AUTHOR’S REVIEW OF HIS WORK

Functionalization of di- and polisaccharides

Dr Stanisław Porwański

Department of Organic and Applied Chemistry,
Faculty of Chemistry, University of Łódź

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Table of contents

1 Personal data

1.1 Name and surname

Stanisław Porwański

1.2 Diplomas

My master thesis entitled *Synthesis and spectral studies on deutheroderivatives of 3-Phenyl-2-methyl-azabicyclobutanes* was conducted under guidance of prof. Romuald Bartnik at the Department of Organic and Applied Chemistry, University of Lodz.

My Ph.D. thesis entitled *Palladium(0)-catalysed formation of glycosides, disaccharides and disaccharide ethers* was conducted in the Department of Organic and Applied Chemistry, University of Lodz under guidance of prof. Bogusław Kryczka in collaboration with the Laboratory of Asymmetric Synthesis at the University Claude Bernard Lyon I (directed by prof. Denis Sinou). I received a series of unsaturated disaccharides in good yields, by alkylation of ethyl α-*O*-Δ^2-glycosides, having a leaving group at C-4 or C-2 position, with various carbohydrates, in the presence of catalytic amounts of Pd(0).

1.3 Employment

01.10.87-05.06.1997 assistant (*Department of Organic and Applied Chemistry, Faculty of Chemistry, University of Łódź)*

06.06.97-30.09.2009 adjunct (*Department of Organic and Applied Chemistry, Faculty of Chemistry, University of Łódź)*

01.10.2009-still – senior lecturer (*Department of Organic and Applied Chemistry, Faculty of Chemistry, University of Łódź)*

1.4 Publications -statistics

Original articles:

–*22* publications (19 experimental papers in the full version, all in foreign journals and 2 review articles: *Wiadomości Chemiczne* and *Polish Journal of Chemistry*); the first author – 6 papers, corresponding author – 2 papers),

– *after obtaining the PhD degree* – 18 publications (the first author – 6 papers, corresponding author – 2 papers).

Total IF of all work: **34,314** (1,56 for one paper)

Total points Ministry of Science and Higher Education (MSHE): **490** (24,50 for one paper)

*Total IF of major publications: **20,84** (2,61 for one paper)*
*Total points MSHE of major publications: **230** (28,75 for one paper)*

Total IF of works before obtaining the degree of doctor: **3,336** (0,83 for one paper)
Total points MSHE before obtaining the degree of doctor: **53** (13,25 for one paper)

Total IF of works after obtaining the degree of doctor: **30,978** (1,72 for one paper)
Total points MSHE after obtaining the degree of doctor: **420** (19,09 for one paper)

Summarized citations: **143** (by Web of Science),– 09.05.2014
H-index : **8** (by Web of Science) – 09.05.2014

Reports on the Polish and international conferences in the form of posters and communications **84**

Impact Factor (IF) of scientific publications are given in accordance with their year of publication.

2 Main scientific achievements

2.1 Major publications

P1. S. Porwanski, P. Salanski, G.Descotes, A.Bouchu, Y.Queneau

Selective Synthesis of 4,6-*O*-Alkenylidene and -Benzylidene Acetals from Unprotected Sucrose by Lanthanide(III) Resin-Catalyzed Transacetalization

Synthesis, **2000.** *4*, 525-528.

IF = 2.19 (**25 pt** MSHE)

My contribution to this work consisted of managing the research project, performing synthesis of all compounds, analyzing the results as well as writing the experimental and discussion parts of the manuscript. I estimate my participation at 70%.

P2. S. Porwanski, P. Salanski, N. Panaud, G. Descotes, A. Bouchu, Y. Queneau

Regioselectivity in acid- or base-catalysed acetalation of sucrose: selection of [OH-2, OH-3] or [OH-4, OH-6] diols

*Top. Catal***., 2000,** *13* (3); 335-338.

IF = 3.24 (**35** pt MSHE)

My contribution to this work consisted of managing the research project, performing synthesis of 4,6-O-acetals of sucrose, analyzing the results as well as writing the experimental and discussion parts of the manuscript. I estimate my participation at 50%.

P3. S. Porwanski, B. Kryczka, A. Marsura**,**

A polymer-supported 'one-pot' phophine imide reaction on cyclodextrins

Tetrahedron Lett. **2002;** *43;* 8441-8443

IF = 2.36 (**25** pt MSHE)

My contribution to this work consisted of managing the research project, performing synthesis of all compounds, analyzing the results as well as writing the experimental and discussion parts of the manuscript. I estimate my participation at 70%.

P4. S. Menuel, **S. Porwanski,** A. Marsura

New synthetic approach to per-O-acetyl-isocyanates, isothiocyanates and thioureas in the disaccharide and cyclodextrin series

New J. Chem. **2006,** *30*, 603-608

IF = 2.65 (30 pt MSHE)

*My contribution to this work consisted of managing the research project, performing synthesis of compounds **29-31** and **34-38**, analyzing the results as well as writing the experimental and discussion parts of the manuscript. I estimate my participation at 50%.*

P5. S. Porwanski, A. Marsura

Tandem Staudinger–Aza-Wittig Templated Reaction: De Novo Synthesis of Sugar–Ureido Cryptands

Eur. J. Org. Chem. **2009**, 2047-2050.

IF = 3.10 (35pt MSHE)

My contribution to this work consisted of managing the research project, performing synthesis of all compounds, analyzing the results as well as writing the experimental and discussion parts of the manuscript. I estimate my participation at 70%.

P6. S. Porwanski, F. Dumarcay-Charbonnier, S. Menuel, J.P. Joly, V. Bulach, A. Marsura

Bis-β-Cyclodextrinyl-And Bis-cellobiosyl-diazacrowns: Synthesis And Molecular Complexation Behaviors Toward Busulfan Anticancer Agent And two Basic Aminoacids"

Tetrahedron, **2009**, 65, 6196-6203

IF=3.22 (30 pt. MSHE**)**

My contribution to this work consisted of managing the research project, performing synthesis of disaccharide derivatives, analyzing the results. I estimate my participation at 50%.

P7. M. Pintal, B. Kryczka, A. Marsura, **S. Porwański*,**

Synthesis of bis-cellobiose and bis-glucose derivatives of azacrown macrocycles as hosts in complexes with acetylsalicylic acid and 4-acetamidophenol

Carbohydr. Res., **2014**, *386*, 18-22

IF=2.04 (25 pt. MSHE**)**

My contribution to this work consisted of managing research project, overseeing the progress of work, analyzing the results as well as writing the manuscript, and editing the response to reviewer comments. I estimate my participation at 65%.

P8. S. Porwański*

New ureas containing glycosyl and diphenylphosphinyl scaffolds: synthesis and the first attempts to use them in asymmetric synthesis

Carbohydr. Res., **2014**, *394*, 7-12

IF=2.04 (25 pt. MSHE**)**

My contribution to this work consisted of managing research project, performing synthesis, analyzing the results as well as writing the manuscript, and editing the response to reviewer comments. I estimate my participation at 100%.

2.2 Introduction to the field of research

Carbohydrates are arguably one of the most important classes of natural products. Carbohydrates are naturally enantiomerically pure compounds which have an interesting stereochemical variety and, in addition, are cheap and readily available in large quantities. They serve as important energy sources and energy storage compounds in both plants and animals, and are essential as integral parts of structural fibres of plants, insects, fungi, crustaceans and spiders. Carbohydrates have been used as starting materials to synthesise enantiomerically pure compounds. However, carbohydrates have never been used as chiral auxiliaries in stereoselective syntheses. About 30 years ago, Vassela reported the earliest example of carbohydrate auxiliary tools in organic synthesis.[1] During the following decades, carbohydrates slowly became recognized as versatile starting materials for chiral auxiliaries in stereoselective reaction, and today a multitude of structures has been developed and applied to various reactions.[2] More recently, carbohydrate derivatives have also been used to obtain chiral ligands for catalysis. Carbohydrate derivatives possess certain distinct advantages as ligands. Carbohydrates, which are inexpensive and readily available natural materials, have recently also been employed as chiral backbones of organocatalysts. Since the beginning of the new century we have been able to witness a remarkable renewal of interest in enantioselective organocatalysis. One factor explaining this observed acceleration was a better understanding of the function and structure of glycoproteins and other naturally occurring sugar derivatives; for example, in the 1990s Shi et al. successfully applied fructose-derived ketones as chiral organocatalysts in asymmetric epoxidation reactions of olefins[3], and Roberts' group described carbohydrate-derived thiols as chiral organocatalysts for enantioselective radical additions[4]. In the chemistry of sugars, a very important group are disaccharides and polysaccharides, which are also of interest to our group. Disaccharides, with their free eight hydroxyl groups, are very difficult objects to test. Sugars are compounds that contain a glycoside bond between carbon 1 of one sugar and a hydroxyl group at any position on the other sugar. The best-known disaccharides are sugars containing two hexose units, such as sucrose in cane sugar, maltose in malt sugar and lactose in milk sugar. These

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[1] Vasella, A., *Helv. Chim. Acta*, **1977**, *60*, 1273

[2] Boysen, M. M. K. *Carbohydrates-Tools for Stereoselective Synthesis*, Wiley-VCH, Weinheim, **2013**.

[3] Wong, O.D., Shi, Y. *Chem. Rev*., **2008**, *108*, 3958.

[4] Roberts, B.P., *Chem. Soc. Rev*., **1999**, *28*, 25.

sugars are hydrolysed into monosaccharides in the digestive track by specific enzymes, and each of these important sugars – sucrose, maltose and lactose – has a role to play in human nutrition. For example, maltose which is a disaccharide obtained by enzyme-catalysed hydrolysis of starch, consists of two D-glucopyranoses joined by a 1,4-beta-glycoside bond. Both maltose and cellobiose, obtained from cellulose, are reducing sugars because the anomeric carbons on the right-hand sugar are part of the hemiacetal. Despite the similarities in their structures, cellobiose and maltose are biologically different. Cellobiose cannot be digested by humans and cannot be fermented by yeast. However, maltose is digested without difficulty and is fermented readily. Lactose is a reducing disaccharide that occurs naturally in both human and cow milk. It is widely used in baking and in commercial infant-milk formulas. Lactose, unlike cellobiose and maltose, contains two different monosaccharide units, with a 1,4-β-linked glycoside. An acidic hydrolysis of lactose yields 1 equivalent of D-glucose and 1 equivalent of D-galactose. Another example of a reducing disaccharide is melibiose, which contains the 1,6–α-glycosidic bond. Sucrose, an ordinary table sugar, is probably the most abundant pure organic chemical in the world and also one of the most widely known to non-chemists chemicals. It is obtained from sugar cane (20% by weight) or sugar beets (15% by weight). Unlike most other disaccharides, sucrose is not a reducing sugar and does not exhibit mutarotation. Formulas of the sugars listed above are shown in Figure 1.

