LAQV

requimte
rede de química e tecnologia

Collaborative topic:

Drug-Discovery

Part 1

By

Dr. K.T. Petrova

Contents

- Identified Calls
- Who we are

  Sustainable Organic Chemistry Group @ LAQV-REQUIMTE

  Prof. Dr. M.T. Barros, mtb@fct.unl.pt, and Dr. K.T. Petrova, k.petrova@fct.unl.pt
- Our expertise

In our laboratories we have synthesized various small organic molecules, functional polymers, polymeric conjugates and polymeric nanoparticles, useful for targeted drug delivery. Our work mainly involves carbohydrates, but is not limited to them. We are able to produce a large variety of structures on demand and we are open for collaborations.

Identified Calls

- The synthetic organic chemists need strong collaborations, first to identify target compounds, which to design and produce, and then to test them and prove their activities.

IMI – Innovative Medicines Initiative
https://www.imi.europa.eu/content/overview-imis-calls-how-participate

InfectEra
http://www.infect-era.eu/4th-call-2016

EuroNanoMed 2
http://www.euronanomed.net/

Worldwide Cancer Research
https://grants.worldwidecancerresearch.org/Login.aspx?ReturnUrl=%2f

Safe by Design
http://www.h2020-prosafe.eu/prosafe/?cat=4

Chronic kidney diseases
https://ec.europa.eu/research/participants/portal/desktop/en/opportunities/topics/17055-pp-1-2016-01

Chemical Processes with Microwaves: mild, fast and energy–efficient procedures

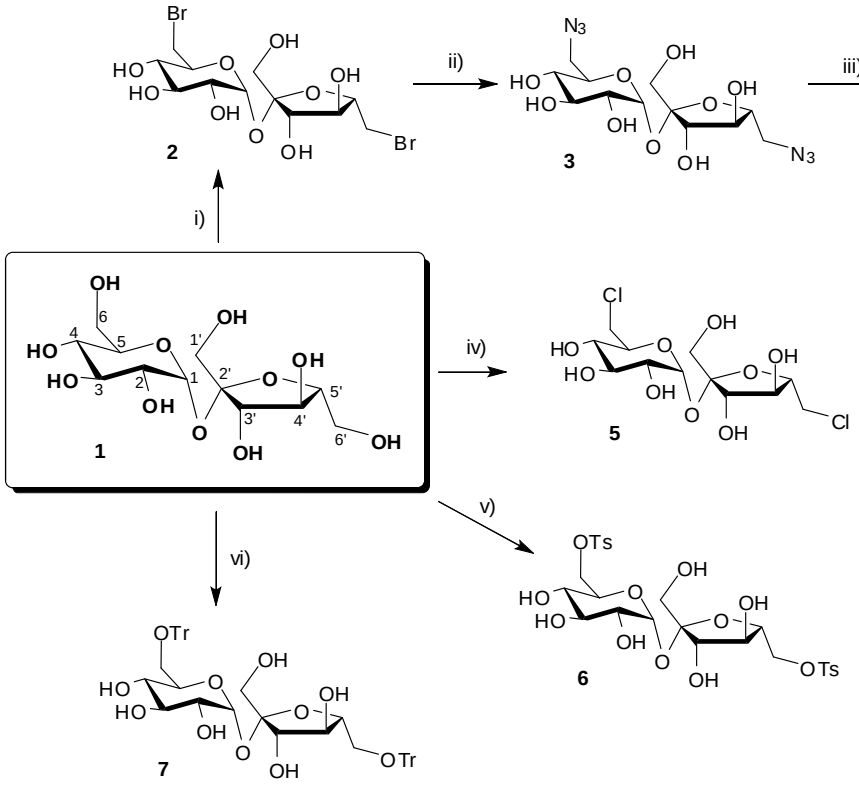
Synthetic Focused Microwave Oven

- Use of especially designed equipment
- The energy is uniformly distributed
- Advanced sensor technologies
- Simplified process monitoring and control
- Reduced amount of solvents, short reaction times

References:

Potentially Biodegradable Polymers based on α- or β-Pinene and Sugar Derivatives or Styrene, Obtained under Normal Conditions and Microwave Irradiation. *Eur. J. Org. Chem.* **2007**, 1357-1363. DOI: 10.1002/ejoc.200600890 | Fast synthesis employing a microwave assisted neat protocol of new monomers potentially useful for the preparation of PDLC films. *Cent. Eur. J. Chem.,* **2011***, 9,* 557-566. DOI: 10.2478/s11532-011-0046-2 | Efficient microwave assisted synthesis of novel 1,2,3-triazole-sucrose derivatives by cycloaddition reaction of sucrose azides and terminal alkynes. *Carbohydr. Res.* **2013,** *379*, 60-67. DOI: 10.1016/j.carres.2013.06.017 | Microwave-Assisted Protocols Applied to the Synthesis of 1',2,3,3',4,4'-Hexa-*O*-Benzylsucrose., *Synthetic Commun*., **2014**, *44*, 3027-3036. DOI: 10.1080/00397911.2014.926555

- We have developed protocols for the fast synthesis of various useful carbohydrate intermediates and biologically active compounds. Many of them have been studied for their antibacterial, antifungal, and cytotoxic activities.

