An efficient synthesis of linear β-(1→6)-galactan oligosaccharides related to plant cell wall glycans

Galactans are linear structures mainly found in arabinogalactan glycans and RG-I side chains. As a follow-up to our work on both β-(1→3)-linked and β-(1→4)-linked galactans, we herein report a convergent synthesis of β-(1→6)-galactan using our previously synthesized 4,6-benzylidene protected disaccharide as a key building block. However, the regioselective reductive opening of the 4,6-benzylidene protected disaccharide turned out to become more challenging as the length of the oligosaccharide increased and a second differential protected disaccharide building block carrying a chloroacetyl group on the 6-position was used to elongate the chain in a more efficient way.

A synthetic glycan microarray enables epitope mapping of plant cell wall glycan-directed antibodies

In the last three decades, more than 200 monoclonal antibodies have been raised against most classes of plant cell wall polysaccharides by different laboratories world-wide. These antibodies are widely used to identify differences in plant cell wall components in mutants, organ and tissue types, and developmental stages. Despite their importance and broad use, the precise binding epitope for only a few of these antibodies has been determined. Here, we use a plant glycan microarray equipped with 88 synthetic oligosaccharides to comprehensively map the epitopes of plant cell wall glycan-directed antibodies. Our results reveal the binding epitopes for 78 arabinogalactan-, rhamnogalacturonan-, xylan-, and
xyloglucan-directed antibodies. We demonstrate that, with knowledge of the exact epitopes recognized by individual antibodies, specific glycosyl hydrolases can be implemented into immunological cell wall analyses, providing a framework to obtain structural information on plant cell wall glycans with unprecedented molecular precision.

**General information**

State: Accepted/In press

Organisations: Department of Chemistry, Organic Chemistry, Max Planck Institute of Colloids and Interfaces, Freie Universität Berlin, Saitama University, University of Leeds, University of Georgia

Authors: Ruprecht, C. (Ekstern), Bartetzko, M. P. (Ekstern), Senf, D. (Ekstern), Dallabernardina, P. (Ekstern), Boos, I. (Intern), Andersen, M. C. F. (Intern), Kotake, T. (Ekstern), Knox, J. P. (Ekstern), Hahn, M. G. (Ekstern), Clausen, M. H. (Intern), Pfrengle, F. (Ekstern)

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BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.864 SNIP 1.857 CiteScore 6.45
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.775 SNIP 1.715
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 4.099 SNIP 1.796
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 4.083 SNIP 1.653
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 4.405 SNIP 1.792
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 3.902 SNIP 1.622
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 3.459 SNIP 1.7
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 3.379 SNIP 1.693
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 3.207 SNIP 1.689
Web of Science (2003): Indexed yes
Chemical Synthesis of Oligosaccharides related to the Cell Walls of Plants and Algae

Plant cell walls are composed of an intricate network of polysaccharides and proteins that varies during the developmental stages of the cell. This makes it very challenging to address the functions of individual wall components in cells, especially for highly complex glycans. Fortunately, structurally defined oligosaccharides can be used as models for the glycans, to study processes such as cell wall biosynthesis, polysaccharide deposition, protein-carbohydrate interactions, and cell-cell adhesion. Synthetic chemists have focused on preparing such model compounds, as they can be produced in good quantities and with high purity. This review contains an overview of those plant and algal polysaccharides, which have been elucidated to date. The majority of the content is devoted to detailed summaries of the chemical syntheses of oligosaccharide fragments of cellulose, hemicellulose, pectin, and arabinogalactans, as well as glycans unique to algae. Representative synthetic routes within each class are discussed in detail and the progress in carbohydrate chemistry over recent decades is highlighted.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Kinnaert, C. (Intern), Daugaard, M. (Intern), Nami, F. (Intern), Clausen, M. H. (Intern)
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Main Research Area: Technical/natural sciences

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Journal: Chemical Reviews
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Scopus rating (2016): CiteScore 42.79 SJR 19.282 SNIP 10.369
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BFI (2015): BFI-level 2
Scopus rating (2015): SJR 18.373 SNIP 11.51 CiteScore 45.92
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 18.369 SNIP 11.47 CiteScore 44.56
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 22.176 SNIP 12.915 CiteScore 49.12
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 20.511 SNIP 11.43 CiteScore 39.08
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Convenient one-step synthesis of 5-carboxy-seminaphthofluoresceins

The one-step synthesis and characterization of a series of regioisomerically pure 5-carboxy-seminaphthofluoresceins (5-carboxy-SNAFLs) is reported. The optical properties were determined in aqueous buffer at around biological pH, and highly pH sensitive, large Stokes-shift fluorophores with emission in the deep-red to near-infrared region were identified.

General information

State: Published
Organisations: Department of Chemistry, Center for Nanomedicine and Theranostics, X-ray Crystallography, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Organic Chemistry, Lund University
Authors: Hammershøj, P. (Intern), Thyhaug, E. (Ekstern), Harris, P. (Intern), Ek, P. K. (Intern), Andresen, T. L. (Intern), Clausen, M. H. (Intern)
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BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.757 SNIP 0.747 CiteScore 2.3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.794 SNIP 0.796 CiteScore 2.41
Web of Science (2014): Indexed yes
Convergent strategy for the synthesis of S-linked oligoxylans

Arabinoxylans (AX) are a major class of hemicellulose and an important polysaccharide component of lignocellulosic biomass. To utilize the glycan polymer effectively, it is desirable to learn more about the enzymatic hydrolysis of AXs. Well-defined glycans can help to elucidate these processes. Here, we report the efficient synthesis of a mixed O- and S-linked tetraxyylan. This thio-oligosaccharide has been developed as a putative inhibitor of arabinoxylan degrading enzymes used for the saccharification of biomass. Two common approaches for the synthesis of thio-oligosaccharides, either involving 1-thioglycoside donors or thioacceptors, are presented and compared regarding byproduct formation and yields. Both methods have shown to be useful for the synthesis of thiolinkages in oligoxylans assembly. However, the success of the reaction is highly dependent on the “match” between donors and acceptors.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics
Authors: Bonora, B. (Intern), Boos, I. (Intern), Clausen, M. H. (Intern)
Diastereoselective Synthesis of Novel Heterocyclic Scaffolds through Tandem Petasis 3-Component/Intramolecular Diels-Alder and ROM-RCM Reactions

A high-yielding, stereoselective and extraordinarily complexity generating Petasis 3-component/intramolecular Diels-Alder reaction has been developed. In combination with ROM-RCM, rapid access to complex sp³-rich heterocyclic scaffolds amenable to subsequent functionalization and library synthesis is provided.
Injectable iodine-125 labeled tissue marker for radioactive localization of non-palpable breast lesions

We have developed a \(^{125}\text{I}\)-radiolabeled injectable fiducial tissue marker with the potential to replace current methods used for surgical guidance of non-palpable breast tumors. Methods in routine clinical use today such as radioactive seed localization, radio-guided occult lesion localization and wire-guided localization suffers from limitations that this injectable fiducial tissue marker offers solutions to. The developed \(^{125}\text{I}\)-radiolabeled injectable fiducial tissue marker is based on highly viscous sucrose acetate isobutyrate. The marker was readily inserted in NMRI mice and proved to be spatially well-defined and stable over a seven day period with excellent CT contrast (>1500 HU), enabling fluoroscopic visualization of markers during placement. The radioactivity remains strongly associated with the marker during the implantation period, which limits exposure to healthy tissue. Biodistribution studies show that there is negligible radioactivity in all non-tumor tissues sampled, with the exception of the thyroid gland, where limited accumulation was observed (0.06% of injected dose after 7 days). Based on the excellent performance of the marker and the fact that it can be delivered through thin hypodermic needles (≥27G), the marker holds great promise for clinical application, since patient discomfort is reduced significantly compared to current methods. Statement of Significance. A new type of tissue marker for local administration to non-palpable breast tumors has been developed. The surgical guidance marker is based on derivatives of the biomaterial sucrose acetate isobutyrate and unlike currently used markers it is injectable in the tissue using thin needles, reducing the discomfort to the patients significantly. The marker confers CT contrast and has radioactive properties, meaning it also could find use in brachytherapy. The design of the iodine-125 labeled fiducial tissue marker enables control of dosimetry as well as a choice of iodine isotope used. The marker is anticipated to be clinical applicable due to its contrast performance in mice and its potential for enhanced flexibility in surgical procedures, compared to current methods.

General information
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Organisations: Department of Chemistry, Center for Nuclear Technologies, The Hevesy Laboratory, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Organic Chemistry, University of Copenhagen
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Publication information
Journal: Acta Biomaterialia
ISSN (Print): 1742-7061
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Synthesis and formulation studies of griseofulvin analogues with improved solubility and metabolic stability

Griseofulvin (1) is an important antifungal agent that has recently received attention due to its antiproliferative activity in mammalian cancer cells. Comprehensive SAR studies have led to the identification of 2'-benzyloxy griseofulvin 2, a more potent analogue with low micromolar anticancer potency in vitro. Analogue 2 was also shown to retard tumor growth through inhibition of centrosomal clustering in murine xenograft models of colon cancer and multiple myeloma. However, similar to griseofulvin, compound 2 exhibited poor metabolic stability and aqueous solubility. In order to improve the poor pharmacokinetic properties, 11 griseofulvin analogues were synthesized and evaluated for biological activity and physiological stabilities including SGF, plasma, and metabolic stability. Finally, the most promising compounds were investigated in respect to thermodynamic solubility and formulation studies. The 2'-benzylamine analogue 10 proved to be the most promising compound with low μM in vitro anticancer potency, a 200-fold increase in PBS solubility over compound 2, and with improved metabolic stability. Furthermore, this analogue proved compatible with formulations suitable for both oral and intravenous administration. Finally, 2'-benzylamine analogue 10 was confirmed to induce G2/M cell cycle arrest in vitro.
Unexpected interactions between gold and N-morpholino-sulfonates

Nanoporous gold (NPG) has a high surface area and excellent conductivity. It is an ideal supporting material for the electrocatalysis, e.g. in fuel cell applications. NPG is traditionally produced by etching a gold/silver alloy. This method has significant drawbacks, such as the introduction of silver into your NPG, and its multi-step fabrication. A method has been discovered for producing NPG as a thin film chemically. This bottom-up approach entails reduction of Au3+ precursor using morpholinoethanesulfonic acid (MES). This produces a thin and highly porous gold film at the air-Water interface1 (for details, see poster by Mikkel Christiansen). This chemical reaction is far more complex than first expected and bi-products, intermediates and reaction mechanisms are the focus of the present work. The chemical reaction and its products have been examined using state-of-the-art nuclear magnetic resonance (NMR), ultraviolet-visible spectroscopy (UV-vis), fluorescence spectroscopy, density functional theory (DFT), mass spectrometry (MS) and Raman spectroscopy. The results illustrate a complex chain of reactions resulting in gold nanoparticles, NPG, and several previously unidentified Au-complexes. N-NMR presented three different 13+/+environments for the N-atom in MES, while the UV-vis results points...
towards some interesting gold complexes. MS identifies several distinct molecular entities demonstrating the reactivity of MES and Au, and fluorescence spectroscopy suggests the formation of polynuclear Au complexes as previously reported where Au nuclei are bridged by C=N functionalities in small organic molecules. This adds up to a complicated reaction mechanism involving some interesting Au $^{3+}/^{1+}$ complexes, deprotonation and oxidation of MES and the formation of molecules that show UV-vis absorbance and fluorescence.

**General information**
State: Published
Organisations: Department of Chemistry, NanoChemistry, Organic Chemistry, University of California, San Diego, University of Copenhagen
Authors: Nielsen, F. S. (Intern), Engelbrekt, C. (Intern), Elliot, S. G. (Intern), Junor, G. (Ekstern), Sørensen, K. (Ekstern), Jensen, K. J. (Ekstern), Clausen, M. H. (Intern), Zhang, J. (Intern)
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**Accessing Tri-substituted γ-Lactam Scaffolds Via Cascade Reactions: What Opportunities For Libraries!**
The European Lead Factory is an EU-based initiative (part of the Innovative Medicines Initiative), which has been set to foster drug discovery in Europe. Among the objectives, a 200,000-compound collection is being generated. Lactams represent a large class of valuable scaffolds for medicinal chemistry and remain a wide and interesting area of study. In this context, 2 libraries based on a 1,4,5 γ-lactam core have been designed and produced using cascade reactions involving an aldehyde moiety, an amine and a nucleophilic partner as the key reaction. One library is focused on a 3-MCR on oxo-esters, while the other is based on a Ritter-type cascade. On several occasions these multi-component and one-pot processes have been used directly as the production step, thus allowing very fast and diverse library syntheses, whereas in other cases, the choice of partners bearing other anchoring groups permitted further functionalization and the production of even more diverse members of the libraries. The > 1,000 compounds based on these scaffolds have been delivered for HTS at the European Screening Center where they are currently being tested.

**General information**
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Organisations: Department of Chemistry, Organic Chemistry, Department of Organic Chemistry, EDELRIS
Authors: Bonnet, K. (Ekstern), Clausen, M. H. (Intern), Fleury-Brégeot, N. (Ekstern), Lardy, C. (Ekstern), Morgentin, R. (Ekstern), Nielseni, T. E. (Intern), Petersen, M. A. (Intern), Rasmussen, M. O. (Ekstern), Roche, D. (Ekstern), Wu, P. (Intern)
Publication date: 2016
Event: Abstract from Experimental biology 2016, San Diego, United States.
Main Research Area: Technical/natural sciences
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http://www.fasebj.org/content/30/1_Supplement/lb473.abstract
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**A metal-catalyzed enyne-cyclization step for the synthesis of bi- and tricyclic scaffolds amenable to molecular library production**
A facile metal-catalyzed diversification step for the synthesis of novel bi- and tricyclic scaffolds from enyne substrates is reported in this study. From a single starting material, topologically diverse scaffolds for library synthesis can be generated and decorated in a few steps. The methodology was used to produce a library of 490 compounds within the European Lead Factory (ELF) Consortium.

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Organisations: Organic Chemistry, Department of Chemistry, EDELRIS
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- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 1.41 SNIP 0.858 CiteScore 3.47
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 1.387 SNIP 0.903 CiteScore 3.5
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 1.481 SNIP 0.897 CiteScore 3.55
- ISI indexed (2013): ISI indexed yes
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- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 1.635 SNIP 0.934 CiteScore 3.47
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- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 1.737 SNIP 0.974 CiteScore 3.71
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 1.775 SNIP 0.951
- Web of Science (2010): Indexed yes
- BFI (2009): BFI-level 2
- Scopus rating (2009): SJR 1.831 SNIP 1.073
- Web of Science (2009): Indexed yes
- BFI (2008): BFI-level 2
- Scopus rating (2008): SJR 1.936 SNIP 1.042
- Web of Science (2008): Indexed yes
- Scopus rating (2007): SJR 1.843 SNIP 0.984
- Web of Science (2007): Indexed yes
- Scopus rating (2006): SJR 1.557 SNIP 0.957
- Web of Science (2006): Indexed yes
- Scopus rating (2005): SJR 1.245 SNIP 1.098
- Web of Science (2005): Indexed yes
- Scopus rating (2004): SJR 1.274 SNIP 0.999
- Web of Science (2004): Indexed yes
- Scopus rating (2003): SJR 0.1
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Characterization of the LM5 pectic galactan epitope with synthetic analogues of β-1,4-d-galactotetraose

Plant cell wall glycans are important polymers that are crucial to plant development and serve as an important source of sustainable biomass. The study of polysaccharides in the plant cell wall relies heavily on monoclonal antibodies for localization and visualization of glycans, using e.g. Immunofluorescent microscopy. Here, we describe the detailed epitope mapping of the mab LM5 that is shown to bind to a minimum of three sugar residues at the non-reducing end of linear beta-1,4-linked galactan. The study uses de novo synthetic analogs of galactans combined with carbohydrate microarray and competitive inhibition ELISA for analysis of antibody-carbohydrate interactions.
Development of peptidic anti-dendrotoxins

The black mamba (Dendroaspis polylepis) is one of the most feared and dangerous snakes in the world, and its bite has a very high mortality and morbidity rate. Dendrotoxins, the most abundant and some of the most toxic components present in black mamba venom, target potassium channels in neuronal tissue, leading to hyper-excitability in victims and prey. Blockage of the potassium channels can lead to respiratory paralysis and eventually death. Early administration of appropriate antivenom is the only effective snakebite therapy to date. However, current antivenoms are still being produced by the very laborious and expensive traditional animal immunization techniques, leading to severe side effects in human recipients due to their heterologous nature. In contrast, novel approaches based on synthetic or recombinant antivenoms may offer an alternative solution, saving cost, limiting side effects, and providing more effective neutralization of snake venom.