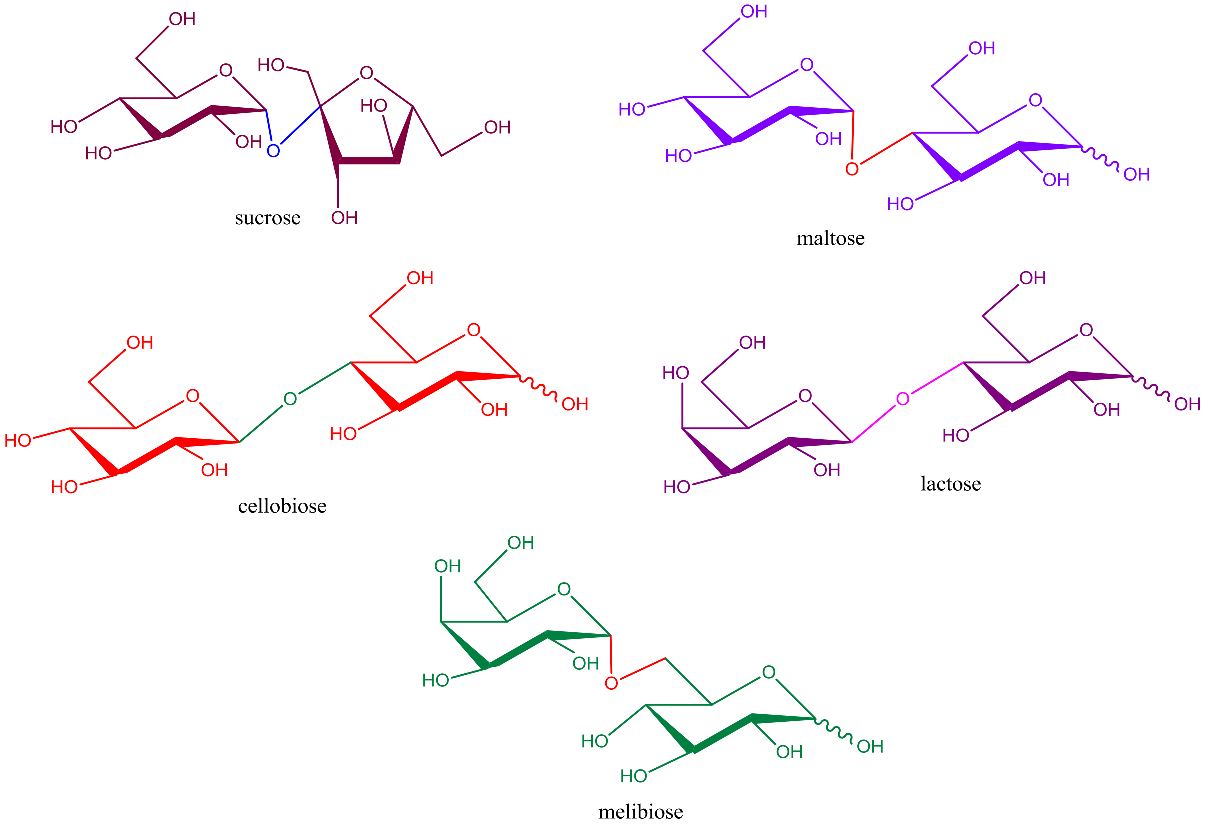
sucrose
maltose
cellobiose
lactose
melibiose

Figure 1

The family of polysaccharides that remains in our circle of interest are cyclodextrins. Cyclodextrins (CyDs) are macrocyclic oligosugars most commonly composed of 6, 7 or 8 glucosidic units bearing 1,4-α-glycoside bond, so-called α-, β- or γ-CyD (Figure 2).

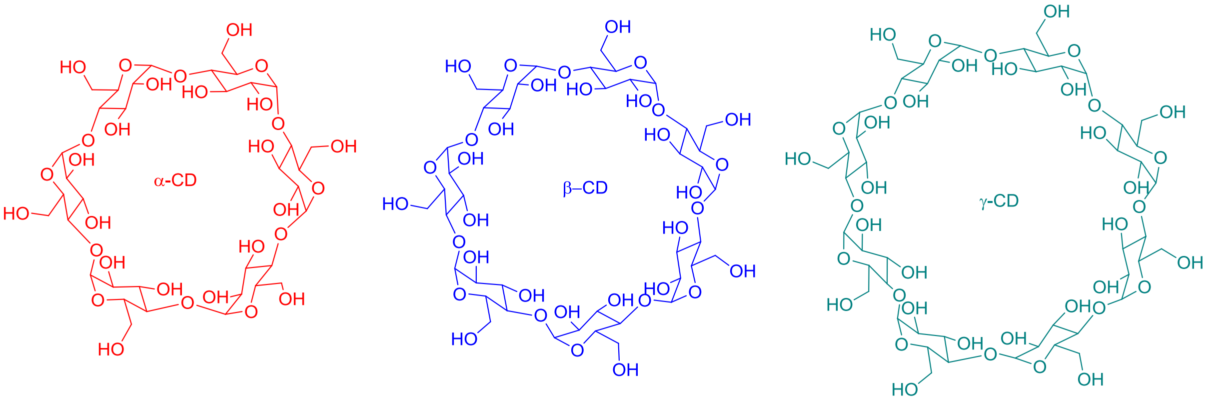

Figure 2

Each of the chiral glucose units is in a rigid $^4C_1$ chair conformation, thus giving the macrocycle shape of a hollow truncated cone with all of the secondary hydroxyl groups located on the wider rim, while all of the primary hydroxyl groups are on the narrower rim (Figure 2). The primary and secondary hydroxyl groups on the outside of the CyD make it water-soluble. CyDs have been studied extensively as hosts in supramolecular chemistry.[5,6] The choice of structure of CyDs is of particular importance for supramolecular host-guest complexes, which are the basis of most cyclodextrin applications in medicine, catalysis, separation and sensor technology as well as the food chemistry.

In the initial period, my research interests were concentrated on the functionalisation of sucrose in interesting and useful products in perfumery and food industry (P1, P2).

Methods for the selective functionalisation of carbohydrates are useful both for the direct transformation of unprotected sugars to low added value derivatives, and for the subtle protection–deprotection strategies in multistep syntheses of complex molecules. In the case of sucrose, which can be considered as a promising raw material for the chemical industry because of its exceptional availability, the presence of eight hydroxyl groups provides an interesting field of experimentation aiming at the control of the regioselectivity and/or the degree of substitution.[7,8] Among the numerous chemical reactions involving the alcohol function, the acetalation reaction is extensively used in the case of carbohydrates, mostly for protection purposes. The fragility of the glycosidic bond of sucrose under acidic conditions, (because of its fructofuranosidic nature) is a strict limitation to acid-catalysed acetalations. Only very reactive carbonyl compounds are reactive enough under appropriate acidic conditions which preserve the disaccharidic integrity of the molecule. Notably, the transacetalation reaction of *α,β*-unsaturated dialkylacetals has been shown to occur under mild conditions by Gelas and co-workers, then by our group, and later by Queneau et al.[9,10]

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[5] Szejtli, J: *Chem. Rev*. **1998**, *98*, 1743

[6] Dodziuk, H., *Cyclodextrins and Their Complexes. Chemistry, Analytical Methods, Application* Wiley-VCH, Weinheim, **2006**.

[7] (a) Khan, R. *Adv. Carbohydr. Chem. Biochem*. **1976**, *33* 235; (b) L. Hough, in: *Carbohydrates as Organic Raw Materials*, ed. F. W. Lichtenthaler (VCH, Weinheim, **1991**) p. 33

[8] Queneau, Y.; Jarosz, S.; Lewandowski, B.; Fitremann, J. *Adv. Carbohydr. Chem. Biochem*. **2007**, *61*, 217.

[9] (a) Fanton, E., Fayet, C., Gelas, J., Jhurry, D., Deffieux A., Fontanille, M. *Carbohydr. Res*. **1992**, *226*, 337; (b) Fanton, E., Fayet C., Gelas, J. *Carbohydr. Res*. **1997**, *198*, 85.

[10] Salanski, P., Descotes, G., Bouchu, A., Queneau, Y. *J. Carbohydr. Chem*. **1998**, *17*, 129.

Sensitivity to the acidic glycoside bond in sucrose has encouraged researchers to seek methods for the preparation of derivatives without bond cleavage. Such requirements are fulfilled by one pot procedure (**P1**, **P2**), in which I have obtained cyclic acetals of sucrose in the presence of lanthanides deposited on the ion exchange resin. As a result, cyclic acetals can be obtained with very good yields without damaging the glycosidic bond. My research was inspired by the work of Yu et al., who used lanthanides embedded in resin for the synthesis of simple acetals of aldehydes and ketones.[11] In addition, I have showed that the catalyst can be recovered and reused without loss of capacity.

Collaboration with Professor Marsure from the University of Nancy resulted in developing the synthesis of many interesting di- and polysaccharide derivatives of urea using the "phosphinimide" reaction. This reaction was first described by Professors Pinter and Marsure and its general scheme is shown below.[12]

$$\text{Azide} \xrightarrow{\text{PPh}_3/\text{CO}_2} \text{Isocyanate} \xrightarrow{\text{Nuclephile}} \text{Product}$$

Scheme 1

If the nucleophile is a primary or secondary amine, the product of this reaction is the urea derivative. Exchanging carbon dioxide for disulfide leads to an isothiocyanate and then to thiourea as the final product.

It is well known that compounds containing the urea or thiourea functionality are of extended biological interest in several classes of drugs.[13] In the carbohydrate field, glycosylureas have been shown also to be useful antidiabetic agents.[14] By carrying out the reaction of di- or polysaccharide azides in the presence of triphenylphosphine, carbon dioxide or disulfide, I have managed to receive a number of derivatives of these compounds with very good yields (P3, P4).

I have developed a method for the synthesis of urea derivatives of β-cyclodextrin in the presence of polymer-supported phosphine (P4). The use of polymer-supported phosphine solved the problem of a phosphine oxide as a by-product that was complexed in the middle of the cone of cyclodextrin and was difficult to remove from the final product. Greatly successful was the separation and full characterisation of isocyanates in anomeric position of the disaccharide which, as highly reactive compounds, had not previously been separated with this method.

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[11] Yu, L.; Chen, D.; Li, J.; Wang, P. G. *J. Org. Chem.* **1997,** *62*, 3575.

[12] (a) Kovacs, J.; Pinter, I.; Messmer, A.; Toth, G. *Carbohydr. Res.* **1985**, *141*, 57; (b) Pinter, I.; Kovacs, J.; Toth, G. *Carbohydr. Res.* **1995**, *273,* 99; (c) Sallas, F.; Kovacs, J.; Marsura, A.; Jicsinszky, L. *Tetrahedron Lett.* **1996**, *37*, 4011.

[13] As antitumor agents see: (a) Gurulingappa, H., Amador, M. L., Zhao, M., Rudek, M. A., Hidalgo M., Khan, S. R. *Bioorg. Med. Chem. Lett*., **2004**, *14*, 2213; (b) Monneret, C., Risse, R., Ardouin P. and Gouyette, A. *Eur. J. Med. Chem*., **2000**, *35,* 137; (c) as an antimalarial agent: Dominguez, J. N., Caritza, L., Rodrigues, J., Gamboa de Dominguez, N., Gut J. and Rosenthal, P. J. *J. Med. Chem*., **2005**, *48*, 3654; (d) as ACAT inhibitors see: Tanaka A., Terasawa, T. *Drugs Future*, **2000**, *25*, 171; (e) Ban, H., Muraoka M., Ohashi, N. *Tetrahedron*, **2005**, *61*, 10081; (f) thiourea derivatives: de Vries, V. G. *US Pat*. 5003106, **1991**; (g) Venkatachalam T. K., Uckun, F. M. S*ynth. Commun*., **2005**, *35*, 2039.

[14] (a) Oikonomakos, N. G., Kosmopoulou, M., Zographos S. E., Leonidas, D. D., Chrysina, E. D., Somsak, L., Nagy, V., Praly, J.-P., Docsa, T., Toth, B., Gergely, P. *Eur. J. Biochem*., **2002**, *269*, 1684; (b) Somsak, L., Nagy, V., Hadaly, Z., Docsa T., Gergely, P. *Curr. Pharm. Des*., **2003**, *9*, 1177.