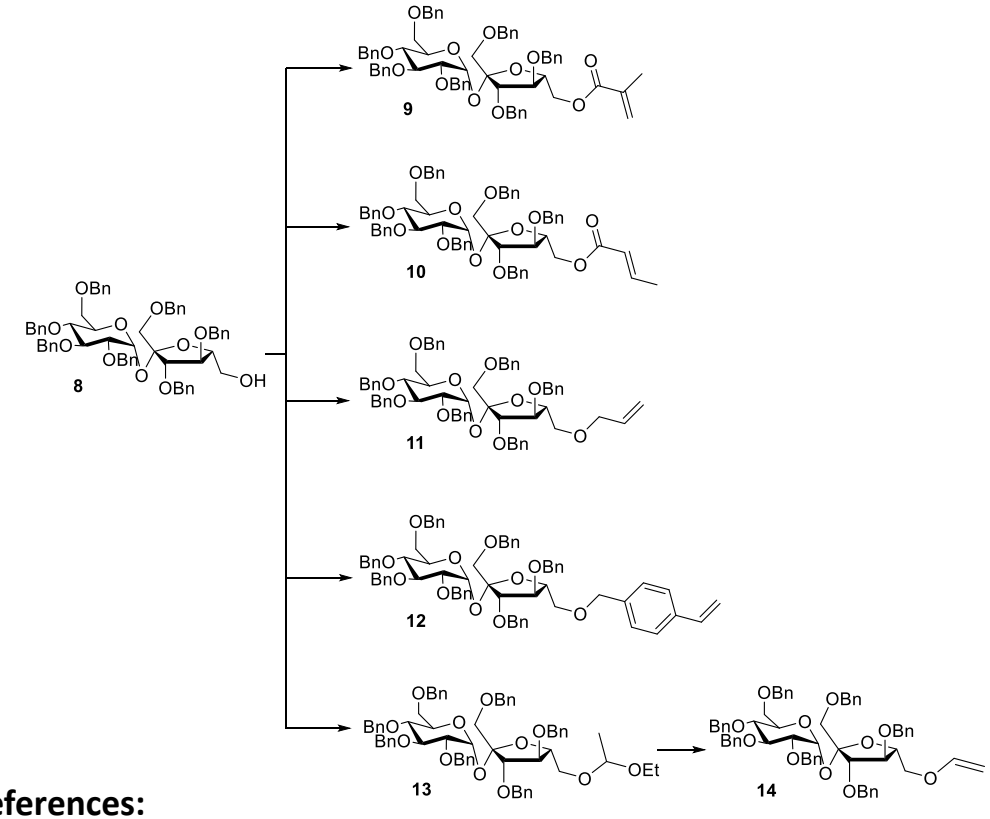


i) CBr_4, PPh_3, pyridine, 90ºC/300W, 10min, 76%;
ii) NaN_3, DMF, 145ºC/300W, 10min, 84%;
iii) PPh_3, dioxane, MeOH, 40ºC/300W, 5min, 65%;
iv) CCl_4, PPh_3, pyridine, 70ºC/300W, 10min, 73%;
v) TsCl, DMAP, pyridine, 90ºC/300W, 5min, 54%;
vi) TrCl, DMAP, pyridine, 90ºC/300W, 5min, 80%.

References:

Library of Mild and Economic Protocols for the Selective Derivatization of Sucrose under Microwave Irradiation. *Green Chem.* **2011,** *13*, 1897-1906. DOI: 10.1039/c1gc15228a | Antimicrobial and cytotoxic activities of 1,2,3-triazole-sucrose derivatives. *Carbohydr. Res.* **2015**, *417*, 66-71. DOI: 10.1016/j.carres.2015.09.003 | Synthesis, Characterization, Antimicrobial and Antitumor Activities of Sucrose Octa(*N*-ethyl)carbamate. *Med. Chem.*, **2016**, *12*, 22-29. DOI: 10.2174/1573406410666150807111029

• We have synthesized a number of novel monomers, focusing on the selectivity of the transformations. These were used to use to obtain functional biodegradable polymers and carbohydrates-decorated polymeric nanoparticles.