General information
State: Published
Organisations: Department of Systems Biology, Department of Chemistry, Organic Chemistry, Technical University of Denmark, University of Copenhagen
Authors: Oscoz, S. (Ekstern), Laustsen, A. H. (Intern), Clausen, M. H. (Intern), Lohse, B. (Ekstern)
Number of pages: 1
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Event: Abstract from 14th Protein.DTU Workshop, Kgs. Lyngby, Denmark.
Main Research Area: Technical/natural sciences
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Observations on the Influence of Precursor Conformations on Macrocyclization Reactions

Macrocycles hold great promise in drug discovery as an underutilized class of lead compounds. The low abundance of these molecules can, in part, be explained by the inherent difficulties in the synthesis of macrocycles and the lack of general methods for their rapid assembly. We have undertaken a research program aimed at developing methods for facile synthesis of macrocycles from simple precursors. The synthesis of two new cyclization precursors is described and the results of their reaction with thionyl chloride are presented and discussed. Whereas one acyclic diol smoothly underwent macrocyclization to afford a mixture of diastereomeric sulfites, subjection of the other precursor to identical reaction conditions resulted in the isolation of the linear dichloride. We hypothesize that there is a difference in the ability of the two molecules to adopt a conformation that is germane to macrocyclization, a proposition that is supported by conformational analyses using molecular mechanics.
Small-molecule kinase inhibitors: an analysis of FDA-approved drugs

Small-molecule kinase inhibitors (SMKIs), 28 of which are approved by the US Food and Drug Administration (FDA), have been actively pursued as promising targeted therapeutics. Here, we assess the key structural and physicochemical properties, target selectivity and mechanism of function, and therapeutic indications of these approved inhibitors. Our analysis showed that >30% of approved SMKIs have a molecule weight (MW) exceeding 500 and all have a total ring count of between three and five. The assumption that type II inhibitors tend to be more selective than type I inhibitors has been proved to be unreliable. Although previous SMKI research was concentrated on tyrosine kinase inhibitors for cancer treatment, recent progress indicates diversification of SMKI research in terms of new targets, mechanistic types, and therapeutic indications.

General information
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Organisations: Department of Chemistry, Organic Chemistry
Authors: Wu, P. (Intern), Nielsen, T. E. (Intern), Clausen, M. H. (Intern)
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.11 SJR 2.124 SNIP 1.7
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.085 SNIP 1.596 CiteScore 5.62
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.84 SNIP 1.61 CiteScore 5.61
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.005 SNIP 1.843 CiteScore 6.04
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.951 SNIP 1.993 CiteScore 5.96
ISI indexed (2012): ISI indexed yes
Strategies for improving the solubility and metabolic stability of griseofulvin analogues

We report two types of modifications to the natural product griseofulvin as strategies to improve solubility and metabolic stability: the conversion of aryl methyl ethers into aryl difluoromethyl ethers at metabolic hotspots and the conversion of the C-ring ketone into polar oximes. The syntheses of the analogues are described together with their solubility, metabolic half-life in vitro and antiproliferative effect in two cancer cell lines. We conclude that on balance, the formation of polar oximes is the most promising strategy for improving the properties of the analogues.

General information

State: Published
Organisations: Department of Chemistry, Organic Chemistry, German Cancer Research Center (DKFZ)
Authors: Petersen, A. B. (Intern), Konotop, G. (Ekstern), Hanafiah, N. H. M. (Ekstern), Hammershøj, P. (Intern), Raab, M. S. (Ekstern), Kraemer, A. (Ekstern), Clausen, M. H. (Intern)
Number of pages: 6
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Publication information

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BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.35 SJR 1.272 SNIP 1.562
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.152 SNIP 1.471 CiteScore 3.87
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.074 SNIP 1.668 CiteScore 3.84
BFI (2013): BFI-level 1
Synthesis of oligo (1→5)-α-L-arabinofuranosides related to the plant polysaccharide pectin

A strong fundamental understanding of plant biology is essential for meeting society's growing demand for safe and nutritious food, dietary fibers, clothes, and renewable energy sources for an increasing global population. The plant cell wall is one of the main targets for biotechnological research, as it represents almost 50% of plant biomass. A major constituent of the plant cell wall is different complex polysaccharides. The knowledge about their detailed structure and function on a molecular level is far from complete, and structural studies are complicated by the great complexity of the cell wall. The diversity of polysaccharides and the microheterogeneity in the cell wall make it extremely challenging to isolate well-defined compounds after partial degradation of plant material. Chemical synthesis, on the other hand, is capable of producing structurally diverse oligosaccharides of excellent purity, and in larger quantities.

The objective of the present study is to design and execute chemical syntheses of well-defined pectic oligosaccharides. These can serve as models for the more complex polysaccharide network found in the plant cell wall. The chemical synthesis of two branched structures of oligo (1→5)-α-L-arabinofuranosides that are prominent side chains in RG-I is presented. By employing a disaccharide donor, the number of glycosylation reactions was reduced significantly and late stage regioselective deprotection made it possible to introduce different sidechains in the oligosaccharides.

The work done during an external research stay at University of Copenhagen is also described. This includes the implementation of a covalent linker system as an alternative to bovine serum albumin (BSA) for oligosaccharides, as well as the development of a microarray-based transglycosylation assay capable of screening for novel glycosyl transferase/hydrolase activities.

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Organisations: Department of Chemistry, Organic Chemistry
Authors: Daugaard, M. (Intern), Clausen, M. H. (Intern)
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Synthesis of S-linked cello-oligosaccharides

Plant cell walls represent almost 50% of the biomass found in plants and therefore constitute one of the main targets for biotechnological research. For this reason, the transition to a sustainable bio-resource for future energy can primarily be founded on plant cell walls. Thus, in order to achieve a sustainable development, it is necessary to optimize plant production and its utilization. The polysaccharides present in the plant cell wall vary depending on the plant species and change during the developmental stage of the plant. As a result, this makes it very challenging to address the function of each individual component. The conversion of lignocellulosic biomass still remains a big challenge nowadays with the enzymatic hydrolysis being the limiting step. Indeed, characterization of the enzymes involved in this process can help the optimization development. For this reason, structurally well-defined oligosaccharides made via chemical synthesis can be used as models for the more complex polysaccharides in the investigation of properties such as polysaccharide biosynthesis, degradation and protein-carbohydrate interactions. For this purpose, non-natural substrate analogues forming irreversible binding to the enzyme can be employed. Thio-oligosaccharides represent the largest class of specific non-natural inhibitors for glycanases. In this thesis the chemical synthesis of some thio-glucans is presented. The formation of thio-linkages using a classical and non-classical method is investigated. Two strategies, relying on either a linear or a convergent strategy, have been employed in the synthesis towards two target molecules. Furthermore, the activity of a glycosyltransferase responsible for the elongation of a pectic polysaccharide has been investigated and partially characterized.

Synthesis of S-linked oligoxylans

The transition from a petroleum-dependent economy to one based on sustainable bio-resources will largely be founded on plant cell walls, as these are the largesource of biomass on earth. However, the development of lignocellulosic biomass conversion to fine chemicals and polymers still remains a big challenge for the biofuel industry. In particular, the enzymatic hydrolysis of lignocellulosic polysaccharides is one of the limiting steps of the entire procedure and therefore the enzymes involved in the degradation process must ideally be characterized and understood. This requires a detailed understanding of cell wall polysaccharide decomposition and architecture. Hemicelluloses are the second most abundant polymers in lignocellulosic biomass. They include different types of polysaccharides such as xyloglucans, xylans, mannans, glucomannans and β-(1→3,1→4)-glucans. Xylans are heteropolymers possessing a β-(1→4)-D-xylopyranose backbone, which is branched by short carbohydrate chains. The branches include D-glucuronic acid and its methyl ether, L-arabinose and/or various oligosaccharides like D-xylose, L-arabinose, D- or L-galactose and D-glucose. The hydrolysis of these polysaccharides is catalyzed by several families of enzymes, collected under the name of Glycosyl...
Hydrolases (GHs). Among other methods, the use of enzyme inhibitors like thio-linked oligosaccharides has for a long time been a common tool to analyze and characterize these enzymes. In the present work, the chemical synthesis of thio-analogs of xylo- and arabinoxyloglycans is presented. Furthermore, the selection of a reliable method for the incorporation of thiolinkages in the synthesis of oligoxylans is also investigated. Therefore, different strategies for assembling S-linked-disaccharides have been approached both involving 1-thioglycoside donors and thioacceptors. Advantages and disadvantages concerning the different methods are described and evaluated in relation to the synthesis of linear and branched oligoxylans.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Joint Bioenergy Institute
Authors: Bonora, B. (Intern), Clausen, M. H. (Intern), Scheller, H. V. (Ekstern)
Number of pages: 168
Publication date: 2016

Synthesis of S-linked oligoxylans
An efficient strategy for the synthesis of complex small molecules from simple building blocks is presented. Key steps of the strategy include tandem Petasis and Diels–Alder reactions, and divergent complexity-generating cyclization cascades from a key dialdehyde intermediate. The methodology is validated through the synthesis of a representative compound set, which has been used in the production of 1617 molecules for the European Lead Factory.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, EDELRIS, Nanyang Technological University
Authors: Flagstad, T. (Intern), Min, G. (Intern), Bonnet, K. (Ekstern), Morgentin, R. (Ekstern), Roche, D. (Ekstern), Clausen, M. H. (Intern), Nielsen, T. E. (Intern)
Pages: 4943-4946
Publication date: 2016
Main Research Area: Technical/natural sciences

Synthesis of sp3-rich scaffolds for molecular libraries through complexity-generating cascade reactions
An efficient strategy for the synthesis of complex small molecules from simple building blocks is presented. Key steps of the strategy include tandem Petasis and Diels–Alder reactions, and divergent complexity-generating cyclization cascades from a key dialdehyde intermediate. The methodology is validated through the synthesis of a representative compound set, which has been used in the production of 1617 molecules for the European Lead Factory.
The synthesis of linear- and (1→6)-branched-β-(1→4)-D-galactans, side chains of the pectic polysaccharide rhamnogalacturonan I is described. The strategy relies on iterative couplings of n-pentenyl disaccharides followed by a late stage glycosylation of a common hexasaccharide core. Reaction with a covalent linker and immobilization on NHS-modified glass surfaces allows for the generation of carbohydrate microarrays. The glycan arrays enables the study of protein-carbohydrate interactions in a high throughput fashion, here demonstrated with binding to mAbs and CBMs.

Synthesis of β-1,4-Linked Galactan Side-Chains of Rhamnogalacturonan I

The synthesis of linear- and (1→6)-branched-β-(1→4)-D-galactans, side chains of the pectic polysaccharide rhamnogalacturonan I is described. The strategy relies on iterative couplings of n-pentenyl disaccharides followed by a late stage glycosylation of a common hexasaccharide core. Reaction with a covalent linker and immobilization on NHS-modified glass surfaces allows for the generation of carbohydrate microarrays. The glycan arrays enables the study of protein-carbohydrate interactions in a high throughput fashion, here demonstrated with binding to mAbs and CBMs.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, University of Copenhagen
Authors: Andersen, M. C. F. (Intern), Kracun, S. (Ekstern), Rydahl, M. (Ekstern), Willats, W. (Ekstern), Clausen, M. H. (Intern)
Number of pages: 6
Pages: 11543-11548
Publication date: 2016
Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 5.03 SJR 2.247 SNIP 1.046
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.416 SNIP 1.184 CiteScore 4.99
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.487 SNIP 1.219 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.604 SNIP 1.239 CiteScore 5.68
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.884 SNIP 1.294 CiteScore 5.55
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.726 SNIP 1.336 CiteScore 5.46
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.527 SNIP 1.292
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.499 SNIP 1.365
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 2.887 SNIP 1.407
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.233 SNIP 1.532
Scopus rating (2006): SJR 2.911 SNIP 1.505
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 2.62 SNIP 1.454
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 2.32 SNIP 1.472
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 2.156 SNIP 1.45
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 2.554 SNIP 1.472
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 2.834 SNIP 1.612
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 2.956 SNIP 1.652
Web of Science (2000): Indexed yes
Tandem Mannich/Diels–Alder reactions for the synthesis of indole compound libraries

A tandem Mannich/Diels–Alder sequence for the synthesis of small-molecule libraries with an indolyl-octahydro-3a,6-epoxy-isindole core structure is demonstrated in this study. Representative diversification examples based on this scaffold were performed, and a library is being produced within the European Lead Factory (ELF) Consortium.

General information

State: Published
Organisations: Department of Chemistry, Organic Chemistry, EDELRIS
Authors: Wu, P. (Intern), Petersen, M. Å. (Intern), Petersen, R. (Intern), Flagstad, T. (Intern), Guilleux, R. (Ekstern), Ohsten Rasmussen, M. (Ekstern), Morgentin, R. (Ekstern), Nielsen, T. E. (Intern), Clausen, M. H. (Intern)
Pages: 46654-46657
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information

Journal: RSC Advances
Volume: 2016
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ISSN (Print): 2046-2069
Ratings:
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  - Web of Science (2017): Indexed yes
  - BFI (2016): BFI-level 1
  - Scopus rating (2016): CiteScore 3.06 SJR 0.875 SNIP 0.743
  - Web of Science (2016): Indexed yes
  - BFI (2015): BFI-level 1
  - Scopus rating (2015): SJR 0.959 SNIP 0.837 CiteScore 3.42
  - Web of Science (2015): Indexed yes
  - BFI (2014): BFI-level 1
  - Scopus rating (2014): SJR 1.114 SNIP 0.965 CiteScore 3.87
  - Web of Science (2014): Indexed yes
  - BFI (2013): BFI-level 1
  - Scopus rating (2013): SJR 1.117 SNIP 0.903 CiteScore 3.74
  - ISI indexed (2013): ISI indexed yes
  - Web of Science (2013): Indexed yes
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Publication: Research - peer-review › Journal article – Annual report year: 2016
Method for the preparation of intermediates for carboxy-fluoresceins and novel carboxy-fluorescein.