Further research in the field of urea derivatives resulted in the development of efficient synthesis of cryptands of di- and polysaccharide derivatives of azacrown ethers as effective receptors for drug and aminoacids in host-guest complexes (P5, P6, P7).

Natural or synthetic macrocyclic molecules are interesting compounds for various applications in supramolecular chemistry.[15] The characterizing feature of supramolecular chemistry is that carefully designed synthetic structures (hosts) recognize target molecules (guests) and form a supramolecular complex through noncovalent interactions. A supramolecular complex is formed when there is attractive interaction between host and guest that includes H-bonding, aromatic-aromatic π-stacking, electrostatic and hydrophobic forces. The development of artificial receptors able to form complexes with specific guest has been important to the progress of supramolecular host-guest chemistry. In designing a suitable hosts you have to consider parameters like host size, charge, character of the donor atom, according to the properties of target molecules. The optimal preorganization of host and guest are obtained in the complementarity of the binding sites of host and guest. Suitable neutral host types known for binding cationic molecules are crown ethers, podands, cryptands, cyclophanes and calixarenes. Very often crown ethers constitute the main part of construction of macrocycles. Crown compounds are capable of selective binding to metal, ions, organic compounds, and neutral molecules.[16] When the metal cation radius exactly fits the size of the crown units, it usually forms a1/1 host/guest complex. In cases when the cation is larger than the crown cavity, a particularly interesting phenomenon is observed, consisting in formation of complexes with 2/1 stoichiometry (sandwich-type complex). Crown ethers and azacrown ethers are important molecular receptors that are currently being used in biological model systems. It has been also shown that sugars are well known to be versatile chiral entities that are particularly suitable for the design of chiral receptors. Crown ethers containing various carbohydrate moieties have received much attention in recent years.[17] Usually, the sugar moieties are mono-, di-, or trisaccharides which are directly incorporated into the crown macrocycle itself or grafted on as pendant arms.[18] Host-guest chemistry, and among others the

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[15] (a) Lehn, J.-M. *Science* **1985**, *227*, 849–856; (b) Muller-Dethlefs, K., Hobza, P. *Chem. Rev*. **2000**, *100*, 143; (c) Davis F., Higson S. "*Macrocycles Construction, Chemistry and Nanotechnology Applications*", John Wiley &Sons **2011**.

[16] (a) Gokel, G.W. *Crown Ethers and Cryptands*; Royal Society of Chemistry: Cambridge, **1991;** (b) Lehn J.M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Weinheim, **1995;** (c) Schneider, H.-J.; Yatsimirsky, A. *Principles end Methods in Supramolecular Chemistry*; Wiley: Chichester, **2000**; (d) Späth, A., König. B. *Beilstein J. Org.Chem*. **2010**, *6*, No.32; (e) Gokel. G.W., Leevy. W.M., Weber. M. E., *Chem. Rev*. **2004**, *104*, 2723.

[17] (a) Jarosz, S.; Listkowski, A. *Curr. Org. Chem*. **2006**, *10*, 643-662; (b) Bakó, P.; Keglevich, G.; Rapi, Z. *Lett. Org. Chem*. **2010**, *7*, 645.

[18] (a) Pietraszkiewicz, M.; Salanski, P.; Jurczak, J. *Tetrahedron* **1984**, *40*, 2971; (b) Van Maarschalkerwaart, D. A. H.; Willard, N. P.; Pandit, U. K. *Tetrahedron* **1992**, *48*, 8825; (c) Joly, J.-P.; Nazhaoui, M.; Dumont, B. *Bull. Soc. Chim. Fr*. **1994**, *131*, 369; (d) Miethchen, R.; Fehring, V. *Synthesis* **1998**, 94; (e) Pietraszkiewicz, M., Koźbiał, M., Pietraszkiewicz, O. *J. Membr. Sc.* **1998**, *138*, 109; (f) Sharma, G. V. M.; Reddy, V. G.; Krishna, P. R. *Tetrahedron: Asymmetry* **1999**, *10*, 3777; (g) Gryko, D.T.; Piatek, P.; Jurczak, J. *Synthesis* **1999**, 336; (h) Wenzel, T. J.; Thurston, J. E.; Sek, D.C.; Joly, J.-P. *Tetrahedron: Asymmetry* **2001**, *12*, 1125; (i) Faltin, F.; Fehring, V.; Miethchen, R. *Synthesis* **2002**, 1851; (j) Bako, T., Bako, P., Keglevich, G., Bombicz, P., Kubinyi, M., Pal, K., Bodor, S., Mako, L., Toke, L. *Tetrahedron Asymmetry* **2004**, *15*, 1589; (k) Bakó, P.; Makó, A.; Keglevich, G.; Kubinyi, M.; Pál, K. *Tetrahedron: Asymmetry* **2005**, *16*, 1861; (l) Menand, M., Blais, J.-C., Valery J.-M., Xie, J. *J. Org. Chem*. **2006**, *71*, 3292; (m) Queneau, Y., Jarosz, S., Lewandowski, B., Fitremann, J. *Adv. Carbohydr. Chem. Biochem*. **2007**, *61*, 217; (n) Coppola, C., Virno, A., De Napoli, L., Randazzo, A.,

sugar macrocycle, is emerging as one of the key elements of science and nonotechnology, that aims to improve systems that exhibit higher association constants and greater selectivity.[19] In this context I had the opportunity to demonstrate that novel C2-symmetrical heterotropic co-receptors 1,10-N,N'-Bis-(*β*-D-ureidocellobiosyl)-4,7,13,16-tetraoxa-1,10 diazacyclooctadecane efficiently encapsulated Busulfan (1,4-butanedioldimethanesulfonate), a powerful antitumour drug in leukemia (**P6**). Our studies had showed two types of interactions in the complex: hydrogen bonds between sulfonic groups and urea bridges and van der Waals forces hydrophobic chain of the busulfan with azacrown protons. In the light of these first results it appears that the next step of our research should be the investigation of other receptors of this type, varying the size of the azacrowns cavity. In addition, the host turned out to be completely non-toxic and the complex showed a very good solubility in water, while Busulfan as a drug is poorly soluble in water. Herein we report two new sugar decorated receptors in which the 1,10-diaza-18-crown-6 has been replaced with 1,4,10-trioxa-7,13-diazacyclopentadecane (Kryptofix 21). The new, obtained macrocycles besides the disaccharides in the urea bridge involve also monosaccharides units. Such derivatives can form dissolved in water the guest-host type complexes with *bis*-substituted aromatic guest (aspirin and paracetamol) (P7).

The use of cesium and sodium cations as a "template" is a successful strategy for the preparation of sugar cryptands (P5). Suitable sucrose and cellobiose derivatives were received in good yields and I have shown that the size of the metal cation determines the structure of the obtained macrocycles.

Another aim of the study was to synthesize the sugar urea derivatives containing the function of chiral phosphine, and to check the effectiveness of these ligands or organocatalysts in asymmetric synthesis. My results are the first examples of applications of sugar urea derivatives with phosphines as effective organocatalysts in the asymmetric Morita-Baylis-Hillman and aza-Henry reactions (P8).

Saccharides, as naturally occurring compounds with defined stereogenic centre, are useful building blocks for many interesting structures.[20] Carbohydrates, which are inexpensive and readily available natural materials, have recently been employed as chiral backbones of organocatalysts. Examples of effective catalysts with a thiourea bridge which are often combined with saccharides, can be found in the literature.[21] Much less examples of

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Montesarchio, D. *Tetrahedron* **2009**, *65*, 9694; (o) Potopnyk, A. M., Lewandowski, B., Jarosz, S. *Tetrahedron: Asymmetry* **2012**, *23*, 1474; (p) Rapi, Z., Bakó, P., Keglevich, G., Szölloősy, Á., Drahos, L., Hegedűs, L. *Carbohydr. Res*. **2013**, *365*, 61; (r) Sabah, J.K., Hashim, R. *Tetrahedron Lett*. **2013**, *54*, 1534; (s) Balbuena, P., Goncalves-Pereira, R., Blanco, L.J., Garcia-Moreno, M. I., Lesur, D.,Ortiz Mellet, C., Garcia Fernandez, J. *J. Org.Chem*. **2013**, *78*, 1390.777

[19] Kinbara, K.; Aida, T. *Chem. Re*v. **2005**, *105*, 1377.

[20] (a) Dieguez, M., Pamies, O., Ruiz, A., Diaz, Y., Castillon, S., Claver, C. *Coord. Chem. Rev.* **2004**, *248*, 2165; (b) Gao, P., Wang, Ch., Wu, Y., Zhou, Z., Tang, Ch. *Eur. J. Org. Chem*. **2008**, 4563; (c) Weihong, Y., Feng, S., Xin, Z., Kui, Y., Xinyan, W. *Chin. J. Chem*. **2012**, *30*, 2652; (d) Lu, A., Hu, K., Wang, Y., Song, H., Zhou, Z., Fang, J., Tang, Ch. *J. Org. Chem*., **2012**, *77*, 6208; (e) Taha, T. A., Richards, M. R., Lowary, T. L. *Chem. Rev*. **2013**, *113,* 1851.

[21] a) Liu, K., Kui, H.-F., Nie, J., Dong, K.-Y., Li, X.-J., Ma, J.-A. *Org. Lett.* **2007**, *9*, 923; (b) Pu, H., Li, P., Peng, F., Li, X., Zhang, H., Shao, Z. *Eur. J. Org. Chem*. **2009**, 4622; (c) Gu, Q., Guo, X-T., Wu, X-Y., *Tetrahedron,* **2009**, *65,* 5265; (d) Wang, Y., Yang, H., Yu, J., Miao, Z., Chen, R. *Adv. Synth. Catal*, **2009,** *351*, 3057; (e) Chen, J.-R., Cao, Y.-J., Zou, Y.-Q., Tan, F., Fu, L., Zhu, X.-Y., Xiao, W.-J., *Org. Biomol. Chem.*, **2010,** *8*, 1275; (f) Ma, H., Liu, K., Zhang, F.G., Zhu, Ch.L., Nie, J., Ma, J.A. J. Org. Chem., **2010**, *75*, 1402; (g)

application of urea saccharide organocatalyst in asymmetric synthesis can be found in the chemical reports.[22]

I received a series of urea derivatives of saccharide with phosphine, which proved to be capable to act as ligands or organocatalysts. Derivative **64** is an effective chiral ligand in the stereoselective synthesis of vinyl-tetrahydrofurans.[23] The positive results of this reaction encouraged us to obtain a larger group of this type of compounds and to study them also as organocatalysts. The saccharide derivatives that include a chiral phosphine moiety were tested as organocatalysts in the Morita-Baylis-Hillman and aza-Henry reaction. There are known examples of effective thiourea sugar derivatives acting as organocatalysts in such type of reactions[21], but there are no reports describing the use of saccharides urea derivatives. My results are the first examples of applications of sugar urea derivatives with phosphines as effective organocatalysts in the asymmetric Morita-Baylis-Hillman and aza-Henry reactions (P8).