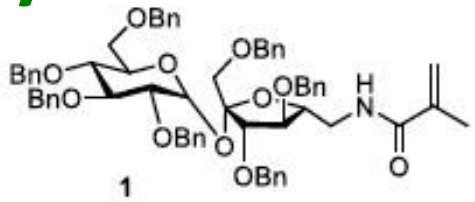


vii) $(CH_2=C(CH_3)CO)_2O$, NEt_3, CH_2Cl_2, MW 35ºC/300W, 10 min, 51%;
viii) $(CH_3CH=CHCO)_2O$, NEt_3, CH_2Cl_2, MW 35ºC/300W, 10 min, 65%;
ix) $CH_2=CHCH_2Br$, NaH, DMF, MW 145ºC/300W, 10 min, 59%;
x) $CH_2=CHC_6H_4CH_2Br$, NaH, DMF, MW 145ºC/300W, 10 min, 50%;
xi) $CH_2=CHOEt$, PPTS, CH_2Cl_2, MW 35ºC/300W, 10 min, 54%;
xii) TMSOTf, NEt_3, CH_2Cl_2, MW 35ºC/300W, 10 min, 30%.

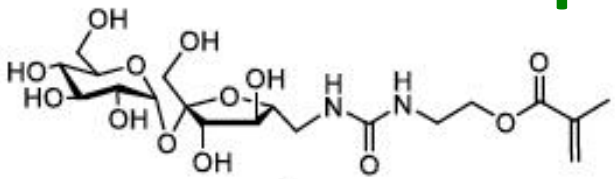
References:

Regioselective Copolymerisation of Acryl Sucrose Monomers. *J. Org. Chem.* **2004**, *69*, 7772-7775. DOI: 10.1021/jo048957y | Novel Unsaturated Sucrose Ethers and Their Application as Monomers. *Molecules* **2008**, *13*, 762-770. DOI: 10.3390/molecules13040762 | Ziegler-Natta catalysed polymerisation for the preparation of copolymers with pendant sucrose moieties. *Eur. Polym. J*. **2009**, *45*, 295-301. DOI: 10.1016/j.eurpolymj.2008.10.013 | Synthesis and biodegradation studies of new copolymers based on sucrose derivatives and styrene. *Eur. Polym. J*. **2010**, *46*, 1151-1157. DOI: 10.1016/j.eurpolymj.2010.02.002 | Synthesis of Hydrophilic and Amphiphilic Acryl Sucrose Monomers and Their Copolymerisation with Styrene, Methylmethacrylate and α- and β-Pinenes. *Int. J. Mol. Sci*. **2010**, *11*, 1792-1807. DOI: 10.3390/ijms11041792 | Chemoselective synthesis of sucrose building blocks and their polymerization. *Curr. Org. Chem*. **2014**, *18*, 1788-1802. DOI: 10.2174/13852728196661405272315

Synthesis of amphiphilic and biodegradable polymers based on renewable compounds



1



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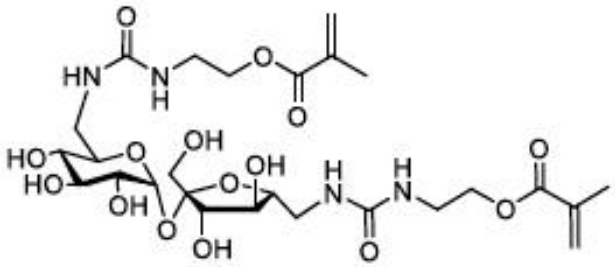