The invention provides a method for the preparation of regioisomerically pure intermediates which are useful for the preparation of carboxy-fluorescein-type compounds. Such compounds have broad applications within bio-conjugation and/or fluorescent imaging.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Hammershøj, P. L. (Ekstern), Clausen, M. H. (Intern)
Publication date: 12 Nov 2015

Publication information
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Patent number: WO2015169854
Date: 12/01/1915
Priority date: 26/03/2015
Priority number: EP20150161033
Original language: English
Main Research Area: Technical/natural sciences
Source: espacenet
Source-ID: WO2015169854
Publication: Research › Patent – Annual report year: 2016

A hydrogel based nanosensor with an unprecedented broad sensitivity range for pH measurements in cellular compartments

Optical pH nanosensors have been applied for monitoring intracellular pH in real-time for about two decades. However, the pH sensitivity range of most nanosensors is too narrow, and measurements that are on the borderline of this range may not be correct. Furthermore, ratiometric measurements of acidic intracellular pH (pH < 4) in living cells are still challenging due to the lack of suitable nanosensors. In this paper we successfully developed a multiple sensor, a fluorophore based nanosensor, with an unprecedented broad measurement range from pH 1.4 to 7.0. In this nanosensor, three pH-sensitive fluorophores (difluoro-Oregon Green, Oregon Green 488, and fluorescein) and one pH-insensitive fluorophore (Alexa 568) were covalently incorporated into a nanoparticle hydrogel matrix. With this broad range quadruple-labelled nanosensor all physiological relevant pH levels in living cells can be measured without being too close to the limits of its pH-range. The nanosensor exhibits no susceptibility to interference by other intracellular ions at physiological concentrations. Due to its positive surface charge it is spontaneously internalized by HeLa cells and localizes to the lysosomes where the mean pH was measured at 4.6. This quadruple-labelled nanosensor performs accurate measurements of fluctuations of lysosomal pH in both directions, which was shown by treatment with the V-ATPase inhibitor bafilomycin A1 or its substrate ATP in HeLa cells. These measurements indicate that this novel quadruple-labelled nanosensor is a promising new tool for measuring the pH of acidic compartments in living cells.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Department of Chemistry, Physical and Biophysical Chemistry, Organic Chemistry, Technical University of Denmark, Shanghai Jiaotong University
Authors: Zhang, M. (Ekstern), Søndergaard, R. V. (Intern), Ek, P. K. (Intern), Henriksen, J. R. (Intern), Cui, D. (Ekstern), Hammershøj, P. (Intern), Clausen, M. H. (Intern), Andresen, T. L. (Intern)
Number of pages: 8
Pages: 7246-7253
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Analyst
Volume: 140
ISSN (Print): 0003-2654
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Allosteric small-molecule kinase inhibitors

Small-molecule kinase inhibitors are invaluable targeted therapeutics for the treatment of various human diseases, especially cancers. While the majority of approved and developed preclinical small-molecule inhibitors are characterized as type I or type II inhibitors that target the ATP-binding pocket of kinases, the remarkable sequential and structural similarity among ATP pockets renders the selective inhibition of kinases a daunting challenge. Therefore, targeting allosteric pockets of kinases outside the highly conserved ATP pocket has been proposed as a promising alternative to overcome current barriers of kinase inhibitors, including poor selectivity and emergence of drug resistance. In spite of the small number of identified allosteric inhibitors in comparison with that of inhibitors targeting the ATP pocket, encouraging results, such as the FDA-approval of the first small-molecule allosteric inhibitor trametinib in 2013, the progress of more than 10 other allosteric inhibitors in clinical trials, and the emergence of a pipeline of highly selective and potent preclinical molecules, have been reported in the past decade. In this article, we present the current knowledge on allosteric inhibition in terms of conception, classification, potential advantages, and summarized debatable topics in the field. Recent progress and allosteric inhibitors that were identified in the past three years are highlighted in this paper.
Cyclic N-acyliminium ions for the diversity-oriented synthesis of functionalized γ-lactams

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Wu, P. (Intern), Nielsen, T. E. (Intern), Clausen, M. H. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from 250th American Chemical Society National Meeting & Exposition, Boston, United States.
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Discovery and optimization of peptide-based anti-cobratoxins

More than 5.5 million people per year are victims of snake envenomation, resulting in 125,000 deaths and 400,000 amputations worldwide. Antivenoms are still produced by animal immunization procedures, and they are associated with a high risk of severe adverse reactions. Alternatively, synthetic peptides may open the possibility for new therapies with better efficacy and safety. Here, we report the discovery and optimization of a synthetic peptide directed against α-cobratoxin (α-CTX), the most toxic component of Monocled cobra (Naja kaouthia).

Facile Large-Scale Synthesis of 5- and 6-Carboxyfluoresceins: Application for the Preparation of New Fluorescent Dyes

A series of fluorescein dyes have been prepared from a common precursor through a very simple synthetic procedure, giving access to important precursors for fluorescent probes. The method has proven an efficient access to regioisomerically pure 5- and 6-carboxyfluoresceins on a large scale, in good yields, and with high regioisomeric purity. Furthermore, we have applied the method to the development of a new type of mixed fluorescein derivatives of 5-carboxyfluorescein. We have demonstrated the scope of the procedure by synthesizing a new type of double chromophore within the fluoro-Jade family.
FDA-approved small-molecule kinase inhibitors

Kinases have emerged as one of the most intensively pursued targets in current pharmacological research, especially for cancer, due to their critical roles in cellular signaling. To date, the US FDA has approved 28 small-molecule kinase inhibitors, half of which were approved in the past 3 years. While the clinical data of these approved molecules are widely presented and structure–activity relationship (SAR) has been reported for individual molecules, an updated review that analyzes all approved molecules and summarizes current achievements and trends in the field has yet to be found. Here we present all approved small-molecule kinase inhibitors with an emphasis on binding mechanism and structural features, summarize current challenges, and discuss future directions in this field.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, Novo Nordisk A/S
Authors: Wu, P. (Intern), Nielsen, T. E. (Ekstern), Clausen, M. H. (Intern)
Number of pages: 18
Injectable Colloidal Gold for Use in Intrafractional 2D Image-Guided Radiation Therapy

In the western world, approximately 50% of all cancer patients receive radiotherapy alone or in combination with surgery or chemotherapy. Image-guided radiotherapy (IGRT) has in recent years been introduced to enhance precision of the delivery of radiation dose to tumor tissue. Fiducial markers are often inserted inside the tumor to improve IGRT precision and to enable monitoring of the tumor position during radiation therapy. In the present article, a liquid fiducial tissue marker...
is presented, which can be injected into tumor tissue using thin and flexible needles. The liquid fiducial has high radio-opacity, which allows for marker-based image guidance in 2D and 3D X-ray imaging during radiation therapy. This is achieved by surface-engineering gold nanoparticles to be highly compatible with a carbohydrate-based gelation matrix. The new fiducial marker is investigated in mice where they are highly biocompatible and stable after implantation. To investigate the clinical potential, a study is conducted in a canine cancer patient with spontaneous developed solid tumor in which the marker is successfully injected and used to align and image-guide radiation treatment of the canine patient. It is concluded that the new fiducial marker has highly interesting properties that warrant investigations in cancer patients.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Department of Applied Mathematics and Computer Science, Image Analysis & Computer Graphics, Colloids and Biological Interfaces, Department of Chemistry, Organic Chemistry, University of Copenhagen, Copenhagen University Hospital
Number of pages: 8
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Publication date: 2015
Main Research Area: Technical/natural sciences

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Journal: Advanced Healthcare Materials
Volume: 4
Issue number: 6
ISSN (Print): 2192-2640
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.26 SJR 1.906 SNIP 1.108
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.323 SNIP 1.172 CiteScore 5.91
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.056 SNIP 1.168 CiteScore 5.29
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.549 SNIP 0.948 CiteScore 4.39
ISI indexed (2013): ISI indexed yes
ISI indexed (2012): ISI indexed no
Web of Science (2012): Indexed yes
Original language: English
Computed tomography, Fiducial markers, Gold nanoparticles, Image-guided radiation therapy, Sucrose acetate isobutyrate
Electronic versions:
DOIs: 10.1002/adhm.201400651
Source: FindIt
Source-ID: 274907740
Publication: Research - peer-review › Journal article – Annual report year: 2015

Optimization of anti-cobratoxins for treatment of neurotoxic envenomings
Cobras (Naja spp.) are some of the most venomous and dangerous snakes worldwide, responsible for high mortality and morbidity. The most toxic components of cobra venoms are cobratoxins, which target the nicotinic acetylcholine receptors (nAChRs) responsible for neuromuscular transmission. Inhibition of nAChRs may lead to respiratory arrest with death as a result within 3-12 hr after a bite from a cobra. Early parental administration of appropriate antivenom is the cornerstone of life saving snakebite therapy. However, current antivenoms are still produced by animal immunization, which is a laborious and expensive process yielding highly immunogenic antivenoms due to the heterologous nature of equine antibodies in
the antivenom. In contrast, novel antivenom based on synthetic peptides may offer an alternative solution, which is less expensive and cause less side effects.

**General information**
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Technical University of Denmark, University of Copenhagen
Authors: Solà, M. (Ekstern), Laustsen, A. H. (Intern), Olsen, L. (Ekstern), Clausen, M. H. (Intern), Lohse, B. (Ekstern)
Number of pages: 1
Publication date: 2015
Event: Abstract from 13th Protein.DTU Workshop, Lyngby, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016

**Reductive Cyclization and Petasis-Like Reaction for the Synthesis of Functionalized γ-Lactams**
An efficient reductive cyclization strategy was employed for the synthesis of N-substituted β,γ-dihydroxy-γ-lactams. A subsequent Petasis-like reaction (PLR) through nucleophilic additions of boronic acids to intermediate N-acyliminium ions produced substituted γ-lactams. Overall, the application of this protocol provides β,γ-dihydroxy-γ-lactams and functionalized γ-lactams with potential interest for synthetic and bioorganic chemistry.

**General information**
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics
Authors: Wu, P. (Intern), Petersen, M. Å. (Intern), Cohrt, A. E. (Intern), Petersen, R. (Intern), Clausen, M. H. (Intern), Nielsen, T. E. (Intern)
Number of pages: 5
Pages: 2346-2350
Publication date: 2015
Main Research Area: Technical/natural sciences

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BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.74 SJR 1.133 SNIP 0.653
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.198 SNIP 0.758 CiteScore 2.88
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.181 SNIP 0.767 CiteScore 2.96
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.292 SNIP 0.796 CiteScore 2.96
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.471 SNIP 0.811 CiteScore 2.93
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.536 SNIP 0.857 CiteScore 3.2
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Ritter-Hydrolysis Cascade Strategy for the Synthesis of Substituted gamma-Lactams

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Wu, P. (Intern), Nielsen, T. E. (Intern), Clausen, M. H. (Intern)
Number of pages: 1
Publication date: 2015
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Main Research Area: Technical/natural sciences
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Synthesis of 1,4,5 trisubstituted γ-lactams via a 3-component cascade reaction
A three component one-pot cascade reaction was developed for the synthesis of 1,4,5-trisubstituted γ-lactams. The resulting scaffold can be modified independently at three positions, two of which are conveniently accessed by changing the components of the one-pot reaction. The phases of building block generation, scaffold synthesis and subsequent
appendage modification were adapted to library production, which resulted in a screening library of 500 compounds.

**General information**
State: Published
Organisations: Department of Chemistry, Organic Chemistry, EDELRIS
Authors: Petersen, M. Å. (Intern), Mortensen, M. A. (Intern), Cohrt, A. E. (Intern), Petersen, R. (Intern), Wu, P. (Intern), Fleury-Brégot, N. (Ekstern), Morgentin, R. (Ekstern), Lardy, C. (Ekstern), Nielsen, T. E. (Intern), Clausen, M. H. (Intern)
Number of pages: 4
Pages: 2695-2698
Publication date: 2015
Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.978 SNIP 0.969 CiteScore 2.96
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.038 SNIP 1.058 CiteScore 3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.01 SNIP 1.101 CiteScore 2.87
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.063 SNIP 1.21 CiteScore 3.08
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.2 SNIP 1.312 CiteScore 3.12
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.145 SNIP 1.285 CiteScore 3.09
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.072 SNIP 1.294
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.121 SNIP 1.353
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.175 SNIP 1.25
Scopus rating (2007): SJR 1.051 SNIP 1.237
Scopus rating (2006): SJR 0.911 SNIP 1.167
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.881 SNIP 0.995
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.802 SNIP 1.012
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.868 SNIP 1.007
Web of Science (2003): Indexed yes
Synthesis of (Arylamido)pyrrolidinone Libraries through Ritter-Type Cascade Reactions of Dihydroxylactams

The Ritter-type reaction of arylnitriles and N-acyliminium ions generated in situ from dihydroxy-γ-lactams gave tetrahydropyrrolo[2,3-d]oxazol-5-ones in excellent yields. A subsequent acidic hydrolysis in EtOH/H₂O/TFA (trifluoroacetic acid) yielded new (arylamido)pyrrolidinones with excellent cis diastereoselectivity. A combined one-step Ritter–hydrolysis procedure proved to be of equal efficiency. This versatile method, which was successfully used for the construction of a screening library containing 706 molecules within the European Lead Factory consortium, provides a simple way to access new compounds incorporating an arylamido and a pyrrolidinone moiety, both of which are widely found in marketed drugs and in biologically active molecules.

Molecular libraries of natural product-like and structurally diverse compounds are attractive in early drug discovery campaigns. In here, we present synthetic methodology for library production of hexahydropyrrolo[2,1-a]isoquinoline (HPIQ) compounds. Two advanced HPIQ intermediates, both incorporating two handles for diversification, were synthesized through an oxidative cleavage/Pictet–Spengler reaction sequence in high overall yields. A subsequent metal-catalyzed cross coupling/amidation protocol was developed and its utility in library synthesis was validated by construction of a 20-membered natural product-like molecular library in good overall yields.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Petersen, R. (Intern), Cohrt, A. E. (Intern), Petersen, M. Å. (Intern), Wu, P. (Intern), Clausen, M. H. (Intern), Nielsen, T. E. (Intern)
Number of pages: 4
Pages: 2646-2649
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Bioorganic & Medicinal Chemistry
Volume: 23
Issue number: 11
ISSN (Print): 0968-0896
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
Distinct substrate specificities of three glycoside hydrolase family 42 β-galactosidases from Bifidobacterium longum subsp. infantis ATCC 15697

Glycoside hydrolase family 42 (GH42) includes β-galactosidases catalyzing the release of galactose (Gal) from the non-reducing end of different β-d-galactosides. Health-promoting probiotic bifidobacteria, which are important members of the human gastrointestinal tract microbiota, produce GH42 enzymes enabling utilization of β-galactosides exerting prebiotic effects. However, insight into the specificity of individual GH42 enzymes with respect to substrate monosaccharide composition, glycosidic linkage and degree of polymerization is lagging. Kinetic analysis of natural and synthetic
substrates resembling various milk and plant galactooligosaccharides distinguishes the three GH42 members, Bga42A, Bga42B and Bga42C, encoded by the probiotic B. longum subsp. infantis ATCC 15697 and revealed the glycosyl residue at subsite +1 and its linkage to the terminal Gal at subsite −1 to be key specificity determinants. Bga42A thus prefers the β1-3-galactosidic linkage from human milk and other β1-3- and β1-6-galactosides with glucose or Gal situated at subsite +1. In contrast, Bga42B very efficiently hydrolyses 4-galactosyllactose (Galβ1-4Galβ1-4Glc) as well as 4-galactobiose (Galβ1-4Gal) and 4-galactotriose (Galβ1-4Galβ1-4Gal). The specificity of Bga42C resembles that of Bga42B, but the activity was one order of magnitude lower. Based on enzyme kinetics, gene organization and phylogenetic analyses, Bga42C is proposed to act in the metabolism of arabinogalactan-derived oligosaccharides. The distinct kinetic signatures of the three GH42 enzymes correlate to unique sequence motifs denoting specific clades in a GH42 phylogenetic tree providing novel insight into GH42 subspecificities. Overall, the data illustrate the metabolic adaptation of bifidobacteria to the β-galactoside-rich gut niche and emphasize the importance and diversity of β-galactoside metabolism in probiotic bifidobacteria.