<u>The aim of the study was to:</u>

1. The design and realisation of the transacetalisation reaction of sucrose with aldehydes and ketone dimethylacetals in the presence of lanthanide cations supported on resin.
    - preparation of lanthanide catalysts,
    - optimization of reaction conditions,
    - isolation in pure form, and full spectroscopic characterisation of sucrose derivatives,
    - checking for the possibility of recovery and reuse of the catalyst.
2. The design and realisation of the synthesis of isocyanates, isothiocyanates, and di- and polysaccharide urea derivatives.
    - The synthesis in the presence of a phosphine deposited on a solid support,
    - The regeneration of phosphine and verification of the effectiveness of its re-use,
    - The isolation of pure isocyanates and isothiocyanates at the anomeric position of the disaccharide.
3. The design and realisation of the synthesis of cryptand derivatives of di- and polysaccharides.
    - checking the influence of metal cations (template) on the structure of cryptands,
    - checking cryptands as hosts in the complexation of drugs and amino acids (guests),
    - determination of the stoichiometry of the obtained complexes.
4. The design and realisation of the synthesis of new ureas containing glycosyl and diphenylphosphinyl scaffolds as chiral ligands and organocatalysts.
    - checking the organocatalysts in the asymmetric Morita-Baylis-Hillman and aza-Henry reaction.

Nie, J., Li, X.-J., Zheng, D.-H., Zhang, F.-G., Cui, S., Ma, J.-A. *J. Fluorine Chem.*, **2011,** *132,* 468; (h) Heravi, M. M., Asadi, S. *Tetrahedron Asymmetry*, **2012**, *23*, 1431; (i) Tsakos, M., Kokotos, Ch.G. *Tetrahedron,* **2013**, *69*, 10199.

[22] (a) Becker, C., Hoben, C., Kunz, H. *Adv. Synt. Catal.* **2007**, *349*, 417; (b) Puglisi, A., Benaglia, M., Raimondi, L., Lay, L., Poletti, L. *Org. Biomol. Chem.* **2011**, *9*, 3295.

[23] Olszewska, B., Szulc, I., Kryczka, B., Kubiak, A., Porwański, S., Zawisza, A. *Tetrahedron: Asymmetry*, **2013**, *24,* 214

2.3 Short description of major publications

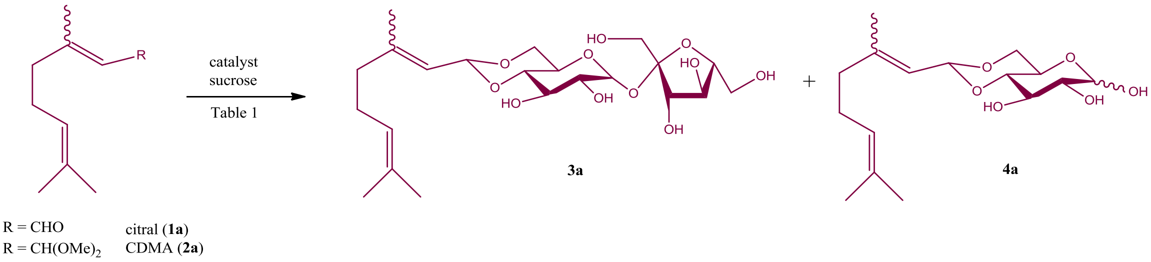
Publication P1

"Selective Synthesis of 4,6-*O*-Alkenylidene and –Benzylidene Acetals from Unprotected Sucrose by Lanthanide (III) Resin Catalyzed Transacetalization",
Synthesis, **2000**, *4*, 525-528.

The paper presents an efficient synthesis of sucrose 4,6-acetals. Lanthanide cation exchanged resins were used as catalysts for the transacetalization of sucrose.

The procedure described by Yu et al.[11] was followed for the preparation of three lanthanide cation exchange resins, using lanthanum, ytterbium and erbium salts.

The acetalization of sucrose (in excess) with citral dimethylacetal (**2a**) in anhydrous DMF was first studied (Scheme 2, Table 1).



Scheme 2

The acetalization of sucrose (in excess) with citral dimethylacetal (**2a**) in anhydrous DMF was first studied (Scheme 1, Table 1). Good yields (based on the starting dimethyl acetal) of the sucrose 4,6-acetal **3a** were obtained using these catalysts (ca. 5 mol% in lanthanide cation equiv) at a higher temperature (80°C) (Table 1).

Table 1 Lanthanide(III)-Mediated Acetalization of Citral with Sucrose

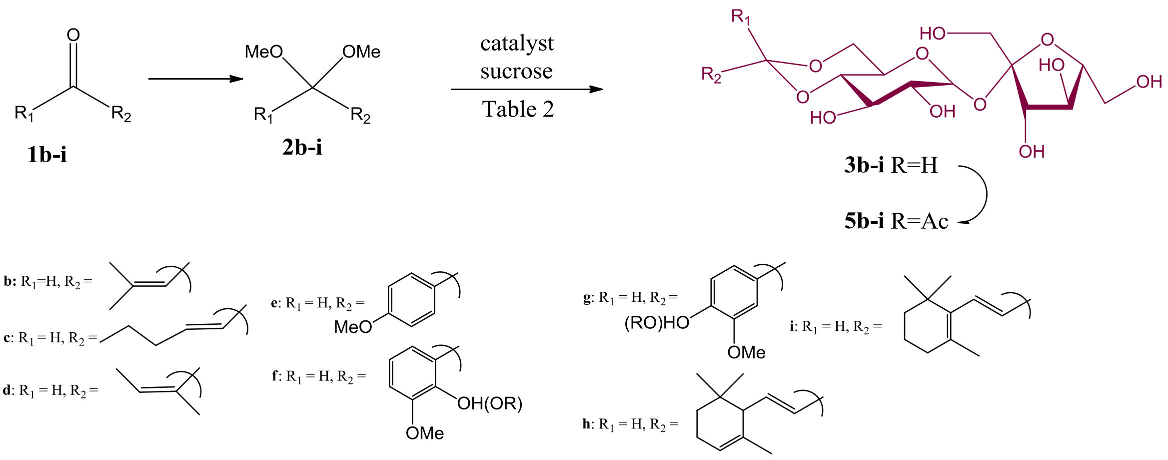
Substrate[a]	Catalyst[b]	Temp. (˚C)	Time (h)	Yields **3a** (+**4a**)
2a	Yb-resin	80	24	66
2a	Yb- resin (recycled)	80	24	55
2a	Yb- resin	100	24	58
1a	Yb- resin (two-step)	80	24	69
2a	$Yb(OTf)_3$	25	46	38 (+9)
2a	$Yb(OTf)_3$	60	24	48 (+14)
2a	La- resin	80	24	44
2a	Er- resin	80	24	77
2a	Er- resin (recycled)	80	24	76
1a	Yb- resin	20-80	24	Traces
1a	$Yb(OTf)_3$	20	24	15 (+8)
1a	$Yb(OTf)_3$	60	24	31 (+13)

[a] 2.3 mmol for 4.6 mmol of sucrose

[b] 100mg of lanthanide resin (5 mol% in lanthanide ions) or 2 mol% of $Yb(OTf)_3$.

The ytterbium(III) and the erbium(III) resins are more effective than the lanthanum(III) one. Filtration of the reaction mixture, followed by washing and drying provided a recycled catalyst which was still active, especially in the case of erbium. Under the same conditions, ytterbium(III) triflate, as an homogeneous catalyst, led to significant acidic cleavage of the intersaccharidic bond, yielding the glucose acetal **4a** (this compound can be obtained from glucose in 54% yield under Yb-resin catalysis). However, a stronger acidity is required to achieve direct acetalization of citral (**1a**) which leads to extensive concomitant glycosidic cleavage.

Using the most available resin prepared from ytterbium sulfate, a series of α,β-unsaturated or aromatic aldehyde acetals were transformed to their corresponding sucrose acetals **3b-g** (Scheme 3, Table 2)



Scheme 3

Aromatic aldehyde and ketone acetals reacted also under these conditions (Table 2).

Table 2 Sucrose Acetalization with a,b-Unsaturated Aldehydes, Ketones, or Acetals Catalyzed by Yb(III) Exchanged Amberlyst Resin (Method A: From Isolated Dialkylacetal; Method B: Two-Step One-Pot Procedure)

Subst.	Methods	Product	Yied (%)	Ac-derivatives(%)	Yield	[α]D
2b	A	**3b**	78	**5b**	66	+75
2c	A	**3c**	53	**5c**	76	+54
1d	B	**3d**	75	**5d**	93	+60
1e	B	**3e**	37	**5e**	71	+41
1f	B	**3f**	60	**5f**	74	+44
1g	B	**3g**	80	**5g**	54	+32
2h	A (4d, 80˚C)	**3h**	13			
2i	A 4d, 50˚C)	**3i**	32			
1i	B (Er-resin, 6d, 40˚C)	**3i**	8			

However, the transacetalization of α,β-unsaturated ketone acetals, such as ionone acetals **2h,i** leading to acetals **3h,i**, was much slower. Reaction of methyl α-D-glucopyranoside with citral dimethylacetal or 3,3-diethoxypropene could proceed in moderate yields.

In conclusion, lanthanide cation-exchanged resins were shown to catalyze smoothly the acetalization of unprotected sucrose by α,β-unsaturated and aromatic aldehydes in a two step one-pot procedure. This method should be useful in the case of acid sensitive substrates, either the polyol or the carbonyl compound. Such sucrose acetals might find applications based on their solubility in water, the temporary protection of the reactive carbonyl centre, and their ability to release the active carbonyl compound, such as citral, vanillin or ionones, under mild and controllable conditions.

Publication P2

"Regioselectivity in acid- or base-catalysed acetalation of sucrose: selection of [OH-2, OH-3] or [OH-4, OH-6] diols" *Top. Catal.*, **2000**, *13* (3); 335-338.

The paper is a continuation of the studies presented in publication P1, and describes the reaction of unprotected sucrose with a α-chloromethyl ketone in the presence of base provided a α-hydroxymethyl 5-membered ring acetal involving OH-2 and OH-3 as the major product, illustrating the pre-eminent reactivity of OH-2 in sucrose and its consequences on the product distribution for reactions under kinetic control. This is another example illustrating the reactivity of groups in sucrose. The general idea of a larger reactivity of primary groups is limited to punctual examples, involving essentially bulky electrophilic species, the steric factors being the key element in the control of the process. Notably, OH-2 and OH-1' have been shown to be more reactive because these groups are involved in a hydrogen bond network which persists in highly polar solvents, and even in aqueous media[24] The etherification reaction, because of the high chemical stability of the products, is a direct tool for comparing the kinetic reactivity of the various nucleophilic groups in a multifunctional substrate. This source of selectivity can also be expressed in a second type of acetalation reactions, i.e., the reaction of sucrose with α-chloromethyl ketones (scheme 4).