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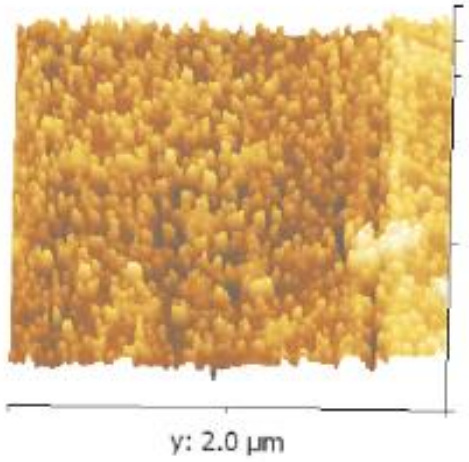
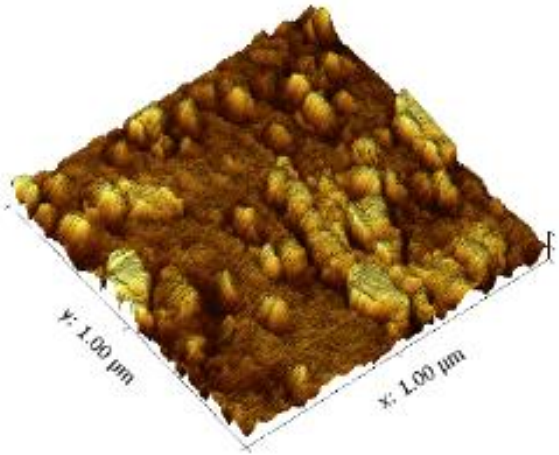
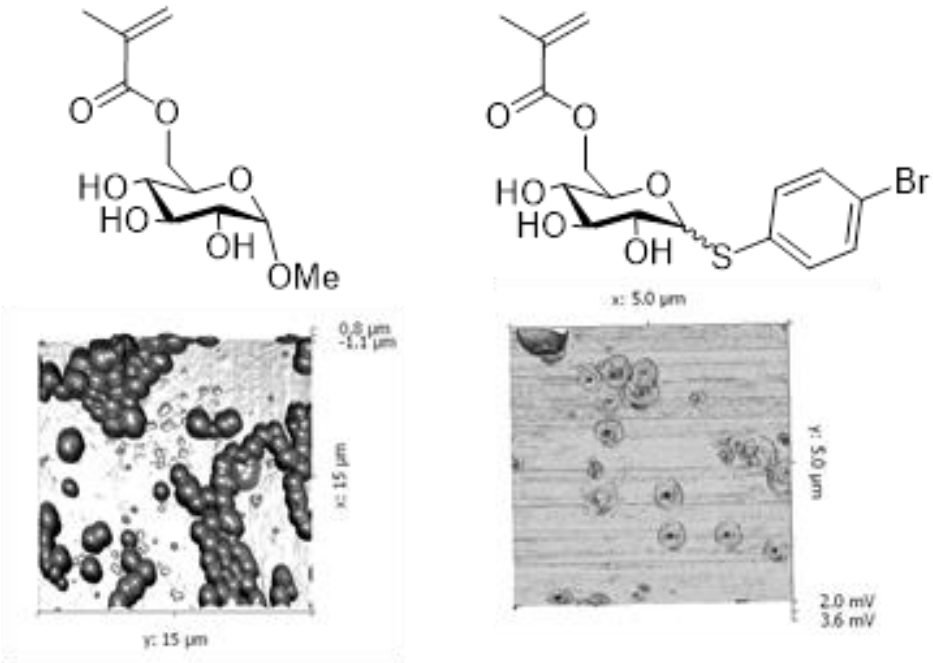




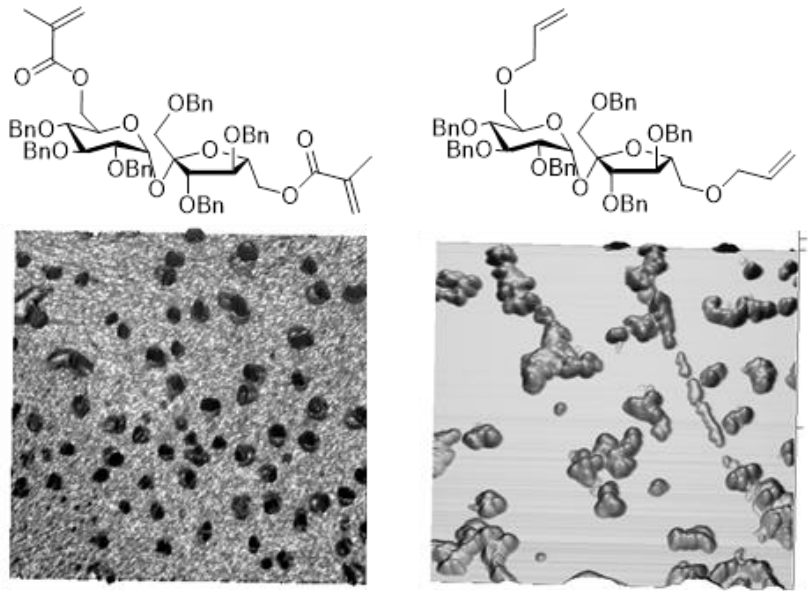
Reference:

Amide-linked N-methacryloyl sucrose containing polymers. *Carbohydr. Polym*. **2014**, *110*, 38-46. DOI: 10.1016/j.carbpol.2014.03.050

Potential applications: sugars-containing polymeric nanoparticles for drug-delivery systems