**General information**

State: Published

Organisations: Department of Systems Biology, Enzyme and Protein Chemistry, Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, Ishikawa Prefectural University, National Agriculture and Food Research Organization, Obihiro University of Agriculture and Veterinary Medicine

Authors: Viborg, A. H. (Intern), Katayama, T. (Extern), Abou Hachem, M. (Intern), Andersen, M. C. F. (Intern), Nishimoto, M. (Extern), Clausen, M. H. (Intern), Urashima, T. (Extern), Svensson, B. (Intern), Kitaoka, M. (Extern)

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Scopus rating (2015): SJR 1.638 SNIP 1.142 CiteScore 3.4

Web of Science (2015): Indexed yes

BFI (2014): BFI-level 1

Scopus rating (2014): SJR 1.535 SNIP 0.954 CiteScore 3.04

Web of Science (2014): Indexed yes

BFI (2013): BFI-level 1

Scopus rating (2013): SJR 1.655 SNIP 1.275 CiteScore 3.76

ISI indexed (2013): ISI indexed yes

BFI (2012): BFI-level 1

Scopus rating (2012): SJR 1.711 SNIP 1.137 CiteScore 3.41

ISI indexed (2012): ISI indexed yes

BFI (2011): BFI-level 1

Scopus rating (2011): SJR 1.573 SNIP 1.199 CiteScore 3.61

ISI indexed (2011): ISI indexed yes

Web of Science (2011): Indexed yes

BFI (2010): BFI-level 1

Scopus rating (2010): SJR 1.829 SNIP 1.201

BFI (2009): BFI-level 1

Scopus rating (2009): SJR 2.139 SNIP 1.313

BFI (2008): BFI-level 1

Scopus rating (2008): SJR 2.247 SNIP 1.34

Scopus rating (2007): SJR 2.204 SNIP 1.177

Scopus rating (2006): SJR 2.14 SNIP 1.247

Web of Science (2006): Indexed yes
Pyrrolidin-2-ones are important heterocyclic motifs found in natural products and biologically active synthetic molecules. Addition of nucleophiles, including allylsilanes, isonitriles and organometallics, to N-acyliminium ions represents one of the most commonly used approaches for the formation of substituted pyrrolidin-2-ones. Only a few studies on the nucleophilic addition of organoboronic acids to N-acyliminium ions have been reported. Herein, we disclose our recent efforts for the synthesis of substituted pyrrolidin-2-ones through Lewis-acid-mediated Petasis-type reactions. By implementing a reductive cyclization reaction, linear L-malic acid derivatives were rapidly converted into cyclic N-acyliminium ions. Under the optimized conditions, entailing the use of HFIP as solvent, both electron-rich and electron-deficient boronic acids were successfully added to a range of cyclic N-acyliminium ions, typically with excellent diastereoselectivity with electron-deficient boronic acids.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Wu, P. (Intern), Clausen, M. H. (Intern), Nielsen, T. E. (Intern)
Publication date: 2014
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Main Research Area: Technical/natural sciences

Publication information
Journal: Abstracts of Papers of the American Chemical Society
ISSN (Print): 0065-7727
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Web of Science (2017): Indexed Yes
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Web of Science (2014): Indexed yes
Scopus rating (2013): SJR 0.101 SNIP 0.003
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 0.1 SNIP 0
Scopus rating (2011): SJR 0.101 SNIP 0
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 0.101 SNIP 0
Scopus rating (2009): SJR 0.101 SNIP 0
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.101 SNIP 0
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.101 SNIP 0
Scopus rating (2006): SJR 0.101
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.101
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.104 SNIP 0.028
Propargylamine-isothiocyanate reaction: efficient conjugation chemistry in aqueous media.
A coupling reaction between secondary propargyl amines and isothiocyanates in aqueous media is described. The reaction is high-yielding and affords cyclized products within 2-24 h. A functionalized ether lipid was synthesized in 8 steps, formulated as liposomes with POPC and conjugated to FITC under mild conditions using this method.
The demand for safe and healthy food is generally increasing and with it the interest in the functional ingredients in the consumed products. Among these ingredients are dietary fibers, which have attracted increased attention in research over the last decades, since the human health benefits from the consumption of fibers were scientifically demonstrated. Detailed studies of dietary fibers on a cellular level in plants benefits greatly from using the newest methods available in biotechnology such as specific monoclonal antibodies, which are a key-tool in protein-carbohydrate interactions, enzyme-linked immunosorbent assay (ELISA) and carbohydrate microarrays. To facilitate the development of monoclonal antibodies and characterization of their binding, it is necessary to obtain highly specific and pure oligosaccharides. However, methods for isolating acceptable quantities of required homogeneity from natural sources are difficult and time consuming, due to the heterogeneity and diversity of the plant cell wall polysaccharides. A alternative to isolation of oligosaccharides from the cell wall is chemical synthesis that makes it possible to obtain larger quantities of well-defined oligosaccharide structures in excellent purity.

This thesis describes the work on a new preparative synthesis method of D-xylose and D-xylobiose building blocks through carbohydrate interconversion of D-glucose and D-cellobiose. A range of methods for the transformation was investigated and the method of dehydrogenative decarbonylation was preferred because of its novelty and versatility. As proof of concept, the building blocks were applied to the synthesis of oligoxylans. Furthermore, the method proved to be an alternative route for selective equatorial deuteration labeling of D-xylose by stereo retention, whereas radical methods mainly afforded axial deuteration.

The work at University of Leeds during the external stay is described. It consisted of the utilization of monoclonal antibodies, ELISA and epitope detecting chromatography for the investigation of polysaccharides found in Arabidopsis thaliana root mucilage and mutants hereof.

**Stereoselective Conversion of Glucosides into Xylosides**

The demand for safe and healthy food is generally increasing and with it the interest in the functional ingredients in the consumed products. Among these ingredients are dietary fibers, which have attracted increased attention in research over the last decades, since the human health benefits from the consumption of fibers were scientifically demonstrated. Detailed studies of dietary fibers on a cellular level in plants benefits greatly from using the newest methods available in biotechnology such as specific monoclonal antibodies, which are a key-tool in protein-carbohydrate interactions, enzyme-linked immunosorbent assay (ELISA) and carbohydrate microarrays. To facilitate the development of monoclonal antibodies and characterization of their binding, it is necessary to obtain highly specific and pure oligosaccharides. However, methods for isolating acceptable quantities of required homogeneity from natural sources are difficult and time consuming, due to the heterogeneity and diversity of the plant cell wall polysaccharides. A alternative to isolation of oligosaccharides from the cell wall is chemical synthesis that makes it possible to obtain larger quantities of well-defined oligosaccharide structures in excellent purity.

This thesis describes the work on a new preparative synthesis method of D-xylose and D-xylobiose building blocks through carbohydrate interconversion of D-glucose and D-cellobiose. A range of methods for the transformation was investigated and the method of dehydrogenative decarbonylation was preferred because of its novelty and versatility. As proof of concept, the building blocks were applied to the synthesis of oligoxylans. Furthermore, the method proved to be an alternative route for selective equatorial deuteration labeling of D-xylose by stereo retention, whereas radical methods mainly afforded axial deuteration.

The work at University of Leeds during the external stay is described. It consisted of the utilization of monoclonal antibodies, ELISA and epitope detecting chromatography for the investigation of polysaccharides found in Arabidopsis thaliana root mucilage and mutants hereof.
Sucrose acetate isobutyrate based nanogels as liquid fiducial tissue markers with potential use in image guided radiotherapy

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Nanomedicine and Theranostics, Department of Chemistry, Organic Chemistry, Colloids and Biological Interfaces, Technical University of Denmark, Copenhagen University Hospital
Authors: Bruun, L. M. (Intern), Schaarup-Jensen, H. (Intern), Jølck, R. I. (Intern), Hansen, A. E. (Intern), Christiansen, A. N. (Ekstern), Clausen, M. H. (Intern), Kjær, A. (Ekstern), Scherman, P. J. B. (Ekstern), Andresen, T. L. (Intern)
Number of pages: 1
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Main Research Area: Technical/natural sciences
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Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014

Sucrose acetate isobutyrate based nanogels as liquid fiducial tissue markers with potential use in image guided radiotherapy

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Nanomedicine and Theranostics, Department of Chemistry, Organic Chemistry, Colloids and Biological Interfaces, Technical University of Denmark, Copenhagen University Hospital
Authors: Bruun, L. M. (Intern), Schaarup-Jensen, H. (Intern), Jølck, R. I. (Intern), Hansen, A. E. (Intern), Christiansen, A. N. (Ekstern), Clausen, M. H. (Intern), Kjær, A. (Ekstern), Scherman, P. J. B. (Ekstern), Andresen, T. L. (Intern)
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Poster presentation
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Sucrose acetate isobutyrate-based nanogels as liquid fiducial tissue markers with potential use in image guided radiotherapy

The poster presents the development of a liquid fiducial tissue marker based on sucrose acetate isobutyrate (SAIB) and uniform, coated gold nanoparticles (AuNPs). The PNIPAM-coated AuNP-SAIB gel provided high CT contrast and high in vivo stability and was assessed to be a suitable tissue marker for image guided radiotherapy (IGRT).

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nanomedicine and Theranostics, Department of Chemistry, Organic Chemistry, Technical University of Denmark, Copenhagen University Hospital
Authors: Bruun, L. M. (Intern), Schaarup-Jensen, H. (Intern), Jølck, R. I. (Intern), Hansen, A. E. (Intern), Christiansen, A. N. (Ekstern), Scherman, P. J. B. (Ekstern), Clausen, M. H. (Intern), Kjær, A. (Ekstern), Andresen, T. L. (Intern)
Synthesis and Application of Plant Cell Wall Oligogalactans

The plant cell walls represent almost 50% of the biomass found in plants and are therefore one of the main targets for biotechnological research. Major motivators are their potential as a renewable energy source for transport fuels, as functional foods, and as a source of raw materials to generate chemical building blocks for industrial processes. To achieve a sustainable development it is necessary to optimize plant production and utilization. This will require a better understanding of the cell wall structure and function at the molecular level.

The cell wall is composed by an intricate network of polysaccharides and proteins that changes during the different developmental stages of the cell. This makes it very challenging to address the function of individual components in living cells. Alternatively, structurally defined oligosaccharides can be used as models for the more complex polysaccharide components in order to investigate a range of properties such as cell wall biosynthesis and protein-carbohydrate interactions. The oligosaccharides can be obtained by chemical or enzymatic degradation of the cell wall. However, although extensive studies have been conducted only a limited range of structures is available and the obtained oligosaccharides require extensive purification. Chemical synthesis, on the other hand, is capable of producing structurally diverse oligosaccharides of excellent purity and in higher quantities.

This thesis presents the chemical synthesis of fragments of galactans and arabinogalactans that are prominent side chains of the pectic polysaccharide rhamnogalacturonan I (RG-I) and the main component of arabinogalactan protein (AGP). In the galactan series, 16 linear or branched β-(1→4)-linked D-galactosides of four to eight residues were prepared by a convergent block strategy. Using a disaccharide donor the number of glycosylations were reduced significantly and late stage regioselective deprotection made it possible to introduce various branches. By the same general strategy, seven linear or branched β-(1→3)-linked- and three linear β-(1→6)-linked D-galactosides were prepared as part of the arabinogalactans series. The fragments were applied in the characterization of a glycosyl transferase, a hydrolase and to study the important cancer biomarker galectin-3. The work done during an external stay at University of Oxford is also presented. This concerns isolation and modification of the carbohydrate-based antibiotic, Tunicamycin. A simple and effective method has been developed for chemo-enzymatic synthesis of the partially protected core tunicaminyl lactol. Furthermore, synthesis of several novel muramic acid donors and attempts to glycosylate the tunicaminyl lactol are discussed.

General information
State: Published
Organisations: Department of Chemistry
Authors: Andersen, M. C. F. (Intern), Clausen, M. H. (Intern)
Number of pages: 244
Publication date: 2014

Synthesis of substituted gamma-lactams through petasis-type addition of boronic acids to N-acyliminium ions

Substituted γ-lactams are important heterocyclic motifs found in various biologically active compounds and marketed drugs, such as glimepiride, doxapram, and levetiracetam. Among available methods for the synthesis of substituted γ-lactams, the addition of nucleophiles to N-acyliminium ions remains the most widely utilized approach. Even though hydroxylactams are important precursors of cyclic N-acyliminium ions, few approaches for their synthesis have been reported so far. By implementing a reductive cyclization reaction, linear L-malic acid derivatives were rapidly converted into cyclic N-acyliminium ions. Under the optimized conditions, entailing the use of HFIP as solvent, both electron-rich and electron-deficient boronic acids were successfully added to a range of cyclic N-acyliminium ions, thereby obtaining a collection of pharmaceutically relevant substituted γ-lactams.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Wu, P. (Intern), Clausen, M. H. (Intern), Nielsen, T. E. (Intern)
The Chemistry of Griseofulvin

Specific synthetic routes are presented in schemes to illustrate the chemistry, and the analogs are presented in a table format to give an accessible overview of the structures. Several patents have been published regarding the properties of griseofulvin and its derivatives including synthesis, formulation, and their medicinal and agricultural applications. The antifungal mode-of-action of griseofulvin has been the subject of considerable research efforts and some debate over the
years, a discussion that is still ongoing. Griseofulvin was one of the first antifungal natural products found in filamentous fungi. During the years, this polyketide has been found to be produced by several Ascomycetes including both closely and distantly related species.

**General information**

State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, Department of Systems Biology
Authors: Petersen, A. B. (Intern), Rønnest, M. H. (Intern), Larsen, T. O. (Intern), Clausen, M. H. (Intern)
Number of pages: 20
Pages: 12088-12107
Publication date: 2014
Main Research Area: Technical/natural sciences

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- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 2
- Scopus rating (2016): CiteScore 42.79 SJR 19.282 SNIP 10.369
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 2
- Scopus rating (2015): SJR 18.373 SNIP 11.51 CiteScore 45.92
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 2
- Scopus rating (2014): SJR 18.369 SNIP 11.47 CiteScore 44.56
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 22.176 SNIP 12.915 CiteScore 49.12
- ISI indexed (2013): ISI indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 20.511 SNIP 11.43 CiteScore 39.08
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 19.538 SNIP 11.534 CiteScore 39.19
- ISI indexed (2011): ISI indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 18.393 SNIP 11.114
- BFI (2009): BFI-level 2
- Web of Science (2009): Indexed yes
- BFI (2008): BFI-level 2
- Scopus rating (2008): SJR 16.038 SNIP 8.682
- Web of Science (2008): Indexed yes
- Scopus rating (2004): SJR 11.196 SNIP 8.924
- Web of Science (2004): Indexed yes
- Scopus rating (2001): SJR 11.072 SNIP 10.832
Tomato Cutin Deficient 1 (CD1) and putative orthologs comprise an ancient family of cutin synthase-like (CUS) proteins that are conserved among land plants

The aerial epidermis of all land plants is covered with a hydrophobic cuticle that provides essential protection from desiccation, and so its evolution is believed to have been prerequisite for terrestrial colonization. A major structural component of apparently all plant cuticles is cutin, a polyester of hydroxy fatty acids; however, despite its ubiquity, the details of cutin polymeric structure and the mechanisms of its formation and remodeling are not well understood. We recently reported that cutin polymerization in tomato (Solanum lycopersicum) fruit occurs via transesterification of hydroxyacylglycerol precursors, catalyzed by the GDSL-motif lipase/hydrolase family protein (GDSL) Cutin Deficient 1 (CD1). Here, we present additional biochemical characterization of CD1 and putative orthologs from Arabidopsis thaliana and the moss Physcomitrella patens, which represent a distinct clade of cutin synthases within the large GDSL superfamily. We demonstrate that members of this ancient and conserved family of cutin synthase-like (CUS) proteins act as polyester synthases with negligible hydrolytic activity. Moreover, solution-state NMR analysis indicates that CD1 catalyzes the formation of primarily linear cutin oligomeric products in vitro. These results reveal a conserved mechanism of cutin polyester synthesis in land plants, and suggest that elaborations of the linear polymer, such as branching or cross-linking, may require additional, as yet unknown, factors.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, Cornell University, City College of New York
Authors: Yeats, T. H. (Ekstern), Huang, W. (Ekstern), Chatterjee, S. (Ekstern), Viart, H. M. (Intern), Clausen, M. H. (Intern), Stark, R. E. (Ekstern), Rose, J. K. (Ekstern)
Pages: 667-675
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Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed Yes
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Scopus rating (2016): SJR 3.351 SNIP 1.508 CiteScore 5.93
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 3.379 SNIP 1.477 CiteScore 5.94
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 3.858 SNIP 1.666 CiteScore 6.42
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 4.362 SNIP 1.831 CiteScore 7.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Tracking developmentally regulated post-synthetic processing of homogalacturonan and chitin using reciprocal oligosaccharide probes.

Polysaccharides are major components of extracellular matrices and are often extensively modified post-synthetically to suit local requirements and developmental programmes. However, our current understanding of the spatiotemporal dynamics and functional significance of these modifications is limited by a lack of suitable molecular tools. Here, we report the development of a novel non-immunological approach for producing highly selective reciprocal oligosaccharide-based probes for chitosan (the product of chitin deacetylation) and for demethylesterified homogalacturonan. Specific reciprocal binding is mediated by the unique stereochemical arrangement of oppositely charged amino and carboxy groups. Conjugation of oligosaccharides to fluorophores or gold nanoparticles enables direct and rapid imaging of homogalacturonan and chitosan with unprecedented precision in diverse plant, fungal and animal systems. We demonstrated their potential for providing new biological insights by using them to study homogalacturonan processing during Arabidopsis thaliana root cap development and by analyzing sites of chitosan deposition in fungal cell walls and arthropod exoskeletons.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, University of Copenhagen, Saclay Plant Sciences, University of Namur, Skidmore College
Pages: 4841-4850
**A Mild Method for Regioselective Labeling of Aromatics with Radioactive Iodine**

A novel technique to label ortho-, meta-, and para-trimethylsilyl-substituted aryl substituents with radioactive iodide is described. The method takes advantage of the ipso-directing and activating properties of trimethylsilyl substituents on the arenes. The method was demonstrated on a griseofulvin analogue with promising anticancer properties and on lidocaine, a widely used local anesthetic drug. Treatment of a trimethylsilyl precursor with Tl(OCOCF3)3 followed by Na125I consistently afforded radioactive purities over 95% in all cases.
Organic synthesis - applications in enzymatic studies, catalysis and surface modification

In a desire to explore various areas of synthetic organic chemistry, different projects have been carried out, and each of the four following chapters will describe the work carried out on each of them. The first three chapters are related in some extent and treat the synthesis and biochemical applications of (phospho)lipids, while the last chapter differs and deals with the synthesis and initial structural studies of a C3 symmetric phosphine oxide.