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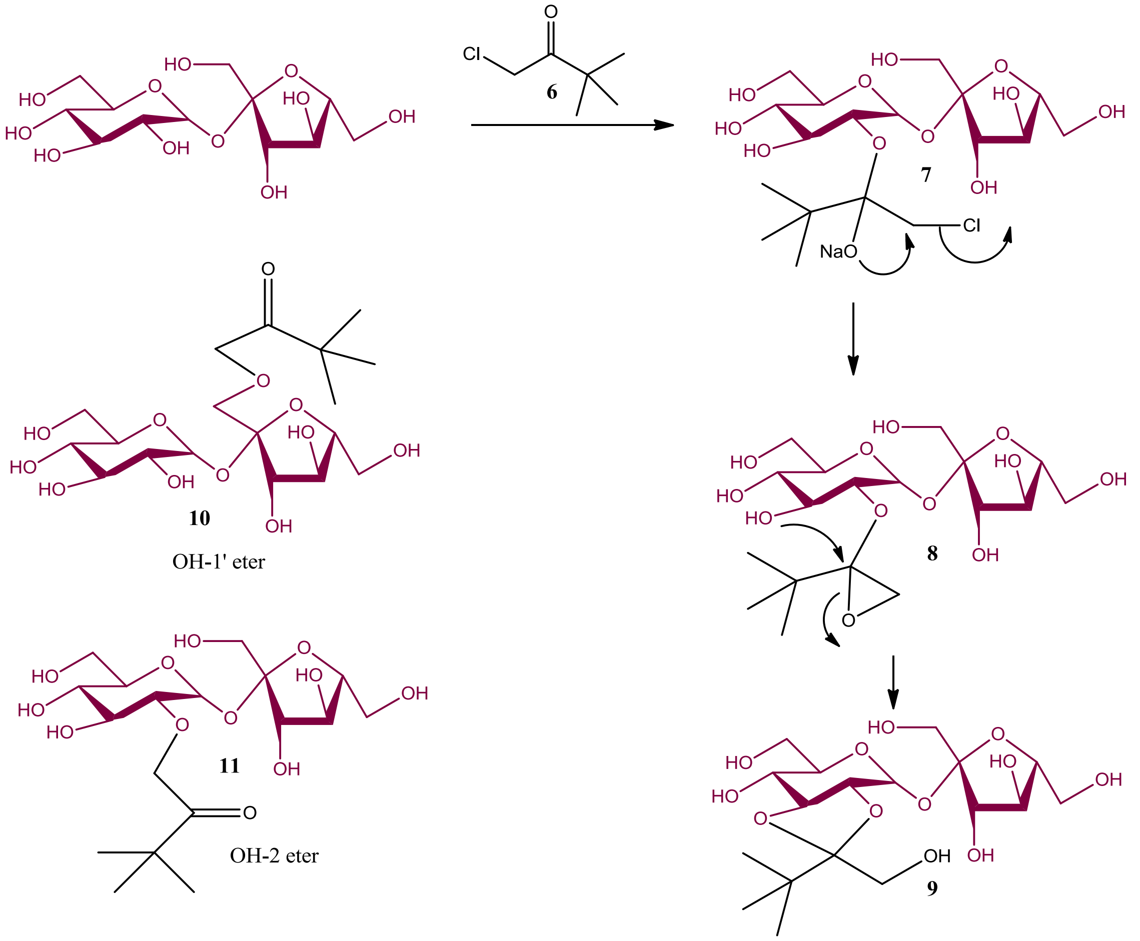
[24] (a) Houdier, S.and Perez, S. *J. Carbohydr. Chem*. **1995** *14,* 1117; Lichtenthaler, F.W., Immel S., Pokinskyj, P. *Liebigs Ann. Chem*. **1995**, 1939; Engelsen, S.B., Herv´e du Penhoat, C., Perez, S. *J. Phys. Chem*. **1995**, *99* 13334; Immel S., Lichtenthaler, F.W., *Liebigs Ann. Chem*. **1995** 1925.



Scheme 4

We found that when sucrose and chloropinacolone (α-chloromethyl *t*-butyl ketone) are heated in DMF in the presence of a base, the major product is an hydroxymethyl acetal involving OH-2 and OH-3, besides the ethers arising from a Williamson[25] reaction at OH-2 and OH-1'. This acetal is produced via the attack of the carbonyl groups of the α-chloromethyl ketone by OH-2, leading to an hemiacetal anion which, upon cyclisation, forms a three-membered ring acetal, subsequently opened at its very reactive acetalic center by the nearest hydroxy group (OH-3). Only one acetal, having the *t*-butyl group close to H-2 (as seen by NOESY NMR experiments) was formed. The acetal linkage can be cleaved under mild acidic conditions (PPTS, MeOH) in a transacetalation process which is able to deliver sucrose with limited concomitant glycosidic bond cleavage.

Herein we have summarised the results of two studies on the acetalation of sucrose which both lead to its direct and selective functionalisation. Smooth and controlled cleavage could be exploited for the slow-release of active molecules, for example in the fragrance industry.

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[25] Giry-Panaud, N., Descotes, G., Bouchu A., Queneau, Y. *Eur. J. Org. Chem*. **1999**, 3393.

Publication P3
“A polymer-supported ‘one-pot’ phophine imide reaction on cyclodextrins”
Tetrahedron Lett. **2002;** *43;* 8441-8443

The present work describes the first example of a polymer-assisted ‘one-pot’ phosphine imide reaction using a polymer-bounded triphenylphosphine. The repeatability of the reaction and the polymer regeneration step were also investigated. On screening the literature for direct, simple and efficient reactions involving cyclodextrins (CDs), the phosphine imide method previously developed by some of us appeared to be a versatile and interesting method for the synthesis of either functionalised, multi-hosted, or tethered CDs derivatives.[26] The goal was to resolve one major problem related to the production of the triphenylphosphine oxide (TPO) by-product, which readily forms strong inclusion complexes with CDs and also to perform a powerful continuous synthetic process including the polymer regeneration step (Scheme 5).

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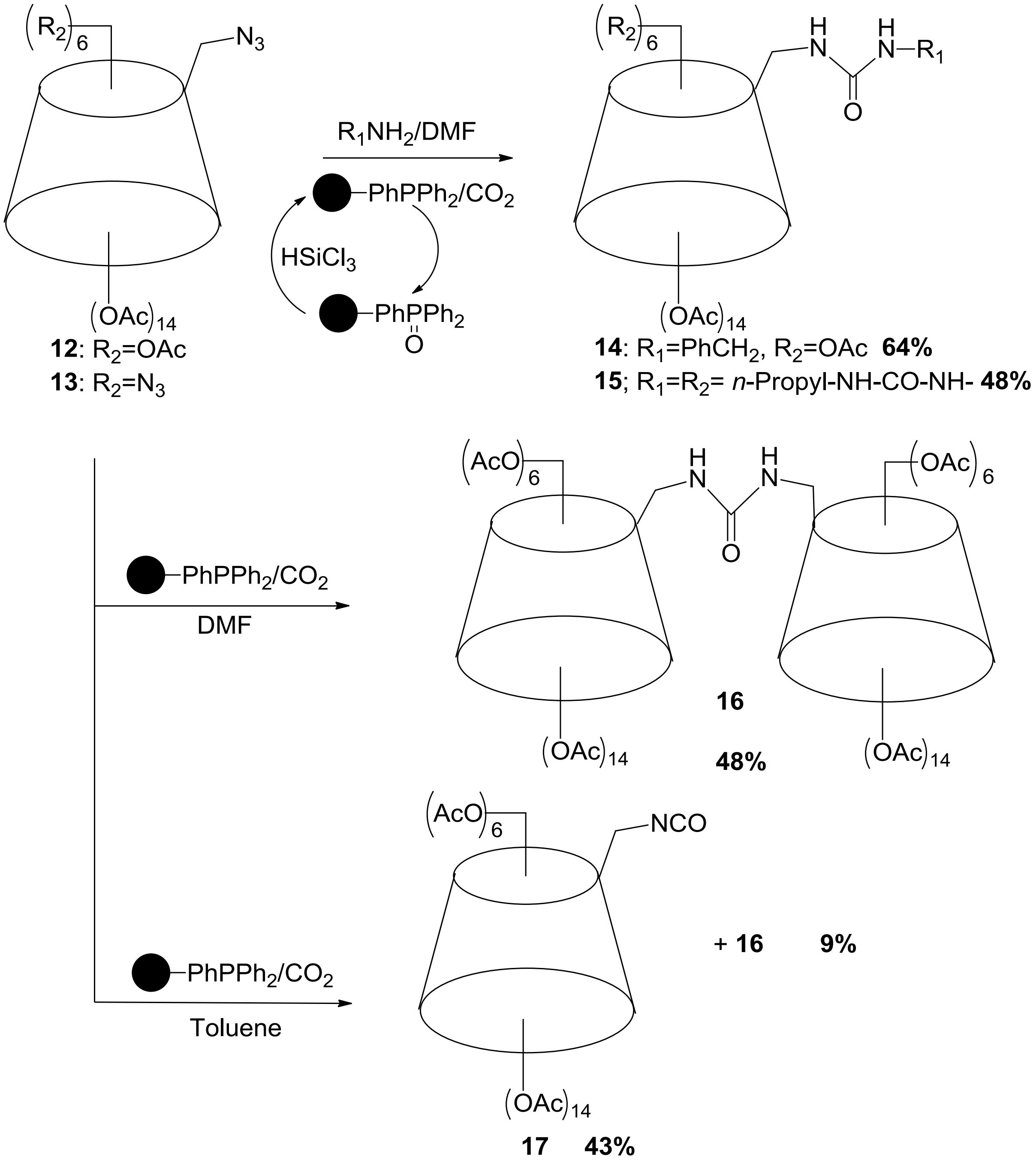
[26] (a) Kovacs, J., Sallas, F., Pinter, I., Jicsinszky, L. *J. Inclusion Phenom. Mol. Recogn. Chem.* **1996**, 25, 53; (b) Charbonnier, F., Humbert, T., Marsura, A. *Tetrahedron Lett.* **1998**, 39, 3481; (c) Sallas, F., Marsura, A., Petot, V., Pinter, I., Kovacs, J., Jicsinszky, L. *Helv. Chim. Acta,* **1998**, 81, 632; (d) Wagner, M., Engrand, P., Regnouf de Vains, J.-B., Marsura, A. *Tetrahedron Lett.* **2001**, 42, 5207; (e) Charbonnier, F., Marsura, A., Pinter, I. *Tetrahedron Lett.* **1999**, 40, 6581.



Scheme 5

All the reactions have been conducted in the same conditions as for the homogeneous reaction in solution (rt/DMF), in a particular reactor for solid-phase peptide synthesis dimensioned for 1 g of resin and equipped with a CO_2 line inlet. The final products **14-17** are obtained in medium yields, slightly lower than in solution but without unfavourable traces of triphenylphosphine oxide during the purification. As shown, in Scheme 5 the triphenyl phosphine oxide polymer is easily regenerated in a second step by refluxing for 3 h in a trichlorosilane/toluene solution.

The reaction repeatability was also investigated. Using as model the benzylamine nucleophile, it was possible to perform the reaction five times with the same polymer sample. The overall yield of the fifth run was 55%, that correspond to less than a 10% decrease which seems to be better attributed to losses during the purification steps than to a decreasing efficiency of the polymer itself.

In this work, we prove that the 'one-pot' phosphine imide reaction could be easily performed with a good repeatability using the triphenylphosphine-grafted polymer assistance. In these conditions, the possibility of building an automated continuous synthetic process with a recyclable polymer reagent should be considered. Attempts to transfer the reaction in supercritical CO2 as, solvent and reagent, are presently in progress.[27]

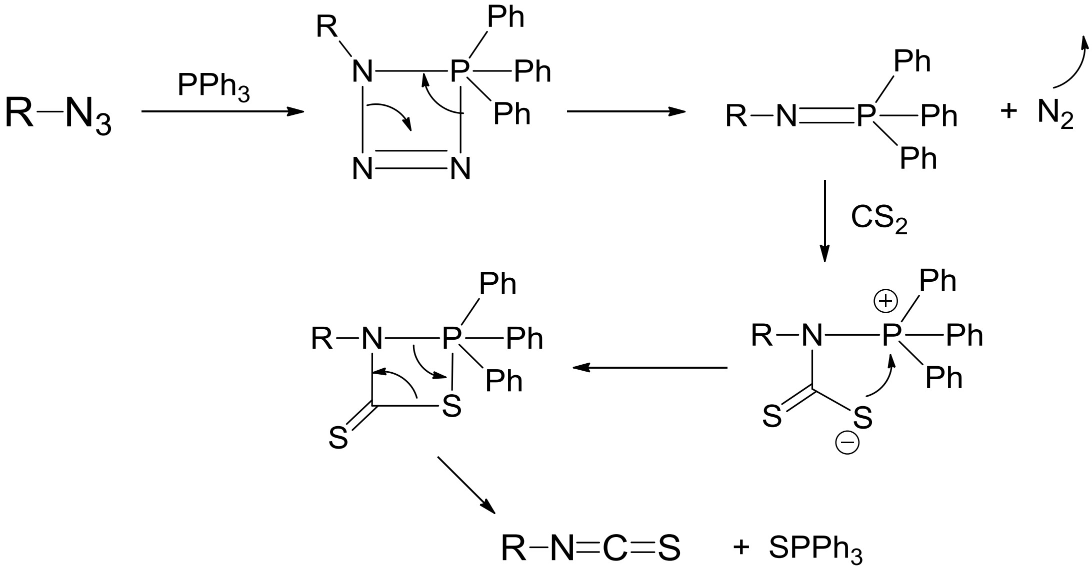
Publication P4

"New synthetic approach to per-*O*-acetyl-isocyanates, isothiocyanates and thioureas in the disaccharide and cyclodextrin series"
New Journal of Chemistry; **2006**, 30, 603-608.