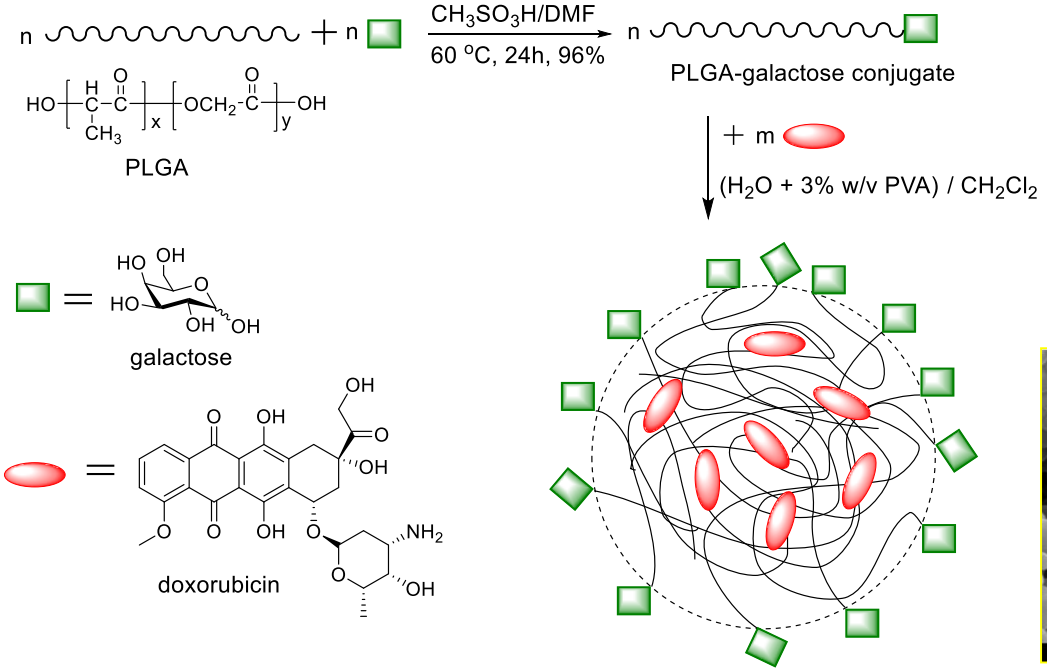
Glucose-containing spherical and core-shell polymeric beads

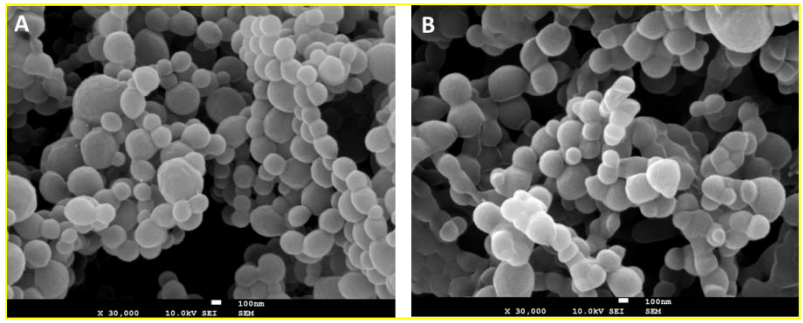


Cross-linked polymeric microparticles containing hexa-*O*-benzylsucrose.

References:
Formation of spherical and core-shell polymeric microparticles from glycopolymers. *Carbohydr. Polym*. **2015**, *125*, 281-287. DOI: 10.1016/j.carbpol.2015.02.052 | Synthesis of cross-linked polymeric microparticles containing hexa-O-benzylsucrose. *Des. Monomers Polym*. **2015**, *18*, 753-760. DOI: 10.1080/15685551.2015.1070507

Smart Nanoparticles for Targeted Drug Delivery





Scheme of PLGA-GAL conjugate synthesis and doxorubicin-loaded nanoparticles formation. Representative scanning electron microscope photographs.

In collaboration with M.M. Cardoso and I.N. Peça

References:

Preparation and Characterization of Polymeric Nanoparticles Composed of Poly(DL-lactide-co-glycolide) and Poly(DL-lactide-co-glycolide)-co-poly(ethylene glycol) 10%Triblock end-capped with a galactose moiety. *React. Funct. Polym*. **2012**, *72*, 729-735. DOI: 10.1016/j.reactfunctpolym.2012.06.019 | Doxorubicin-loaded galactoseconjugated poly(d,l-lactide-co-glycolide) nanoparticles as hepatocyte-targeting drug carrier. *J. Microencapsul*. **2016**, DOI: 10.1080/02652048.2016.1185474

Thank you for your kind attention!