In the first chapter, a series of phospholipids have been synthesised in order to perform a short structure-activity relationship study of an enzyme, secretory phospholipase A2 (sPLA2) capable of hydrolysing phospholipids in the sn-2 position specifically. This enzyme is over-expressed in several types of cancer and is under evaluation as a potential trigger for drug release from a new generation of liposomal drug delivery systems. However, little is known about the steric and electronic requirements in the vicinity of the sn-2 position for an effective hydrolysis catalysed by the enzyme. Based on previous observations and on MD experiments, we developed a theory to predict and/or explain the activity of the enzyme on engineered phospholipids. According to our theory, two aspects of the enzyme-substrate interactions are primordial for an effective hydrolysis to occur: the formation of a constructive Michaelis-Menten complex, and access of water to the hydrolysis site. In order to verify this theory, the synthesised phospholipids were formulated as liposomes and the enzymatic activity was studied. Hydrolysis (or absence of hydrolysis) was monitored by MALDI-TOF-MS. The results observed in these experiments are compared to MD predictions and confirm them.

The second chapter deals with surface functionalization of liposomes. The copper mediated [3+2] azide-alkyne cycloaddition has been successfully applied for this purpose by different groups, but no general optimization has been developed for the reaction on functionalized liposomes. Since the reaction generally takes place between one functionality on the surface of the liposomes membrane and a functionality covalently linked to a coupling partner (such as small molecule, peptide, etc.), we investigated the efficiency of the reaction depending on the position of the functional groups (whether on the liposome or on the coupling partner). Our results indicate that the reaction is most efficient when the liposome carries the alkyne functionality rather than the azide. We also investigated and developed a novel selective method for functionalizing liposomes, which has not yet been reported in the literature, based on the reaction between propargyl-amine decorated liposomes and isothiocyanate derived coupling partners that results in a coupling via formation of an iminothiazolidine.

In the third chapter, the synthesis of sn-2 glyceryl 10,16-dihydroxyhexadecanoate is reported, in the context of the identification of the process of formation of the cutin polymer, one of the primary protective components of the epidermis of land plants. The enzyme responsible for the polymerization (CD1), as well as its substrate, has been identified, and the role of the enzyme has been demonstrated by its activity on the synthetic dihydroxyacylglycerol.

Finally, the last chapter differs greatly from the first three by its focus: a C3 symmetric phosphine oxide has been synthesised, which we intend to test, after reduction to the phosphin, as a ligand in organometallic catalysed reactions. The ultimate goal is to obtain enantioselectivity, introduced by the organization of aryl substituents around phosphorous in our ligand.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Viart, H. M. (Intern), Clausen, M. H. (Intern)
Number of pages: 164
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Publisher: Technical University of Denmark (DTU)
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Synthesis of a Backbone Hexasaccharide Fragment of the Pectic Polysaccharide Rhamnogalacturonan I

Synthesis of the fully unprotected hexasaccharide backbone of the pectic polysaccharide rhamnogalacturonan I is described. The strategy relies on iterative coupling of a common pentenyl disaccharide glycosyl donor followed by a late-stage oxidation of the C-6 positions of the galactose residues. The disaccharide donor is prepared by an efficient chemoselective armed-disarmed coupling of a thiophenyl rhamnoside donor with a pentenyl galactoside acceptor bearing the strongly electron-withdrawing pentafluorobenzoyl ester (PFBz) protective group.

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Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics
Authors: Zakharova, A. N. (Intern), Madsen, R. (Intern), Clausen, M. H. (Intern)
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Web of Science (2017): Indexed Yes
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 3.055 SNIP 1.336 CiteScore 6.38
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.958 SNIP 1.324 CiteScore 6.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 3.144 SNIP 1.329 CiteScore 6.12
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.312 SNIP 1.355 CiteScore 5.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.271 SNIP 1.377 CiteScore 5.81
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.985 SNIP 1.307
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.048 SNIP 1.37
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.263 SNIP 1.295
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.185 SNIP 1.296
Scopus rating (2006): SJR 2.936 SNIP 1.352
Web of Science (2006): Indexed yes
Synthesis of Oligosaccharide Fragments of the Pectic Polysaccharide Rhamnogalacturonan I

Pectin is a highly heterogeneous polysaccharide of plant origin. It is found in the primary cell wall and contributes to various cell functions, including support, defense, signaling, and cell adhesion. Pectin also plays an important role as a food additive, serving as stabilizing and thickening agent in products such as jams, yoghurts, and jellies. Rhamnogalacturonan I is one of the structural classes of pectic polysaccharides, along with homogalacturonan and rhamnogalacturonan II. The chemical structure of rhamnogalacturonan I is complex having a backbone consisting of alternating L-rhamnose and D-galacturonic acid units with numerous branches of arabinans, galactans, or arabinogalactans positioned at C-4 of the rhamnose residues. The structural complexity of pectin together with the wide range of its practical applications and a desire to understand its structure and functions in detail have inspired many researchers to pursue chemical syntheses of pectic oligosaccharides. Herein, the strategies for chemical synthesis of linear and branched oligosaccharide fragments of rhamnogalacturonan I are presented. The first successful synthesis of a fully unprotected linear hexasaccharide fragment of the rhamnogalacturonan I backbone has been accomplished. The strategy employs a highly modular approach that takes advantage of the armed-disarmed effect to generate the key n-pentenyl disaccharide donor in a chemoselective fashion. Two protected n-pentenyl tetrasaccharide intermediates bearing the digalactan and the diarabinan side-chains have been synthesized. The suitably protected mono- and disaccharide donors have been utilized in the chemoselective glycosylations. The protective group pattern is designed to allow the assembly of larger branched rhamnogalacturonan I fragments.

General information
State: Published
Organisations: Department of Chemistry, Organic Chemistry
Authors: Zakharova, A. (Intern), Clausen, M. H. (Intern), Madsen, R. (Intern)
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Carbohydrate Microarrays in Plant Science
Almost all plant cells are surrounded by glycan-rich cell walls, which form much of the plant body and collectively are the largest source of biomass on earth. Plants use polysaccharides for support, defense, signaling, cell adhesion, and as energy storage, and many plant glycans are also important industrially and nutritionally. Understanding the biological roles of plant glycans and the effective exploitation of their useful properties requires a detailed understanding of their structures, occurrence, and molecular interactions. Microarray technology has revolutionized the massively high-throughput analysis of nucleotides, proteins, and increasingly carbohydrates. Using microarrays, the abundance of and interactions between hundreds and thousands of molecules can be assessed simultaneously using very small amounts of
Here we show that carbohydrate microarrays are multifunctional tools for plant research and can be used to map glycan populations across large numbers of samples to screen antibodies, carbohydrate binding proteins, and carbohydrate binding modules and to investigate enzyme activities.

**General information**

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Organisations: Department of Chemistry, Organic Chemistry, University of Copenhagen
Authors: Fangel, J. U. (Forskerdatabase), Pedersen, H. (Intern), Vidal-Melgosa, S. (Ekstern), Ahl, L. I. (Forskerdatabase), Salmean, A. (Ekstern), Egelund, J. (Forskerdatabase), Rydahl, M. G. (Forskerdatabase), Clausen, M. (Intern), Willats, W. G. T. (Forskerdatabase)
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ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.699 SNIP 0.369 CiteScore 1.26
ISI indexed (2012): ISI indexed no
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Scopus rating (2011): SJR 0.699 SNIP 0.258 CiteScore 1.17
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.71 SNIP 0.254
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Scopus rating (2008): SJR 0.574 SNIP 0.257
Scopus rating (2007): SJR 0.633 SNIP 0.181
Scopus rating (2006): SJR 0.599
Scopus rating (2005): SJR 0.484
Scopus rating (2004): SJR 0.362
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.424
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Disparate SAR Data of Griseofulvin Analogues for the Dermatophytes Trichophyton mentagrophytes, T. rubrum, and MDA-MB-231 Cancer Cells

Griseofulvin and 53 analogues of this compound have been tested against the pathogenic dermatophytes Trichophyton rubrum and Trichophyton mentagrophytes as well as against the breast cancer cell line MDA-MB-231. The modifications to griseofulvin include the 4, 5, 6, 2', 3', and 4' positions. The SAR of the griseofulvin analogues toward the two fungi followed the same trend with the majority being less active than griseofulvin and none had more than twice the potency of the parent compound. A comparison of the antifungal and the anticancer SAR revealed distinct differences, as the majority of analogues showed increased activity against the cancer cell line MDA-MB-231, highlighted by 2'-benzyloxy-2'-demethoxy-griseofulvin, which showed low activity against both fungi but was among the most potent compounds against MDA-MB-231 cancer cells. Tubulin has been proposed as the target of griseofulvin in both fungal and mammalian cells, but the differences revealed by this SAR study strongly suggest that the mode-of-action of the compound class toward fungi and mammalian cancer cells is different.
GF-15, a Novel Inhibitor of Centrosomal Clustering, Suppresses Tumor Cell Growth In Vitro and In Vivo

In contrast to normal cells, malignant cells are frequently aneuploid and contain multiple centrosomes. To allow for bipolar mitotic division, supernumerary centrosomes are clustered into two functional spindle poles in many cancer cells. Recently, we have shown that griseofulvin forces tumor cells with supernumerary centrosomes to undergo multipolar mitoses resulting in apoptotic cell death. Here, we describe the characterization of the novel small molecule GF-15, a derivative of griseofulvin, as a potent inhibitor of centrosomal clustering in malignant cells. At concentrations where GF-15 had no significant impact on tubulin polymerization, spindle tension was markedly reduced in mitotic cells upon exposure to GF-15. Moreover, isogenic cells with conditional centrosome amplification were more sensitive to GF-15 than parental controls. In a wide array of tumor cell lines, mean inhibitory concentrations (IC50) for proliferation and survival were in the range of 1 to 5 μmol/L and were associated with apoptotic cell death. Importantly, treatment of mouse xenograft models of human colon cancer and multiple myeloma resulted in tumor growth inhibition and significantly prolonged survival. These results show the in vitro and in vivo antitumor efficacy of a prototype small molecule inhibitor of centrosomal clustering and strongly support the further evaluation of this new class of molecules. Cancer Res; 72(20); 5374–85. ©2012 AACR.
Pectin Biosynthesis: GAL1 in Arabidopsis thaliana Is a β-1,4-Galactan β-1,4-Galactosyltransferase

β-1,4-Galactans are abundant polysaccharides in plant cell walls, which are generally found as side chains of rhamnogalacturonan I. Rhamnogalacturonan I is a major component of pectin with a backbone of alternating rhamnose and galacturonic acid residues and side chains that include α-1,5-arabinans, β-1,4-galactans, and arabinogalactans. Many enzymes are required to synthesize pectin, but few have been identified. Pectin is most abundant in primary walls of expanding cells, but β-1,4-galactan is relatively abundant in secondary walls, especially in tension wood that forms in response to mechanical stress. We investigated enzymes in glycosyltransferase family GT92, which has three members in...
Arabidopsis thaliana, which we designated GALACTAN SYNTHASE1, (GALS1), GALS2 and GALS3. Loss-of-function mutants in the corresponding genes had a decreased β-1,4-galactan content, and overexpression of GALS1 resulted in plants with 50% higher β-1,4-galactan content. The plants did not have an obvious growth phenotype. Heterologously expressed and affinity-purified GALS1 could transfer Gal residues from UDP-Gal onto β-1,4-galactopentaose. GALS1 specifically formed β-1,4-galactosyl linkages and could add successive β-1,4-galactosyl residues to the acceptor. These observations confirm the identity of the GT92 enzyme as β-1,4-galactan synthase. The identification of this enzyme could provide an important tool for engineering plants with improved bioenergy properties.
Synthesis and Stability Studies of α,α-Difluoro Ester Phospholipids

The synthesis of two new α,α-difluoro ester phospholipid conjugates is described and the stability of their liposomal formulations in three different aqueous buffers (pH 4.5, 7.5 and 8.5) has been investigated. The studies confirmed that α,α-difluoro esters are much more prone to hydrolysis when positioned close to the hydrophilic head group of phospholipids than when the functionality is placed in the lipophilic part of the bilayer in liposomes. This observation lends further support to the concept of protecting hydrolysable functionalities by formulation as part of the membrane of liposomes.

General information
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Organisations: Department of Chemistry, Center for Nanomedicine and Theranostics, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Organic Chemistry
Authors: Pedersen, P. J. (Intern), Andresen, T. L. (Intern), Clausen, M. H. (Intern)
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Scopus rating (2014): SJR 1.181 SNIP 0.767 CiteScore 2.96
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BFI (2012): BFI-level 1
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Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.536 SNIP 0.857 CiteScore 3.2
Synthesis of tocopheryl succinate phospholipid conjugates and monitoring of phospholipase A2 activity

Tocopheryl succinates (TOSs) are, in contrast to tocopherols, highly cytotoxic against many cancer cells. In this study the enzyme activity of secretory phospholipase A2 towards various succinate-phospholipid conjugates has been investigated. The synthesis of six novel phospholipids is described, including two TOS phospholipid conjugates. The studies revealed that the TOS conjugates are poor substrates for the enzyme whereas the phospholipids with alkyl and phenyl succinate moieties were hydrolyzed by the enzyme to a high extent.

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Organisations: Department of Chemistry, Organic Chemistry, Department of Micro- and Nanotechnology, Colloids and Biological Interfaces, Center for Nanomedicine and Theranostics
Authors: Pedersen, P. J. (Intern), Viart, H. M. (Intern), Melander, F. (Intern), Andresen, T. L. (Intern), Madsen, R. (Intern), Clausen, M. H. (Intern)
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The identification of cutin synthase: formation of the plant polyester cutin

A hydrophobic cuticle consisting of waxes and the polyester cutin covers the aerial epidermis of all land plants, providing essential protection from desiccation and other stresses. We have determined the enzymatic basis of cutin polymerization through characterization of a tomato extracellular acyltransferase, CD1, and its substrate, 2-mono(10,16-dihydroxyhexadecanoyl)glycerol. CD1 has in vitro polyester synthesis activity and is required for cutin accumulation in vivo, indicating that it is a cutin synthase.
Versatile High Resolution Oligosaccharide Microarrays for Plant Glycobiology and Cell Wall Research

Microarrays are powerful tools for high throughput analysis, and hundreds or thousands of molecular interactions can be assessed simultaneously using very small amounts of analytes. Nucleotide microarrays are well established in plant research, but carbohydrate microarrays are much less established, and one reason for this is a lack of suitable glycans with which to populate arrays. Polysaccharide microarrays are relatively easy to produce because of the ease of immobilizing large polymers noncovalently onto a variety of microarray surfaces, but they lack analytical resolution because polysaccharides often contain multiple distinct carbohydrate substructures. Microarrays of defined oligosaccharides potentially overcome this problem but are harder to produce because oligosaccharides usually require coupling prior to immobilization. We have assembled a library of well characterized plant oligosaccharides produced either by partial hydrolysis from polysaccharides or by de novo chemical synthesis. Once coupled to protein, these neoglycoconjugates are versatile reagents that can be printed as microarrays onto a variety of slide types and membranes. We show that these microarrays are suitable for the high throughput characterization of the recognition capabilities of monoclonal antibodies, carbohydrate-binding modules, and other oligosaccharide-binding proteins of biological significance and also that they have potential for the characterization of carbohydrate-active enzymes.

