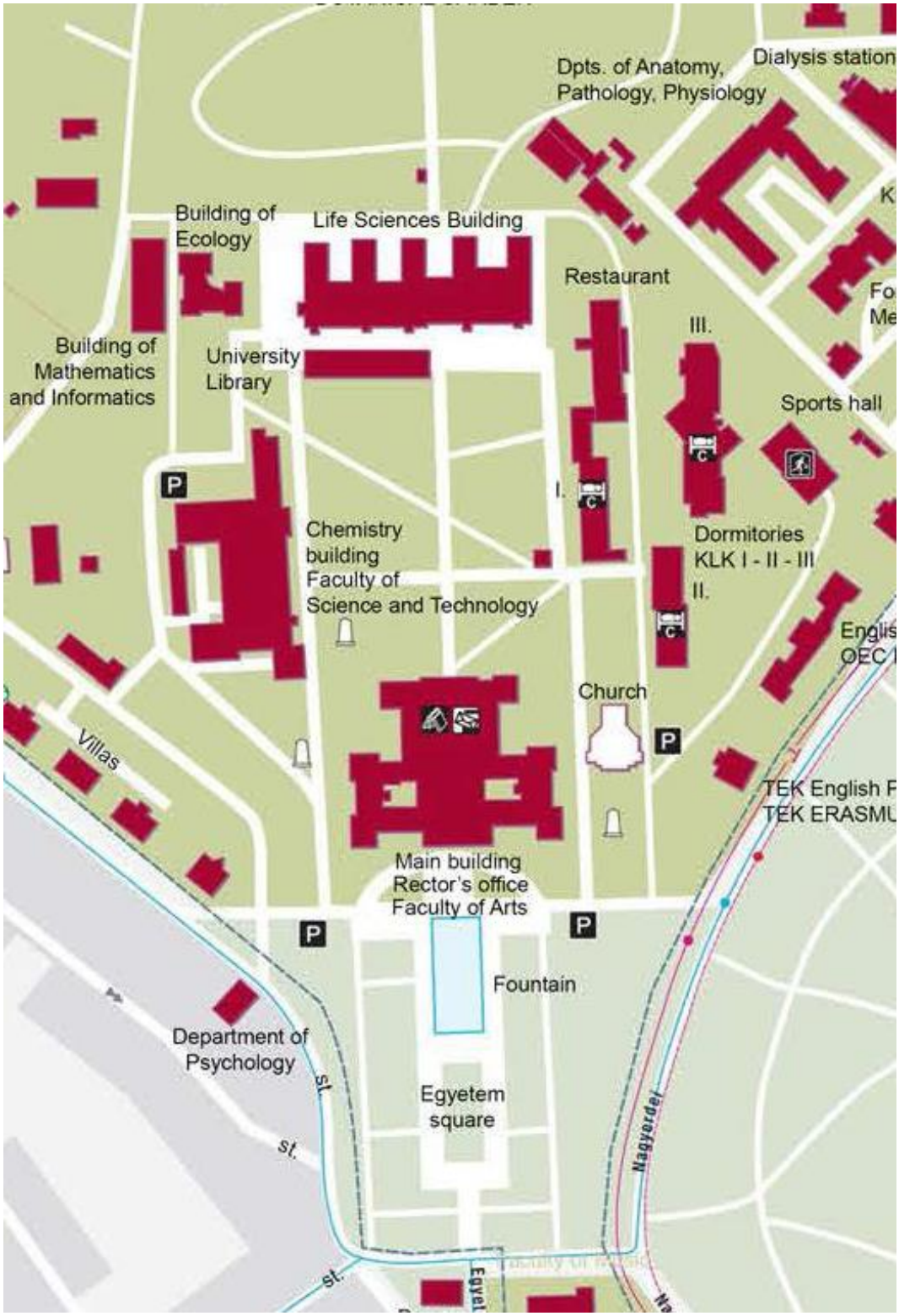

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