The paper presents an efficient synthesis of per-*O*-acetyl-isocyanates, isothiocyanates and thioureas in the disaccharide and cyclodextrin series and is a continuation of research on phosphine imide reaction**.** The method allows easy access to urea functionality and other main quadrivalent functions of chemistry as e.g. isocyanate, carbodiimide, thiourea.

As noted in the introduction of work, compounds containing the urea or thiourea functionality are of extended biological interest in several classes of drugs[13,14], therefore, it seemed to be necessary to take such a research.

Continuing our research on the scope and limitations of the phosphine imide reaction and considering results previously obtained with CO_2, we performed the reaction with CS_2 expecting that CDs-isothiocyanates and/or other isothiocyanates, could be interestingly prepared in this way in pure form and in high yields (Scheme 6).



Scheme 6

Exchanging carbon dioxide for disulfide leads to an isothiocyanate and then to thiourea as the final product (Scheme 7)

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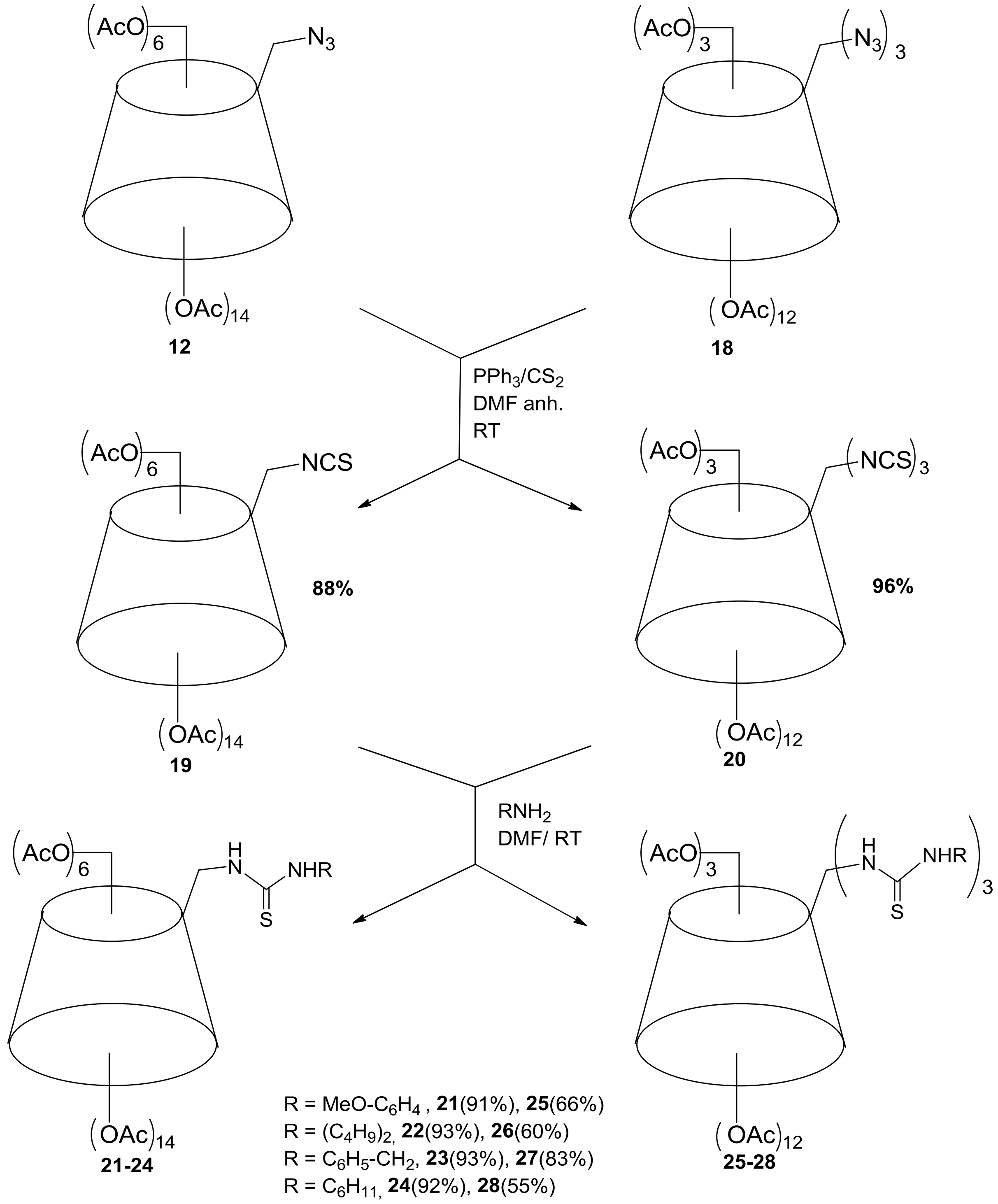
[27] Scondo, A., Dumarcay, F., Marsura, A., Barth, D. *J. Supercrit. Fluids,* **2010,** *53,* 60.

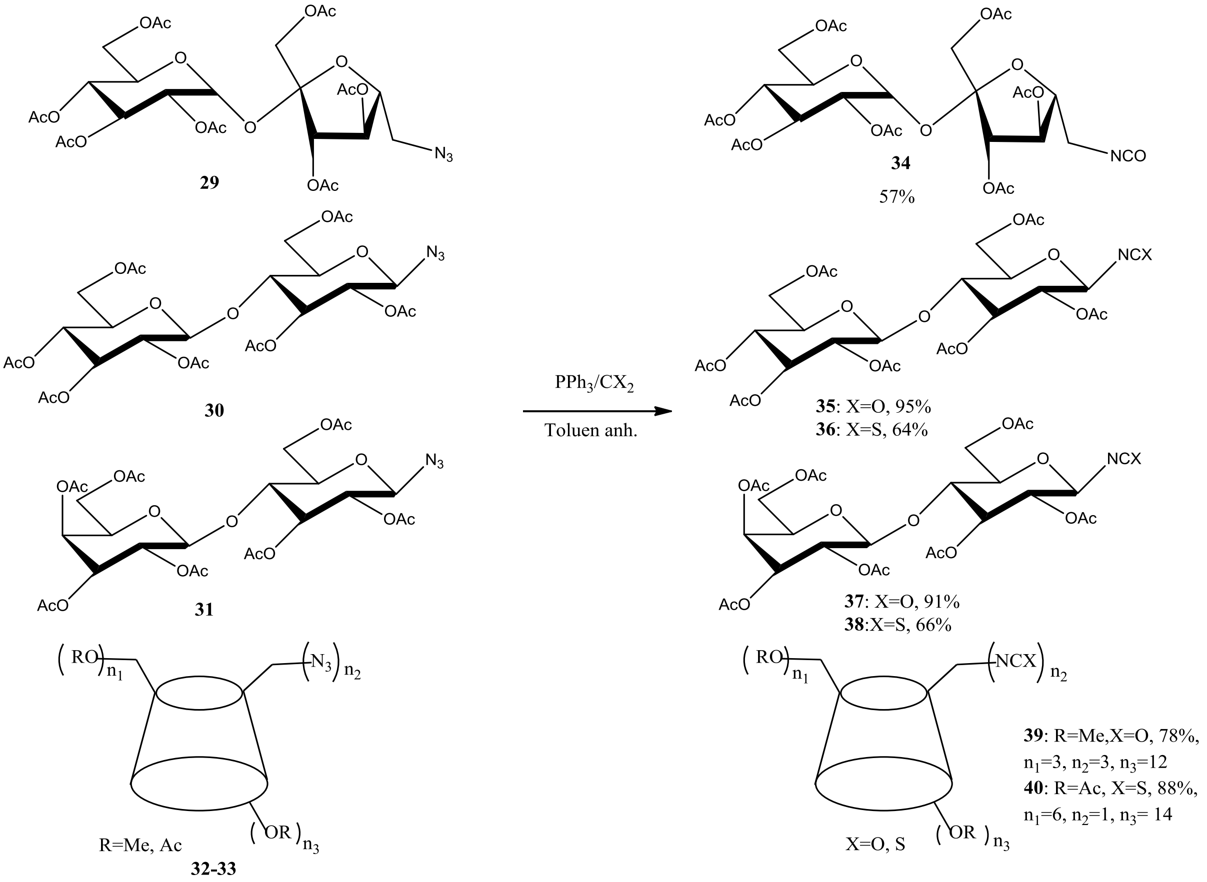


R = MeO-C_6H_4 , **21**(91%), **25**(66%)
R = $(C_4H_9)_2$, **22**(93%), **26**(60%)
R = C_6H_5-CH_2, **23**(93%), **27**(83%)
R = C_6H_{11}, **24**(92%), **28**(55%)

Scheme 7

These are, the first successful synthesis of the 6-monoisothiocyanato-per-O-acetyl-β cyclodextrin **19** and the ^{ACE}tris-6-isothiocyanatoper-O-acetyl-α-cyclodextrin **20** (Scheme 7) through the ‘‘thiophosphine imide reaction’’ (so named by analogy with the initial phosphine imide reaction with CO_2) by the action of carbon disulfide on the 6^A-azido-6^A-deoxy-per-O-acetyl-β-cyclodextrin **12** or the ^{ACE}tris-6-azido-per-O-acetyl-α-cyclodextrin **18**. To the best of our knowledge, only one example of a multistep synthesis of an a-CD isothiocyanate was reported in the patent literature,[28] but other CDs-isothiocyanates have not been obtained before.

This method has been used to synthesis of isocyanates di- and polisaccharides (Scheme 8).



Scheme 8

These were also the first attempts to obtain of per-O-acetyl disaccharides and cyclodextrin isocyanates by the phosphine imide strategy.

To our knowledge, this practical one-pot preparation is the first example reported, of a direct and scale-up preparation of isocyanates and isothiocyanates of oligosaccharides at the anomeric position from their corresponding azides. In comparison rare examples of oligosaccharidyl isothiocyanate synthesis at the 6-primary alcohol position have been reported earlier, from amines by reaction with thiophosgene,[29] and two other monosaccharidyl isocyanates have been recently claimed to be formed, but not isolated, using triphosgene in a biphasic water–CH_2Cl_2 medium.[30]

In summary, we find that the proposed phosphine imide reaction and its thio-variant, bring efficient high yielding, soft and safe (without hazardous phosgene or analogues)

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[28] Hiramatsu, M., Suzuki, T., Satozono H., Misuzawa, Y. *Ger. Offen.* DE 19627474 A1, **1997**.