General information
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Organisations: Department of Chemistry, Organic Chemistry, Center for Nanomedicine and Theranostics, Megazyme International Ireland Ltd., John Innes Centre, National Institute for Agronomic Research, Slovak Academy of Sciences, Lund University, University of Leeds, University of Copenhagen
Authors: Pedersen, H. L. (Ekstern), Fangel, J. U. (Forskerdatabase), McCleary, B. (Ekstern), Ruzanski, C. (Ekstern), Rydahl, M. G. (Forskerdatabase), Ralet, M. (Ekstern), Farkas, V. (Ekstern), von Schantz, L. (Ekstern), Marcus, S. E. (Ekstern), Andersen, M. C. F. (Intern), Field, R. (Ekstern), Ohlin, M. (Ekstern), Knox, J. P. (Ekstern), Clausen, M. H. (Intern), Willats, W. G. T. (Forskerdatabase)
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BFI (2015): BFI-level 2
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 3.254 SNIP 1.222 CiteScore 4.5
Web of Science (2014): Indexed yes
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Scopus rating (2013): SJR 3.369 SNIP 1.231 CiteScore 4.87
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 3.361 SNIP 1.244 CiteScore 4.97
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 3.495 SNIP 1.26 CiteScore 4.97
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New Principles for Targeting Cancer - a Rational Small Molecule Approach

General information
State: Published
Organisations: Center for Microbial Biotechnology, Department of Systems Biology, Organic Chemistry, Department of Chemistry
Authors: Rønnest, M. H. (Intern), Larsen, T. O. (Intern), Clausen, M. H. (Intern)
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Biophysical Characterization of Interactions of a-helical amphipathic peptides with membranes

General information
Biologically Active Macrocyclic Compounds – from Natural Products to Diversity-Oriented Synthesis

Macrocyclic compounds are attractive targets when searching for molecules with biological activity. The interest in this compound class is increasing, which has led to a variety of methods for tackling the difficult macrocyclization step in their synthesis. This microreview highlights some recent developments in the synthesis of macrocycles, with an emphasis on chemistry developed to generate libraries of putative biologically active compounds.
(+)-Geodin from Aspergillus terreus.
The fungal metabolite (+)-geodin [systematic name: (2R)-methyl 5,7-dichloro-4-hydroxy-6'-methoxy-6-methyl-3,4'-dioxospiro[benzofuran-2,1'-cyclohexa-2',5'-diene]-2'-carboxylate], C(17)H(12)Cl(2)O(7), was isolated from Aspergillus terreus. The crystal structure contains two independent molecules in the asymmetric unit. Molecules denoted 1 interact through O-H...O hydrogen bonds creating chains of molecules parallel to the crystallographic 2(1) screw axis. Molecules denoted 2 interact through an O...Cl halogen bond, also creating chains of molecules parallel to the crystallographic 2(1) screw axis. Molecules 1 and 2 interact through another O...Cl halogen bond. The two molecules are similar but molecules 2 have a slightly more planar cyclohexadiene ring than molecules 1. The absolute structure of (+)-geodin has been unequivocally assigned with the spiro centre having the R configuration in both molecules. The structurally related (+)-griseofulvin has an S configuration at the spiro centre, a difference of potential biological and biosynthetic relevance.

General information
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Organisations: Organic Chemistry, Department of Chemistry, Center for Microbial Biotechnology, Department of Systems Biology, X-ray Crystallography, University of Heidelberg
Authors: Rønnest, M. H. (Intern), Nielsen, M. T. (Intern), Leber, B. (Ekstern), Mortensen, U. H. (Intern), Krämer, A. (Ekstern), Clausen, M. H. (Intern), Larsen, T. O. (Intern), Harris, P. (Intern)
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Web of Science (2017): Indexed Yes
Lipid conjugated prodrugs for enzyme-triggered liposomal drug delivery to tumors

For some time we have been developing novel enzyme-triggered prodrugs for drug delivery targeting cancer. The liposomal prodrugs take advantage of the EPR effect to localize to tumors and of the local over-expression of secretory phospholipase A2 in tumors. Compared to conventional liposomal drug delivery systems, our prodrug-lipid conjugates have two main advantages: 1) the drugs are covalently linked to the lipids and thus leakage is circumvented and 2) the lipophilic bilayer of the formulated liposomes effectively shields the drugs from the aqueous environment in vivo. Consequently, the strategy accommodates therapeutic agents with otherwise unfavorable pharmacokinetic properties. We have designed and synthesized different prodrugs, including published examples using capsaicin, chlorambucil and all-trans retinoic acid as the cytotoxic agents. Currently, we are investigating more potent agents targeting nuclear receptors.
Selective Acylation Enhances Membrane Charge Sensitivity of the Antimicrobial Peptide Mastoparan-X

The partitioning of the wasp venom peptide mastoparan-X (MPX) into neutral and negatively charged lipid membranes has been compared with two new synthetic analogs of MPX where the Nα-terminal of MPX was acylated with propanoic acid (PA) and octanoic acid (OA). The acylation caused a considerable change in the membrane partitioning properties of MPX and it was found that the shorter acylation with PA gave improved affinity and selectivity toward negatively charged membranes, whereas OA decreased the selectivity. Based on these findings, we hypothesize that minor differences in the embedding and positioning of the peptide in the membrane caused by either PA or OA acylation play a critical role in the fine-tuning of the effective charge of the peptide and thereby the fine-tuning of the peptide's selectivity between neutral and negatively charged lipid membranes. This finding is unique compared to previous reports where peptide acylation...
enhanced membrane affinity but also resulted in impaired selectivity. Our result may provide a method of enhancing selectivity of antimicrobial peptides toward bacterial membranes due to their high negative charge—a finding that should be investigated for other, more potent antimicrobial peptides in future studies.

**General information**

State: Published
Organisations: Colloids and Biological Interfaces Group, Self-organizing materials for nanotechnology Section, Department of Micro- and Nanotechnology, Biomedical Tracers, Radiation Research Division, Risø National Laboratory for Sustainable Energy, Organic Chemistry, Department of Chemistry
Authors: Etzerodt, T. P. (Intern), Henriksen, J. R. (Intern), Rasmussen, P. (Intern), Clausen, M. H. (Intern), Andresen, T. L. (Intern)
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.06 SJR 1.946 SNIP 1.018
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.145 SNIP 1.173 CiteScore 3.3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.203 SNIP 1.166 CiteScore 3.33
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.229 SNIP 1.165 CiteScore 3.64
ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.343 SNIP 1.154 CiteScore 3.57
ISI indexed (2012): ISI indexed yes
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BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.322 SNIP 1.204 CiteScore 3.75
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.646 SNIP 1.303
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.953 SNIP 1.361
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.222 SNIP 1.416
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.119 SNIP 1.422
Web of Science (2007): Indexed yes
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Web of Science (2006): Indexed yes
Synthesis and application of plant cell wall oligosaccharides

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Organisations: Organic Chemistry, Department of Chemistry
Authors: Clausen, M. H. (Intern)
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Scopus rating (2014): SJR 0.101 SNIP 0.013
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Scopus rating (2012): SJR 0.1 SNIP 0
Scopus rating (2011): SJR 0.101 SNIP 0
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 0.101 SNIP 0
Scopus rating (2009): SJR 0.101 SNIP 0
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.101 SNIP 0
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.101 SNIP 0
Scopus rating (2006): SJR 0.101
Web of Science (2006): Indexed yes
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Web of Science (2004): Indexed yes
Synthesis and structure-activity relationship of liposomal substrates for phospholipase A(2)

A recent innovation in the use of liposomes as drug delivery systems consists of covalently attaching an anticancer drug at the sn-2 position of phospholipids. However, some of those lipids could not be hydrolyzed by sPLA2. Steric bulk in the vicinity of the sn-2 position appears to prevent hydrolysis of the substrate. Structurally different lipids have been synthesized and formulated as liposomes, subjected to sPLA2 and the hydrolysis rates have been compared to Molecular Dynamics simulations of the enzyme/substrate complexes.
Liposomal Drug Delivery of Anticancer Agents: Synthesis, Biophysical Characterization and Biological Studies of Enzyme Sensitive Phospholipid Prodrugs

In the first part of the thesis the work towards a new generation of liposomal drug delivery systems for anticancer agents is described. The drug delivery system takes advantage of the elevated level of secretory phospholipase A2 (sPLA2) IIA in many tumors and the enhanced permeability and retention (EPR) effect. The liposomes consists of sPLA2 IIA sensitive phospholipids having anticancer drugs covalently attached to the sn-2 position of the glycerol backbone in the phospholipids, hence drug leakage is avoided from the carrier system. Various known anticancer agents, like chlorambucil, all-trans retinoic acid, α-tocopheryl succinate and calcitriol were examined for their ability to be incorporated into the investigated drug delivery system and syntheses of the phospholipid prodrugs are described. The majority of the phospholipid prodrugs were able to form particles with diameters close to 100 nm upon extrusion at 20 °C indicating that unilamellar vesicles are formed. When subjected to sPLA2 the phospholipid prodrugs were converted into cytotoxic lysolipids and along with the released anticancer drug a chemotherapeutic cocktail is formed. Cytotoxicity studies in several cancer lines revealed that upon sPLA2 triggering the formulated phospholipid prodrugs displayed IC50 values in range from 3–36 µM and complete cell death was observed when higher drug concentrations were applied. Promising for the drug delivery system the majority of the phospholipid prodrugs remain non-toxic in the absence of the enzyme meaning the prodrugs will not damage healthy tissue during the transport in the body. In the second part of the thesis the synthetic studies towards a library of small natural product-like molecules are described. The collection of molecules was synthesized via a diversity oriented synthesis (DOS) based strategy using a limited number of reaction types. Upon coupling of unsaturated building blocks ring closing metathesis cascades were used to “reprogram” the molecular scaffold and highly diverse structures were obtained. In total 20 novel compounds with a broad structural diversity were prepared in 5 or 6 synthetic steps.

GRISEOFULVIN ANALOGUES FOR THE TREATMENT OF CANCER BY INHIBITION OF CENTROSOMAL CLUSTERING

The invention relates to compounds of the formula (I), where the symbols have the meaning given in the specification, for use in a method for treating cancer, to use of these compounds for the manufacture of a pharmaceutical composition for the treatment of cancer, and to methods of treatment for said diseases employing a compound of formula (I).
Isomerization of all-(E)-Retinoic Acid Mediated by Carbodiimide Activation - Synthesis of ATRA Ether Lipid Conjugates

Treatment of the lysolipid 1-O-hexadecyl-sn-phosphatidylcholine with all-(E)-retinoic acid, DCC and DMAP resulted in poor acylation and caused (Z)/(E) isomerization of the alpha-beta double bond. In the presence of a proton source, the carbodiimide-activated all-(E)-retinoic acid undergoes fast isomerization to give a final mixture of (13E)/(13Z) isomers in a 3:1 ratio. Similar treatment of (13Z)-retinoic acid leads to the same isomer ratio. The isomerization was circumvented successfully by using a Mitsunobu reaction, which provided an efficient synthesis of all-(E)-retinoic acid sn-2-conjugated to phosphatidylcholine and phosphatidylglycerol ether lipids.
Liposomal Formulation of Retinoids Designed for Enzyme Triggered Release

The design of retinoid phospholipid prodrugs is described based on molecular dynamics simulations and cytotoxicity studies of synthetic retinoid esters. The prodrugs are degradable by secretory phospholipase A(2) IIA and have potential in liposomal drug delivery targeting tumors. We have synthesized four different retinoid phospholipid prodrugs and shown that they form particles in the liposome size region with average diameters of 94-118 nm. Upon subjecting to phospholipase A(2), the lipid prodrugs were hydrolyzed, releasing cytotoxic retinoids and lysolipids. The formulated lipid prodrugs displayed IC50 values in the range of 3-19 μM toward HT-29 and Colo205 colon cancer cells in the presence of phospholipase A(2), while no significant cell death was observed in the absence of the enzyme.

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BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.06
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.529 SNIP 1.631 CiteScore 5.66
Prostaglandin phospholipid conjugates with unusual biophysical and cytotoxic properties

The synthesis of two secretory phospholipase A(2) IIA sensitive 15-deoxy-Delta(12,14)-prostaglandin J(2) phospholipid conjugates is described and their biophysical and biological properties are reported. The conjugates spontaneously form particles in the liposome size region upon dispersion in an aqueous buffer and both phospholipids are hydrolyzed by phospholipase A(2), but with different conversion rates and extent of hydrolysis. The cytotoxicity was evaluated in HT-29 and Colo205 cells and the conjugates induced cell death in the presence of phospholipase A(2) and surprisingly also in the absence of the enzyme.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry, Colloids and Biological Interfaces Group, Self-organizing materials for nanotechnology Section, Department of Micro- and Nanotechnology, LiPlasome Pharma ApS
Authors: Pedersen, P. J. (Intern), Adolph, S. K. (Ekstern), Andresen, T. L. (Intern), Madsen, M. W. (Ekstern), Madsen, R. (Intern), Clausen, M. H. (Intern)
Pages: 4456-4458
Publication date: 2010
Structural Insights into Substrate Specificity and the anti beta-Elimination Mechanism of Pectate Lyase

Pectate lyases harness anti beta-elimination chemistry to cleave the alpha-1,4 linkage in the homogalacturonan region of plant cell wall pectin. We have studied the binding of five pectic oligosaccharides to Bacillus subtilis pectate lyase in crystals of the inactive enzyme in which the catalytic base is substituted with alanine (R279A). We discover that the three
central subsites (-1, +1, and +2) have a profound preference for galacturonate but that the distal subsites call accommodate methylated galacturonate. It is reasonable to assume therefore that pectate lyase call cleave pectin with three consecutive galacturonate residues. The enzyme in the absence of substrate binds a single calcium ion, and we show that two additional calcium ions bind between enzyme and substrate carboxylates occupying the +1 subsite in the Michaelis complex. The substrate binds less intimately to the enzyme in a complex made with a catalytic base in place but in the absence of the calcium ions and an adjacent lysine, in this complex, the catalytic base is correctly positioned to abstract the C5 proton, but there are no calcium ions during the carboxylate at the +1 subsite. It is clear, therefore, that the catalytic calcium ions and adjacent lysine promote catalysis by acidifying the a-proton, facilitating its abstraction by the base. There is also clear evidence that binding distorts the relaxed 21 or 31 helical conformation of the oligosaccharides in the region of the scissile bond.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry
Authors: Seyedarabi, A. (Ekstern), To, T. (Ekstern), Ali, S. (Ekstern), Hussain, S. (Ekstern), Fries, M. (Ekstern), Madsen, R. (Intern), Clausen, M. H. (Intern), Teixeira, S. (Ekstern), Brocklehurst, K. (Ekstern), Pickersgill, R. (Ekstern)
Pages: 539-546
Publication date: 2010
Main Research Area: Technical/natural sciences

Publication information
Journal: Biochemistry
Volume: 49
Issue number: 3
ISSN (Print): 0006-2960
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.8
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 3.02
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 2.96
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 3.28
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.33
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 3.3
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Web of Science (2008): Indexed yes
Web of Science (2007): Indexed yes
Web of Science (2006): Indexed yes
Web of Science (2005): Indexed yes
Web of Science (2004): Indexed yes
Web of Science (2003): Indexed yes
Synthesis and single crystal X-ray analysis of two griseofulvin metabolites
The two phenols, 6-O-desmethyl griseofulvin and 4-O-desmethyl griseofulvin are metabolites of the antifungal drug griseofulvin. Herein, we present an improved synthesis of the 6-phenol derivative, and an unequivocal proof of both structures by single-crystal X-ray analysis.
Synthesis of new diverse macrocycles from diol precursors

The formation of a library of diverse macrocycles with different ring sizes from two easily accessible building blocks is presented. Reacting diol precursors with electrophilic reagents lead to 17-membered sulfites and 19-membered malonates in 34–79% yield. Double-reductive amination of dialdehyde analogs of the diol precursors leads to 15-membered amines in yields ranging from 9 to 60%, reflecting large differences in reactivity based on steric environment.

General information

State: Published
Organisations: Organic Chemistry, Department of Chemistry, Technical University of Denmark
Authors: Madsen, C. M. (Intern), Hansen, M. (Intern), Thrane, M. V. (Ekstern), Clausen, M. H. (Intern)
Pages: 9849-9859
Publication date: 2010
Main Research Area: Technical/natural sciences

Publication information

Journal: Tetrahedron
Volume: 66
Issue number: 52
ISSN (Print): 0040-4020
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.907 SNIP 0.742 CiteScore 2.54
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.954 SNIP 0.84 CiteScore 2.72
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.971 SNIP 0.905 CiteScore 2.79
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
The formation of a library of diverse macrocyclic compounds with different functionalities and ring sizes in a few steps from two easily accessible α,ω-diol building blocks is presented. The building blocks are combined by esterifications in four different ways leading to the formation of four structurally isomeric diol precursors. These are then reacted with electrophilic reagents leading to 17-membered sulfites and 19-membered malonates in reasonable yields, and 20-22-membered phthalates and an 18-membered oxalate in low yields. Double-reductive amination of dialdehyde analogs of the diol precursors leads to 15-membered amines in yields ranging from 9 to 60%, reflecting large differences in reactivity based on steric environment. The conversion of the two least sterically hindered diols into diiodide analogs is also presented. However, the desired cyclizations of these precursors have not been successful.