[29] Garcia-Fernandez, J. M., Ortiz-Mellet, C., Jimenez-Blanco, J. L., Mota, J. F., Gadelle, A., Coste-Sarguet, Defaye, J. *Carbohydr. Res.*, **1995**, *268*, 57.

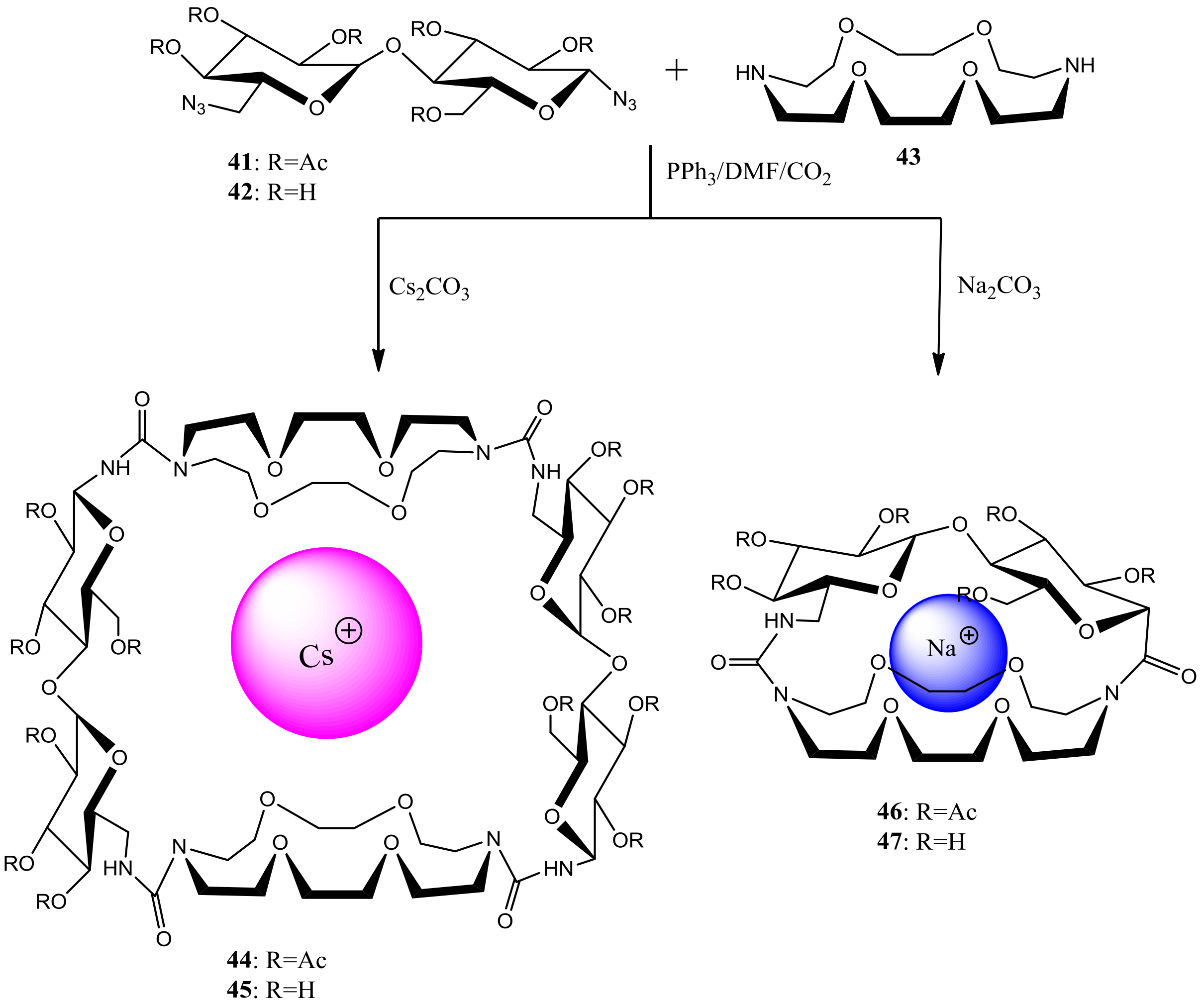
[30] (a) Maya, I., Lopez, O., Maza, S., Fernandez-Bolanos J. G., Fuentes, J. *Tetrahedron Lett.*, **2003**, *44*, 8539; (b) Lopez, O., Maza, S., Maya, I., Fuentes J., Fernandez-Bolanos, J. G. *Tetrahedron*, **2005**, *61*, 9058.

synthetic methodologies for CDs and disaccharide isothiocyanate and isocyanate scale-up preparation.

Publication P5

“Tandem Staudinger–Aza-Wittig Templated Reaction: De Novo Synthesis of Sugar–Ureido Cryptands”
Eur. J. Org. Chem. **2009**, 2047-2050.

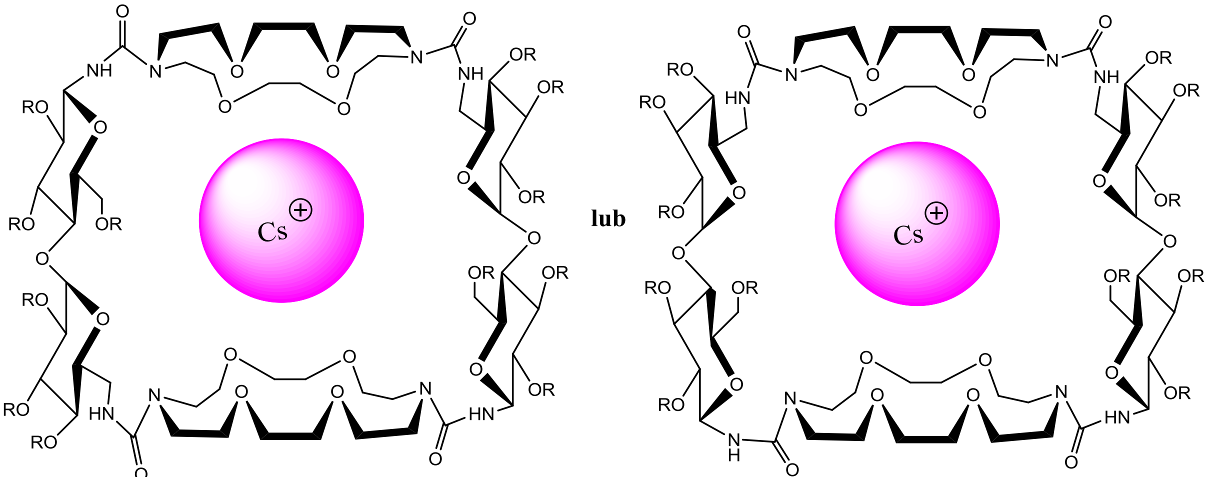
The paper presents the synthesis of cryptand derivatives of disaccharides from azacrown ethers by the tandem SAW reaction in anhydrous DMF by using the alkali cation template effect (Scheme 9). As noted in the introduction of work, crown ethers and azacrown ethers,are important molecular receptors that are currently used in biological model systems. It has been also shown that sugars are well known to be versatile chiral entities that are particularly suitable for the design of chiral receptors.[17,18]



Scheme 9

Cryptates **44** to **47** were synthesised in one pot and in fairly good yields (40–47%) from 2,2’,3,3’,4’,6-hexa-*O*-acetyl-1,6’-diazido-1,6’-dideoxy-β-D-cellobiose (**41**) or 1,6’-

diazido- 1,6’-dideoxy-β-D-cellobiose (**42**) and tetraoxadiazacyclooctadecane **43** by the tandem SAW reaction in anhydrous DMF by using the alkali cation template effect. Thus, from **41** and **42** respectively, in the presence of Na_2CO_3 monocellobiosylsodium cryptates **46** and **47** were obtained. Differently, as shown in Scheme 1, the same reaction from **41** or **42** in the presence of Cs_2CO_3 led only to bis(cellobiosyl)cesium cryptate **44** or **45**. The reaction performed without the cation template effect afforded, as expected, a mixture of the two cryptates, one with the two disaccharides in a parallel direction (**B**) and the other one with the two disaccharides in an antiparallel direction (**A**)(Figure 3).



A **B**

Figure 3

Unfortunately, at that point, the lack of X-ray structural data did not allow us to confirm the sructures. Anyway, we suggested, on the basis of the best geometry adopted around a templating sphere, that the antiparallel arrangement is closer to a spherical spatial organisation and should be preferred over the parallel arrangement, which is more like a coneshaped spatial organisation. Our assumptions were correct. Later multistep synthesis of macrocycle **B** and spectral analysis confirmed the raised thesis.[31]

In conclusion, an efficient, selective and rapid method for the preparation of a new family of macrobicyclic and macrotricyclic molecular receptors has been presented. It was demonstrated that high selectivity occurs in the reaction in the presence of sodium or cesium alkali cations and confirms that the macrocyclisation step was under the control of cations size.

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[31] Porwański, S. Unpublished materials.

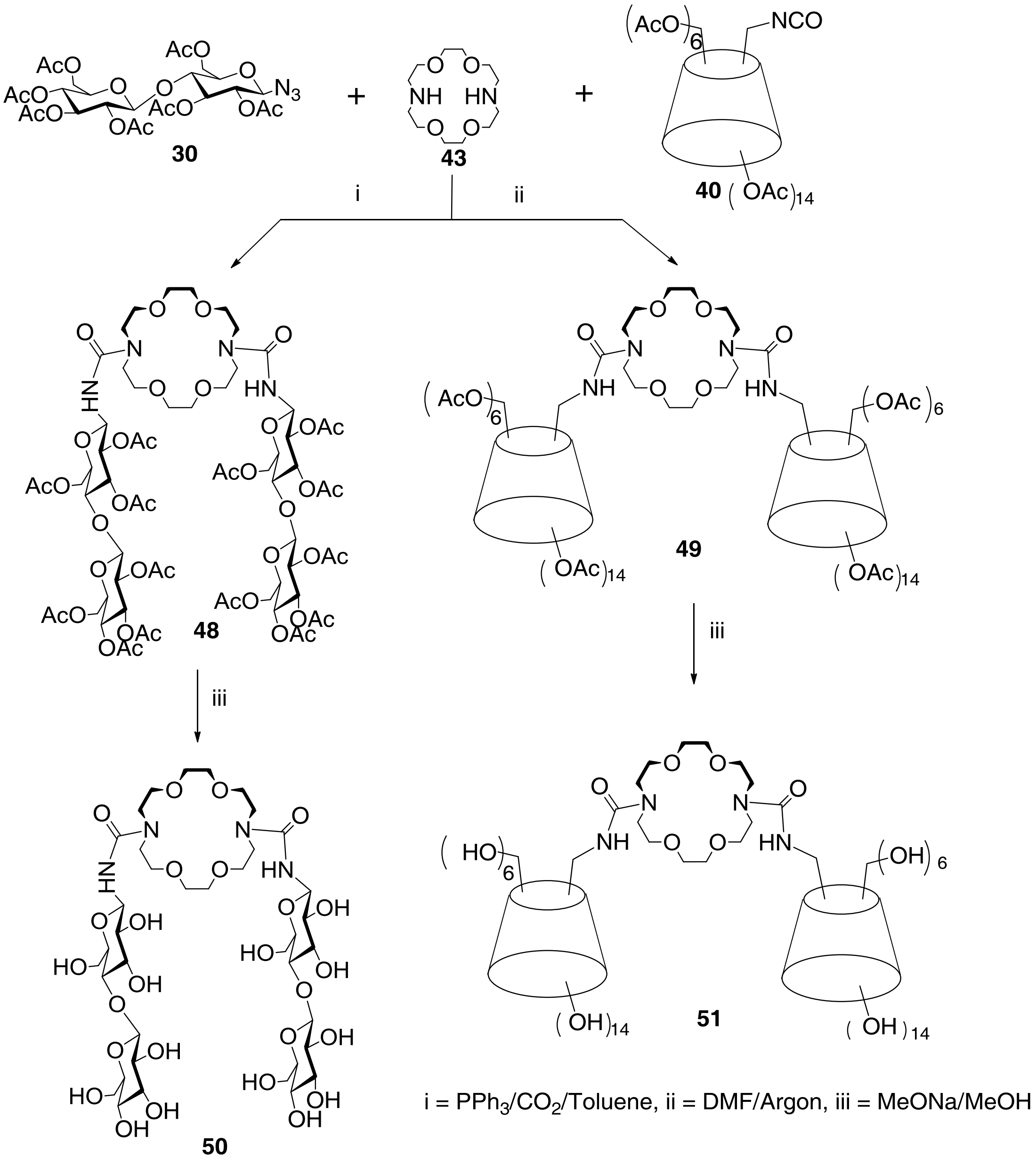
Publication P6

“Bis-β-Cyclodextrinyl-And Bis-cellobiosyl-diazacrowns: Synthesis And Molecular Complexation Behaviors Toward Busulfan Anticancer Agent And two Basic Aminoacids”
Tetrahedron, **2009**, 65, 6196-6203