Part II

The formation and subsequent coupling of a monosilver(I) acetylide of 2,3-diethynyltriptycene is presented. The silver(I) acetylide is formed in high yield from both 2,3-diethynyltriptycene and 2,3-di(trimethylsilyl)ethynyltriptycene by use of the same reagent. Coupling of the silver(I) acetylide with 1-iodoadamantane is demonstrated. Furthermore, attempts at the synthesis of 1,3-difluoro-5,7-diodoadamantane from 1,3,5,7-tetraiodoadamantane are presented. Unfortunately, the reaction is found to be uncontrollable by use of two different reagents, giving a mixture of uoro-iodoadamantanes. However, overall the results provide a good starting point for the synthesis of new triptycene and adamantane-containing molecules that can interact with carbon nanotubes.
Rapid synthesis of macrocycles from diol precursors
A method for the formation of synthetic macrocycles with different ring sizes from diols is presented. Reacting a simple diol precursor with electrophilic reagents leads to a cyclic carbonate, sulfite or phosphate in a single step in 25-60% yield. Converting the cyclization precursor to a bis-electrophilic iodide or aldehyde enables preparation of a cyclic sulfide and amine, respectively, the latter using a double reductive amination to induce ring closure.
Synthesis and Biophysical Characterization of Chlorambucil Anticancer Ether Lipid Prodrugs

The synthesis and biophysical characterization of four prodrug ether phospholipid conjugates are described. The lipids are prepared from the anticancer drug chlorambucil and have C16 and C18 ether chains with phosphatidylcholine or phosphatidylglycerol headgroups. All four prodrugs have the ability to form unilamellar liposomes (86-125 nm) and are hydrolyzed by phospholipase A2, resulting in chlorambucil release. Liposomal formulations of prodrug lipids displayed cytotoxicity toward HT-29, MT-3, and ES-2 cancer cell lines in the presence of phospholipase A2, with IC50 values in the 8-36 μM range.

General information
State: Published
Organisations: Department of Chemistry, Department of Micro- and Nanotechnology, University of Southern Denmark, LiPlasome Pharma ApS
Authors: Pedersen, P. J. (Intern), Christensen, M. S. (Intern), Ruysschaert, T. (Ekstern), Linderoth, L. (Intern), Andresen, T. L. (Intern), Melander, F. (Ekstern), Mouritsen, O. G. (Ekstern), Madsen, R. (Intern), Clausen, M. H. (Intern)
Pages: 3408-3415
Publication date: 2009
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Medicinal Chemistry
Volume: 52
Issue number: 10
ISSN (Print): 0022-2623
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.06
Synthesis and Structure-Activity Relationship of Griseofulvin Analogues as Inhibitors of Centrosomal Clustering in Cancer Cells

Griseofulvin was identified as an inhibitor of centrosomal clustering in a recently developed assay. Centrosomal clustering is an important cellular event that enables bipolar mitosis for cancer cell lines harboring supernumerary centrosomes. We report herein the synthesis and SAR of 34 griseofulvin analogues as inhibitors of centrosomal clustering. The variations in the griseofulvin structure cover five positions, namely the 4, 5, 2', 3', and 4' positions. Modification of the 4 and 5 positions affords inactive molecules. The enol ether must be at the 2' position, and the 4' position needs to be Sp2 hybridized. The most active analogues were the 2'-benzyloxy and 2'-(4-methylbenzyloxy) analogues as well as the oxime of the former with a 25-fold increase of activity compared to griscofulvin. Comparison of the results obtained in this work with prior reported growth inhibition data for dermatophytic fungi showed both similarities and differences.

General information

State: Published
GF-15, a Novel Inhibitor of Centrosomal Clustering, Suppresses Tumor Growth in Vivo

General information
State: Published
Organisations: Department of Systems Biology, Organic Chemistry, Department of Chemistry, Center for Microbial Biotechnology
Authors: Raab, M. S. (Ekstern), Breitkreutz, I. (Ekstern), Rebacz, B. (Intern), Nguyen, T. (Ekstern), Hayden, P. J. (Ekstern), Clausen, M. H. (Intern), Larsen, T. O. (Intern), Fruehauf, J. (Ekstern), Anderson, K. C. (Ekstern), Kraemer, A. (Ekstern)
Pages: 578-579
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication Information
Journal: Blood
Volume: 112
Issue number: 11
ISSN (Print): 0006-4971
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): SJR 5.842 SNIP 2.479 CiteScore 6.93
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 6.42 SNIP 2.656 CiteScore 7.23
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 6.417 SNIP 2.722 CiteScore 7.21
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 6.66 SNIP 2.433 CiteScore 7.26
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 5.667 SNIP 2.365 CiteScore 7.24
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 6.193 SNIP 2.394 CiteScore 7.35
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 6.127 SNIP 2.343
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 5.725 SNIP 2.362
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 5.437 SNIP 2.153
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 5.344 SNIP 2.251
Scopus rating (2005): SJR 4.872 SNIP 2.281
Web of Science (2005): Indexed yes
GRISEOFULVIN ANALOGUES FOR THE TREATMENT OF CANCER BY INHIBITION OF CENTROSOMAL CLUSTERING
The present invention relates to uses of compounds having a structure as shown by formula (I) for the manufacture of a pharmaceutical composition for the treatment of cancer. Moreover, the present invention encompasses methods of treatment for said diseases.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry, Center for Microbial Biotechnology, Department of Systems Biology, DKFZ Deutsches Krebsforschungszentrum
Authors: Clausen, M. H. (Intern), Larsen, T. O. (Intern), Krämer, A. (Ekstern), Rebacz, B. (Ekstern)
Publication date: 2008

Publication information
Patent number: WO2009000937
Date: 31/12/2008
Original language: English

Bibliographical note
International application published under the World Intellectual Property Organization (WIPO)
Main Research Area: Technical/natural sciences
Source: orbit
Source-ID: 266115
Publication: Research › Patent – Annual report year: 2008

Regio- and stereoselective hydrosilylation of immobilized terminal alkynes
Regio- and stereoselective hydrosilylation of terminal alkynes on solid support using diisopropyl hydrosilanes yielding b-(E)-vinyl silanes with excellent selectivity is reported. The hydrosilylation is catalyzed by Pt(DVDS)/P(iBuNCH2CH2)3N (DVDS = 1,3-divinyl-1,1,3,3-tetramethyl-disiloxane), in which the bulky proazaphosphatrane ligand plays a key role for the selectivity. The immobilized products are characterized with gel phase 13C NMR and 1H high resolution magic angle spinning NMR.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry
Authors: Pedersen, P. J. (Intern), Henriksen, J. (Ekstern), Gotfredsen, C. H. (Intern), Clausen, M. H. (Intern)
Pages: 6220-6223
Publication date: 2008
Main Research Area: Technical/natural sciences

Publication information
Journal: Tetrahedron Letters
Volume: 49
Issue number: 43
ISSN (Print): 0040-4039
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Structural characterization of homogalacturonan by NMR spectroscopy - assignment of reference compounds

Complete assignment of 1H and 13C NMR of six hexagalactopyranuronic acids with varying degree and pattern of methyl esterification is reported. The NMR experiments were run at room temperature using approximately 2 mg of sample making this method convenient for studying the structure of homogalacturonan oligosaccharides.

General information
Identification of griseofulvin as an inhibitor of centrosomal clustering in a phenotype-based screen.

General information
State: Published
Organisations: Center for Microbial Biotechnology, Department of Systems Biology, Organic Chemistry, Department of Chemistry
Authors: Rebacz, B. (Ekstern), Larsen, T. O. (Intern), Clausen, M. H. (Intern), Rønnest, M. H. (Intern), Löffler, H. (Ekstern), Ho, A. (Ekstern), Krämer, A. (Ekstern)
Pages: 6342-6350
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Cancer Research
Issue number: 67
ISSN (Print): 0008-5472
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 8.55 SJR 4.753 SNIP 1.986
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 5.324 SNIP 2.017 CiteScore 8.57
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 5.655 SNIP 2.092 CiteScore 8.69
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 5.624 SNIP 2.098 CiteScore 8.75
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 5.028 SNIP 2.033 CiteScore 8.38
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 5.288 SNIP 1.838 CiteScore 7.88
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 5.345 SNIP 1.805
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 5.205 SNIP 1.795
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 5.175 SNIP 1.773
Web of Science (2008): Indexed yes
Study of the mode of action of a polygalacturonase from the phytopathogen Burkholderia cepacia

We have recently isolated and heterologously expressed BcPeh28A, an endopolygalacturonase from the phytopathogenic Gram-negative bacterium Burkholderia cepacia. Endopolygalacturonases belong to glycoside hydrolase family 28 and are responsible for the hydrolysis of the non-esterified regions of pectins. The mode of action of BcPeh28A on different substrates has been investigated and its enzymatic mechanism elucidated. The hydrolysis of polygalacturonate indicates that BcPeh28A is a non-processive enzyme that releases oligomers with chain lengths ranging from two to eight. By inspection of product progression curves, a kinetic model has been generated and extensively tested. It has been used to derive the kinetic parameters that describe the time course of the formation of six predominant products. Moreover, an investigation of the enzymatic activity on shorter substrates that differ in their overall length and methylation patterns sheds light on the architecture of the BcPeh28A active site. Specifically the tolerance of individual sites towards methylated saccharide units was rationalized on the basis of the hydrolysis of hexagalacturonides with different methylation patterns.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry
Authors: Massa, C. (Ekstern), Clausen, M. H. (Intern), Stojan, J. (Ekstern), Lamba, D. (Ekstern), Campa, C. (Ekstern)
Pages: 207-217
Publication date: 2007
Main Research Area: Technical/natural sciences

Publication information
Journal: Biochemical Journal
Volume: 407
ISSN (Print): 0264-6021
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 2.341 SNIP 0.99 CiteScore 3.63
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.56 SNIP 1.123 CiteScore 3.85
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.865 SNIP 1.216 CiteScore 4.25
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 3.056 SNIP 1.343 CiteScore 4.99
We report the isolation and characterization of a monoclonal antibody, designated LM9, against feruloylated-(1→4)-β-D-galactan. This epitope is a structural feature of cell wall pectic polysaccharides of plants belonging to the family Amaranthaceae (including the Chenopodiaceae). Immuno-assays and immunofluorescence microscopy indicated that LM9 binding is specific to samples and cell walls obtained from species belonging to this family. In a series of competitive-inhibition enzyme-linked immunosorbert assays with potential oligosaccharide haptens, the most effective inhibitor was O-[6-O-(trans-feruloyl)-β-D-galactopyranosyl]-(1→4)-β-D-galactopyranose (Gal(2)F). LM9 is therefore a useful antibody probe for the analysis of phenolic substitution of cell wall pectic polymers and of cell wall structure in the Amaranthaceae including sugar beet (Beta vulgaris L.) and spinach (Spinacia oleracea L.).

General information
State: Published
Organisations: Department of Chemistry, University of Leeds
Authors: Clausen, M. H. (Intern), Ralet, M. (Ekstern), Willats, W. G. T. (Ekstern), McCartney, L. (Ekstern), Marcus, S. E. (Ekstern), Thibault, J. (Ekstern), Knox, J. P. (Ekstern)
Pages: 1036-1041
Synthesis of oligogalacturonates conjugated to BSA

The synthesis of three oligogalacturonates with an aldehyde spacer attached at the reducing end is described. Trigalacturonates a-D-GalpA-(1-4)-a-D-GalpA-(1-4)-a-D-GalpA-(1-O(CH2)7CHO and a-D-GalpA(Me)-(1-4)-a-D-GalpA(Me)-(1-4)-a-D-GalpA-(1-O(CH2)7CHO as well as hexagalacturonate a-D-GalpA-(1-4)-[a-D-GalpA-(1-4)]4-a-D-GalpA-(1-O(CH2)7CHO are prepared by stepwise coupling of galactose units followed by oxidation of the 6-positions. The
a-linkages are formed by employing n-pentenyl galactosides as glycosyl donors and N-iodosuccinimide/triethylsilyl triflate as
the promoter. Deprotection furnishes the three target oligogalacturonates, which are subsequently linked to bovine serum albumin by reductive amination. These neoglycoproteins will serve as immunogens for generation of new antibodies that can be used for localization and characterization of pectin in plants.

General information
State: Published
Organisations: Organic Chemistry, Department of Chemistry
Authors: Clausen, M. H. (Intern), Madsen, R. (Intern)
Pages: 2159-2169
Publication date: 2004
Main Research Area: Technical/natural sciences

Publication information
Journal: Carbohydrate Research
Volume: 339
Issue number: 13
ISSN (Print): 0008-6215
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.03 SJR 0.654 SNIP 0.801
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.59 SNIP 0.839 CiteScore 1.98
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.638 SNIP 0.856 CiteScore 2.01
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.639 SNIP 0.86 CiteScore 2.22
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.773 SNIP 1.017 CiteScore 2.2
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.76 SNIP 1.062 CiteScore 2.43
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.722 SNIP 0.868
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.883 SNIP 1.031
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.851 SNIP 0.943
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.751 SNIP 0.89
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.638 SNIP 0.906
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.683 SNIP 1.002
Scopus rating (2004): SJR 0.631 SNIP 0.96
Web of Science (2004): Indexed yes
Synthesis of Hexasaccharide Fragments of Pectin

Short syntheses of five partially methyl-esterified hexagalacturonates are described as part of the development of strategies for the preparation of larger pectic oligosaccharides. The methodology is based on the repeated coupling of galactose mono- and disaccharide donors onto a galactose acceptor until a hexagalactan is obtained. All glycosylations are carried out with n-pentenyl glycosides to provide good yields of the desired α anomers. Pentenyl disaccharide donors are prepared by coupling of two pentenyl galactosides controlled by either the armed-disarmed effect or by converting one pentenyl galactoside into the corresponding galactosyl bromide or fluoride. Two orthogonal protecting groups are employed at C6, which makes it possible to oxidize these positions to either the carboxylic acid or to the methyl ester. Each hexagalactan is therefore able to bifurcate into two different hexagalacturonates with a reverse methyl-esterification pattern. The methyl ester distribution in the hexagalacturonates is confirmed by tandem mass spectrometry.

General information
State: Published
Organisations: Department of Chemistry
Authors: Clausen, M. H. (Intern), Madsen, R. (Intern)
Pages: 3821-3832
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: Chemistry - A European Journal
Volume: 9
Issue number: 16
ISSN (Print): 0947-6539
Ratings:
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 5.03 SJR 2.247 SNIP 1.046
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.416 SNIP 1.184 CiteScore 4.99
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.487 SNIP 1.219 CiteScore 5.51
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.604 SNIP 1.239 CiteScore 5.68
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.884 SNIP 1.294 CiteScore 5.55
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Synthetic methyl hexagalacturonate hapten inhibitors of antihomogalacturonan monoclonal antibodies LM7, JIM5 and JIM7

A range of synthetic methyl hexagalacturonates were used as potential hapten inhibitors in competitive-inhibition enzyme-linked immunosorbent assays (ELISAs) with anti-homogalacturonan monoclonal antibodies LM7, JIM5 and JIM7. The selective inhibition of these antibodies by different haptens provides insight into the structures of the partially methyl-esterified pectin epitopes of these widely used monoclonal antibodies.

General information
State: Published
Organisations: Department of Chemistry, University of Leeds
Authors: Clausen, M. H. (Intern), Willats, W. G. T. (Ekstern), Knox, J. P. (Ekstern)
Pages: 1797-1800
Publication date: 2003
Main Research Area: Technical/natural sciences

Publication information
Journal: Carbohydrate Research
Volume: 338
Issue number: 17
ISSN (Print): 0008-6215
Ratings:
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
A strategy for chemical synthesis of selectively methyl-esterified oligomers of galacturonic acid

The synthesis of monomethyl-esterified trigalacturonans 1-3 is described as part of a general strategy towards pectic oligosaccharides. The necessary monomeric building blocks were all prepared on a large scale from galactose pentaacetate. The glycosylations were carried out between galactose glycosyl donors and acceptors using the n-pentenyl glycosylation technique. Yields of the desired alpha-anomers were in the 50 to 74% range. The trigalactans thus obtained were then subjected to oxidation at C-6. Depending on the protecting group at this position the oxidation either produced...
the carboxylic acid or the corresponding methyl ester. Hereby, oligomers of galacturonic acid can be prepared with methyl esters introduced in a regiocontrolled fashion.

General information
State: Published
Organisations: Department of Chemistry
Authors: Clausen, M. H. (Intern), Jørgensen, M. R. (Intern), Thorsen, J. (Ekstern), Madsen, R. (Intern)
Pages: 543-551
Publication date: 2001
Main Research Area: Technical/natural sciences

Publication information
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Web of Science (2002): Indexed yes
Web of Science (2001): Indexed yes
Web of Science (2000): Indexed yes
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Source: orbit
Source-ID: 43221
Publication: Research - peer-review › Journal article – Annual report year: 2001

Projects:

Novel Tools for Ultra-Specific Targeting of Nucleic Acids
Department of Chemistry
Period: 15/10/2017 → 14/04/2019
Number of participants: 3
Phd Student:
Taskova, Maria (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Astakhova, Kira (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Samfinansieret - Andet
Project: PhD

Metal-Catalyzed Dehydrogenation of Alcohols
Department of Chemistry
Period: 01/04/2017 → 31/03/2020
Number of participants: 3
Phd Student:
Samuelsen, Simone Vestermann (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD
Development of Novel Anti-Cancer Drugs using Fragment-Based Drug Discovery

Department of Chemistry
Period: 01/01/2017 → 31/12/2019
Number of participants: 3
PhD Student:
Andersen, Nikolaj Sten (Intern)
Supervisor:
Gotfredsen, Charlotte Held (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Metal Catalysts for Dehydrogenation and Decarbonylation of Primary Alcohols

Department of Chemistry
Period: 01/10/2016 → 30/09/2019
Number of participants: 3
PhD Student:
Monda, Fabrizio (Ekstern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Eksternt finansieret virksomhed
Project: PhD

Metal Catalysts for Dehydrogenation and Decarbonylation of Primary Alcohols

Department of Chemistry
Period: 01/10/2016 → 30/09/2019
Number of participants: 3
PhD Student:
Monda, Fabrizio (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Fonde
Project: PhD

Metal-Catalyzed Dehydrogenation and Decarbonylation of Primary Alcohols

Department of Chemistry
Period: 01/05/2016 → 30/04/2019
Number of participants: 3
PhD Student:
Bottaro, Fabrizio (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Eksternt finansieret virksomhed
Project: PhD

New Glycosylation Methods for Oligosaccharide Synthesis
Department of Chemistry
Period: 01/12/2015 → 30/11/2018
Number of participants: 3
Phd Student:
Underlin, Emilie Nørmølle (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Culticular Polyesters
Department of Chemistry
Period: 15/12/2014 → 14/12/2017
Number of participants: 2
Phd Student:
Martinez San Segundo, Ignacio (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Polyesters from Plant Cutin
Department of Chemistry
Period: 15/12/2014 → 14/12/2017
Number of participants: 2
Phd Student:
Scavée, Gauthier Mike Luc (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Eksternt finansieret virksomhed
Project: PhD

Synthesis and investigation of prodrugs
Department of Chemistry
Period: 01/05/2014 → 14/09/2017
Number of participants: 5
Phd Student:
Peiro, Jorge (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:

Astakhova, Kira (Intern)
Almqvist, Fredrik (Ekstern)
Olsen, Christian Adam (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Synthesis of plant cell wall oligosaccharides
Department of Chemistry
Period: 01/12/2013 → 15/08/2017
Number of participants: 5
Phd Student:
Mancuso, Enzo (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:

Gotfredsen, Charlotte Held (Intern)
Jensen, Henrik Helligsø (Ekstern)
Lowary, Todd L. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Nanoguide: Development of targeted nanoparticles for improving image-guided radiotherapy
Department of Chemistry
Period: 01/03/2013 → 21/06/2017
Number of participants: 5
Phd Student:
Schaarup-Jensen, Henrik (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Urquhart, Andrew (Intern)
Jensen, Knud Jørgen (Intern)
Ovaa, Huib (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

Synthesis of algaloligosaccharides
Department of Chemistry
Period: 01/03/2013 → 21/06/2017
Number of participants: 5
Phd Student:
Kinnaert, Christine (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Madsen, Robert (Intern)
Jensen, Henrik Helligsø (Ekstern)
Pfrengle, Fabian (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Chemical Synthesis of Hemicellulose Fragments
Department of Chemistry
Period: 01/12/2012 → 26/10/2016
Number of participants: 5
Phd Student:
Böhm, Maximilian Felix (Intern)
Main Supervisor:
Madsen, Robert (Intern)
Examiner:
Clausen, Mads Hartvig (Intern)
Oscarson, Stefan (Ekstern)
Pedersen, Christian Marcus (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering

Relations
Publications:
Chemical Synthesis of Hemicellulose Fragments
Project: PhD

Synthesis of Oligosaccharides related to the plant polysaccharide hemicellulose
Department of Chemistry
Period: 01/11/2012 → 20/04/2016
Number of participants: 5
Phd Student:
Bonora, Beatrice (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Gotfredsen, Charlotte Held (Intern)
Jensen, Henrik Helligsø (Ekstern)
Werz, Daniel B. (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering

Relations
Publications:
Synthesis of S-linked oligoxylans
Project: PhD

Synthesis of thioligosaccharides related to the plant polysaccharide cellulose
Department of Chemistry
Period: 15/07/2012 → 14/12/2016
Number of participants: 5
Phd Student:
Nami, Faranak (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Gotfredsen, Charlotte Held (Intern)
Galan, Carmen (Ekstern)
Werz, Daniel B. (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering

**Relations**
Publications:
Synthesis of S-linked cello-oligosaccharides
Project: PhD

**Ruthenium-catalyzed tandem reactions**
Department of Chemistry
Period: 01/09/2011 → 03/06/2015
Number of participants: 6
Phd Student:
Petersen, Mette Terp (Intern)
Supervisor:
Nielsen, Thomas Eiland (Intern)
Main Supervisor:
Tanner, David Ackland (Intern)
Examiner:
Clausen, Mads Hartvig (Intern)
Skrydstrup, Troels (Ekstern)
Spring, David Robert (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU) Samf.
Project: PhD

**Syntese af oligosakkarider relateret til plantepolysakkaridet hemicellulose**
Department of Chemistry
Period: 01/06/2011 → 11/03/2015
Number of participants: 5
Phd Student:
Pedersen, Martin Jæger (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Fristrup, Peter (Intern)
Pedersen, Christian Marcus (Ekstern)
Scanlan, Eoin M. (Ekstern)

**Financing sources**
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

**Syntese af oligosakkarider relateret til plantepolysakkaridet pektin**
Department of Chemistry
Period: 01/05/2011 → 20/09/2016
Number of participants: 5
Phd Student:
Daugaard, Mathilde (Intern)

Main Supervisor:
Clausen, Mads Hartvig (Intern)

Examiner:
Duus, Jens Øllgaard (Intern)
Codée, Jeroen Dirk Cornelis (Ekstern)
Nielsen, Poul (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering

Relations
Publications:
Synthesis of oligo (1→5)-α-L-arabinofuranosides related to the plant polysaccharide pectin

Design, Synthesis and Characterization of Novel Bioimetric Oligomers
Department of Chemistry
Period: 15/10/2010 → 07/05/2014
Number of participants: 5
Phd Student:
Laursen, Jonas Striegler (Intern)
Main Supervisor:
Olsen, Christian Adam (Intern)
Examiner:
Clausen, Mads Hartvig (Intern)
Albericio, Fernando (Ekstern)
Franzyk, Henrik (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Novel Analytical Technologies
Department of Chemistry
Period: 01/09/2010 → 07/05/2014
Number of participants: 5
Phd Student:
Andersen, Mathias Christian Franch (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Madsen, Robert (Intern)
Oscarson, Stefan (Ekstern)
Pedersen, Christian Marcus (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Oligosaccharide synthesis
Department of Chemistry
Period: 15/03/2010 → 24/06/2013
Number of participants: 6
Phd Student:
Zakharova, Alexandra (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Madsen, Robert (Intern)
Examiner:
Duus, Jens Ølgaard (Intern)
Field, Robert A. (Ekstern)
Hindsgaul, Ole (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Marie Curie (EU-stipendium)
Project: PhD

Bioorganic Chemistry
Department of Chemistry
Period: 01/01/2010 → 19/08/2013
Number of participants: 5
Phd Student:
Viart, Helene Marie-France (Intern)
Main Supervisor:
Clausen, Mads Hartvig (Intern)
Examiner:
Tanner, David Ackland (Intern)
Nielsen, Poul (Ekstern)
Wärnmark, B. Kenneth (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut stipendie (DTU)
Project: PhD

Dehydrogenative Coupling of Alcohols and Amines
Department of Chemistry
Period: 01/11/2009 → 19/03/2013
Number of participants: 5
Phd Student:
Maggi, Agnese (Intern)
Main Supervisor:
Madsen, Robert (Intern)
Examiner:
Clausen, Mads Hartvig (Intern)
Jensen, Henrik Helligsø (Ekstern)
Somfai, Peter (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Catalytic Routes to Renewable Polymer Building Blocks
Department of Chemistry
Period: 01/06/2008 → 14/12/2011
Number of participants: 6
Phd Student:
Hansen, Thomas Søndergaard (Intern)
Supervisor:
Woodley, John (Intern)
Main Supervisor:
Riisager, Anders (Intern)
Examiner:
Clausen, Mads Hartvig (Intern)
Bols, Mikael (Ekstern)
Leitner, Walter (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU-lønnet stipendie
Project: PhD

New Principles for Targeting Cancer - a Rational Small Molecule Approach
Department of Systems Biology
Period: 01/02/2008 → 21/09/2011
Number of participants: 6
Phd Student:
Rønnest, Mads Holger (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Main Supervisor:
Larsen, Thomas Ostenfeld (Intern)
Examiner:
Frisvad, Jens Christian (Intern)
Christensen, Søren Brugger (Ekstern)
Sterner, Olov (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Synthesis and Characterization of Membrane Active Peptides - Towards the Development of Novel Drug Delivery Systems
Department of Micro- and Nanotechnology
Period: 01/09/2007 → 24/08/2011
Number of participants: 7
Phd Student:
Etzerodt, Thomas Povl (Intern)
Supervisor:
Clausen, Mads Hartvig (Intern)
Rasmussen, Palle (Intern)
Main Supervisor:
Andresen, Thomas Lars (Intern)
Examiner:
Berg, Rolf Henrik (Intern)
Thompson, David H. (Ekstern)
Westh, Peter (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Institut/centerfinansieret
Project: PhD

Tools for Chemical Biology: New Macrocyclic Antibiotics from Diversity Oriented Synthesis
Department of Chemistry
Period: 01/04/2007 → 24/11/2010  
Number of participants: 6  
Phd Student:  
Madsen, Charlotte Marie (Intern)  
Supervisor:  
Gotfredsen, Charlotte Held (Intern)  
Main Supervisor:  
Clausen, Mads Hartvig (Intern)  
Examiner:  
Nielsen, Thomas Eiland (Intern)  
Nelson, Adam S. (Ekstern)  
Nielsen, John (Intern)  

Financing sources  
Source: Internal funding (public)  
Name of research programme: Institut/centerfinansieret  
Project: PhD

**Liposomale prodrugsystemer - syntese, biofysiske og biologiske studier**  
Department of Chemistry  
Period: 01/03/2007 → 01/09/2010  
Number of participants: 7  
Phd Student:  
Pedersen, Palle Jacob (Intern)  
Supervisor:  
Andresen, Thomas Lars (Intern)  
Madsen, Robert (Intern)  
Main Supervisor:  
Clausen, Mads Hartvig (Intern)  
Examiner:  
Tanner, David Ackland (Intern)  
Jensen, Knud Jørgen (Intern)  
Thompson, David H. (Ekstern)  

Financing sources  
Source: Internal funding (public)  
Name of research programme: Forskningsrådsfinansiering  
Project: PhD

**Metalorganiske Amineringsreaktioner**  
Department of Chemistry  
Period: 01/04/2006 → 22/10/2009  
Number of participants: 5  
Phd Student:  
Jensen, Thomas (Intern)  
Main Supervisor:  
Madsen, Robert (Intern)  
Examiner:  
Clausen, Mads Hartvig (Intern)  
Skrydstrup, Troels (Ekstern)  
Wärnmark, B. Kenneth (Ekstern)  

Financing sources  
Source: Internal funding (public)  
Name of research programme: DTU-lønnet stipendie  
Project: PhD
Tools for Chemical Biology: New Macrocyclic Antibiotics from Diversity Oriented Synthesis

Department of Chemistry
Period: 01/02/2006 → 31/12/2006
Number of participants: 3
Phd Student: Boet efter, John Magnus (Ekstern)
Supervisor: Clausen, Mads Hartvig (Intern)
Main Supervisor: Gotfredsen, Charlotte Held (Intern)

Financing sources
Source: Internal funding (public)
Name of research programme: DTU, Samfinansiering
Project: PhD

Elucidation of Functional Groups in Pectin
Pectin is a polysaccharide found in many fruits such as apples and citrus fruits. Danisco-Cultor A/S has a dominating role for production of pectin as a functional food ingredient. In order to obtain better control of properties of pectin in existing applications or to add new application areas it is necessary to strengthen the fundamental research of the molecular structure of pectin. Danisco-Cultor has obtained fundings (centerkontrakt) from the Danish research councils to a collaboration with DTU (Department of Organic Chemistry and Department of Biotechnology) and Southern University of Denmark, Odense, for this purpose. The current project aims at developing methods for esterification of raw-pectin (possibly for industrial uses), and smaller pectin-fragments, delivered by Danisco. Analytical tools for determining the degree of esterification have to be developed, including using NMR-spectroscopy. Other selective modifications of the carboxylic groups within pectin should be investigated. The modified pectin (fragments) might induce different enzymatic degradation and thus lead to new properties of pectin. Another part of the synthetic project, headed by associate professor Robert Madsen, aims at synthesizing defined building blocks of smaller protected fragments of di-tri- and tetra-saccharides of the galacturonic acids, which is the monomeric carbohydrate building the core structure of pectin. This strategy would lead to the final goal, namely to prepare tailor-made smaller pectin fragments with specific structure/substitution pattern, used for evaluation of mass spectrometric analytical methods by other partners in the project.

Department of Organic Chemistry

Danisco-Cultor
Period: 01/09/1999 → 31/08/2002
Number of participants: 6
Project participant:
Rosenbohm, Christoph (Intern)
Madsen, Robert (Intern)
Clausen, Mads Hartvig (Intern)
Christensen, Tove (Ekstern)
Mikkelsen, Jørn Dalgård (Ekstern)
Project Manager, organisational:
Lundt, Inge (Intern)

Financing sources
Source: Unknown
Name of research programme: Ukendt
Amount: 1,654,000.00 Danish Kroner
Project

Kemisk syntese af oligosakkarider indeholdt i petkin
Department of Chemistry
Period: 01/06/1999 → 28/02/2003
Number of participants: 6
Phd Student: Clausen, Mads Hartvig (Intern)
Supervisor: Lundt, Inge (Intern)
Main Supervisor:
Madsen, Robert (Intern)
Examiner:
Tanner, David Ackland (Intern)
Bock, Klaus (Ekstern)
Wengel, Jesper (Ekstern)

Financing sources
Source: Internal funding (public)
Name of research programme: Forskningsrådsfinansiering
Project: PhD

Activities:

23rd International Symposium on Glycoconjugates
Period: 16 May 2015
Mads Hartvig Clausen (Participant)
Department of Chemistry
Organic Chemistry

Description
CPH assay: high-throughput screening of endo-glycoside hydrolases using novel chromogenic polysaccharide substrates
Participation and poster presentation

Related event
23rd International Symposium on Glycoconjugates
15/09/2015 → 20/09/2015
Split, Croatia
Activity: Attending an event › Participating in or organising a conference

Chemical Biology of the Plant Cell Wall
Mads Hartvig Clausen (Invited speaker)
Department of Chemistry
Organic Chemistry

Related event
Nordic Chemical Biology Meeting
05/05/2015 → 06/05/2015
Stockholm, Sweden
Activity: Talks and presentations › Conference presentations