The work is a continuation of research in field cryptands of sugar derivatives and presents one-step synthesis of C2-symetrical cryptand derivatives of di- and polysaccharides as effective receptors for drug and aminoacids in host-guest complexes.

Bis-cellobiosyl-diazacrown ligand **50** was synthesized in two steps in high yield (99%) from the hepta-O-acetyl-azido-β-D-cellobiose **30** and the tetraoxa-diazacyclooctadecane **43** via a tandem Staudinger–aza-Wittig one-pot coupling reaction (alias phosphineimide reaction) and after a quantitative deacetylation step of ligand **48** using Zemple´n conditions (Scheme 9).

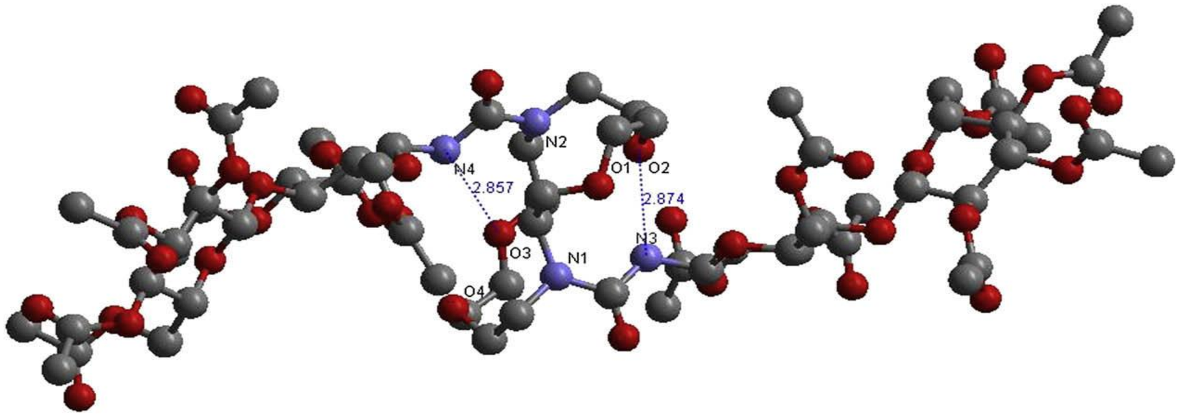
Likewise, a similar synthesis strategy was used for the bis-β-cyclodextrin ligand derivative **51** obtained over one step in a moderate 38% yield from the 6^{A}-isocyanato-6^{A}-deoxy-per-O-acetylated-β-cyclodextrin **40** as starting material (Scheme 10).



i = PPh_3/CO_2/Toluene, ii = DMF/Argon, iii = MeONa/MeOH

Scheme 10

Spectroscopic data of **50** and **51** by IR, NMR, ESIMS, and elemental analysis are in full accordance with the proposed structures. Crystallization of the peracetylated bis-cellobiosyl podand **48** gave us the opportunity to perform X-ray diffraction analysis and allowed its structural determination (Rysunek 4). Single crystals of **48** were obtained by slow diffusion of hexane into a solution of **48** in CH_2Cl_2.



Rysunek 4

Cryptand **50** as the host proved to be effective in the complexation of the busulfan anticancer agent.

Signs of interaction were firstly detected by chemical-induced shifts (CIS) of protons of the guest signals compared to those of the free compounds in D_2O. The signals of both sulfomethyl and methylene protons of the butyl chain are downfield shifted (-0.28 ppm) and upfield (+0.15 ppm), respectively. The stoichiometries of the complexes were established on the basis of the Job plots continuous variation method, values of Rw0.5 being reached at the maximum, which ascertain the 1:1 stoichiometry of these complexes. Complexation constants (Ka) were determined using Scott's plot method[32] and found to be ca. 2600 M^{-1} and 2700 M^{-1}, respectively, for [Busulfan/**50**] and [Busulfan/**51**] at 300 K. Indeed, the 2D ROESY spectrum of the [Busulfan/**50**] complex in D_2O displays two characteristic cross-peaks, a first one between the sulfomethylene protons and the H-1 anomeric proton of the cellobiose units and a second one between the methylene protons of the Busulfan-butyl chain and the oxo-methylene protons of the crown ether.

As previously observed for Busulfan1 as guest and on the ground of structural and electronic similarities with basic aminoacids, formation of host–guest complexes 1/1 between hosts **50**, **51** and L-arginine and L-lysine was investigated.

The main achievements of this part of the study include the:

- synthesis two soluble in water cryptands in good yields,
- solution and establish of the structure the acetyl cryptand derivative **48**,
- proof that obtained cryptand derivatives of di- and polysaccharides as effective hosts in host-guest complexes,
- confirm the type of interactions in the complexes,
- demonstration that complex of cryptand **50** with busulfan is very soluble in water.

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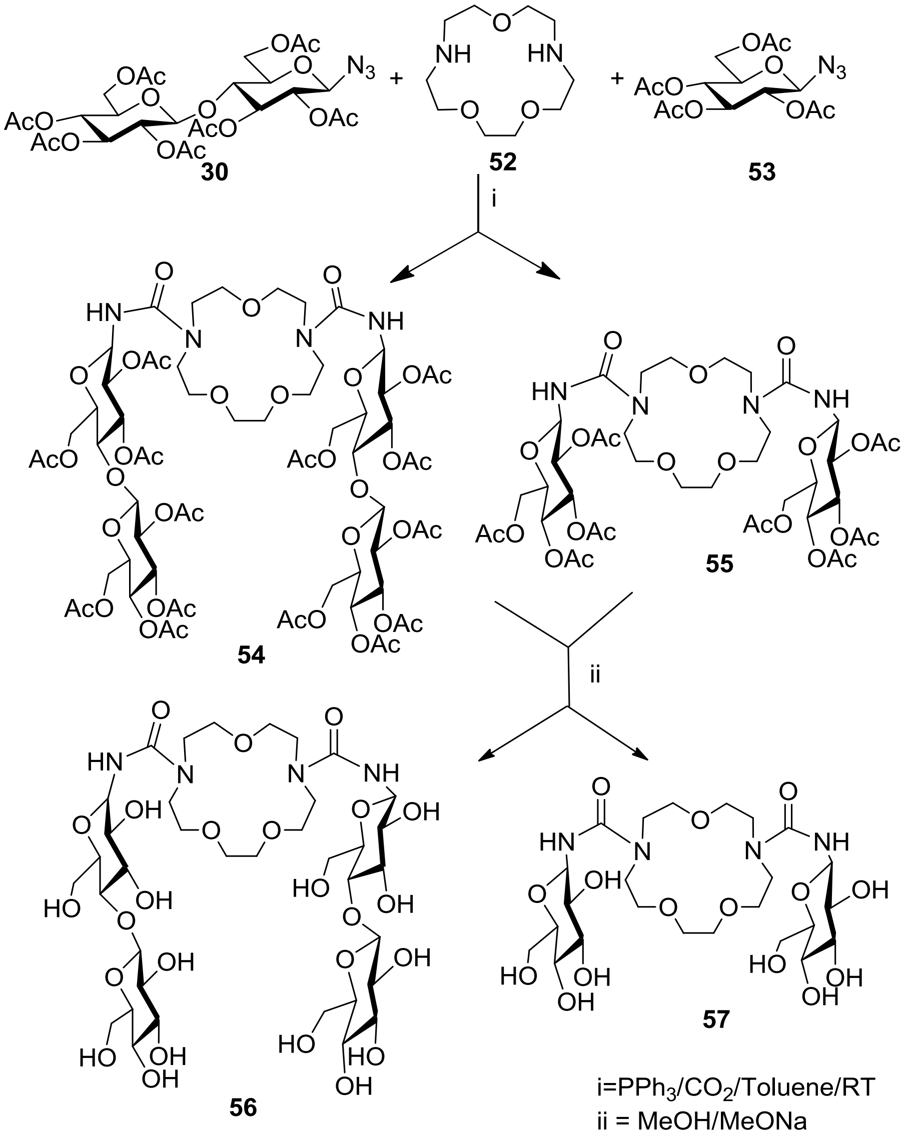
[32] Scott, R. L. *Recl. Trav. Chim. Pays-Bas*, **1956**, 75, 787.

Publication P7

"Synthesis of bis-cellobiose and bis-glucose derivatives of azacrown macrocycles as hosts in complexes with acetylsalicylic acid and 4-acetamidophenol".
Carbohydr. Res., **2014**, *386*, 18-22

The work refers to previous studies and presents the search for other receptors, which are different in size of azacrown ethers. We obtained few new sugar decorated receptors in which the 1,10-diaza-18-crown-6 has been replaced with 1,4,10-trioxa-7,13-diazacyclopentadecane (Kryptofix 21). The new, obtained macrocycles besides the disaccharides in the urea bridge involve also monosaccharide units. Bis-cellobiosyl-diazacrown ligand **56** was synthesised in two steps (Scheme 11) in high yield (92%) from hepta-O-acetyl-azido-β-D-cellobiose **30** and 4,7,13-trioxa-1,10-diazacyclopentadecane **52** via a tandem Staudinger/aza-Wittig/one-pot coupling reaction and after a 96% deacetylation step of ligand **54** using Zemplen conditions



i=PPh_3/CO_2/Toluene/RT
ii = MeOH/MeONa

Scheme 11

Likewise, a similar synthesis strategy was used for β-glucosyl ligand derivative **57** obtained in two steps in high 98% yield from penta-O-acetyl-azido-*β*-D-glucose **53** as the starting material.

The spectroscopic data of **54-57** by IR, 1H NMR and elemental analysis are in full accordance with the proposed structures.

The host–guest properties of receptors 6 and 7 towards paracetamol and aspirin (Figure 5) were explored by 1H NMR spectroscopy in mixture D_2O/Pyridine-d_5 at 293 K.

The sugar area in ^{1}H NMR spectrum is quite complicated (with the exception of anomeric proton), therefore at this stage of our research we chose a well-defined signals from the guests (Figure 5) for an example complex **57**/paracetamol.

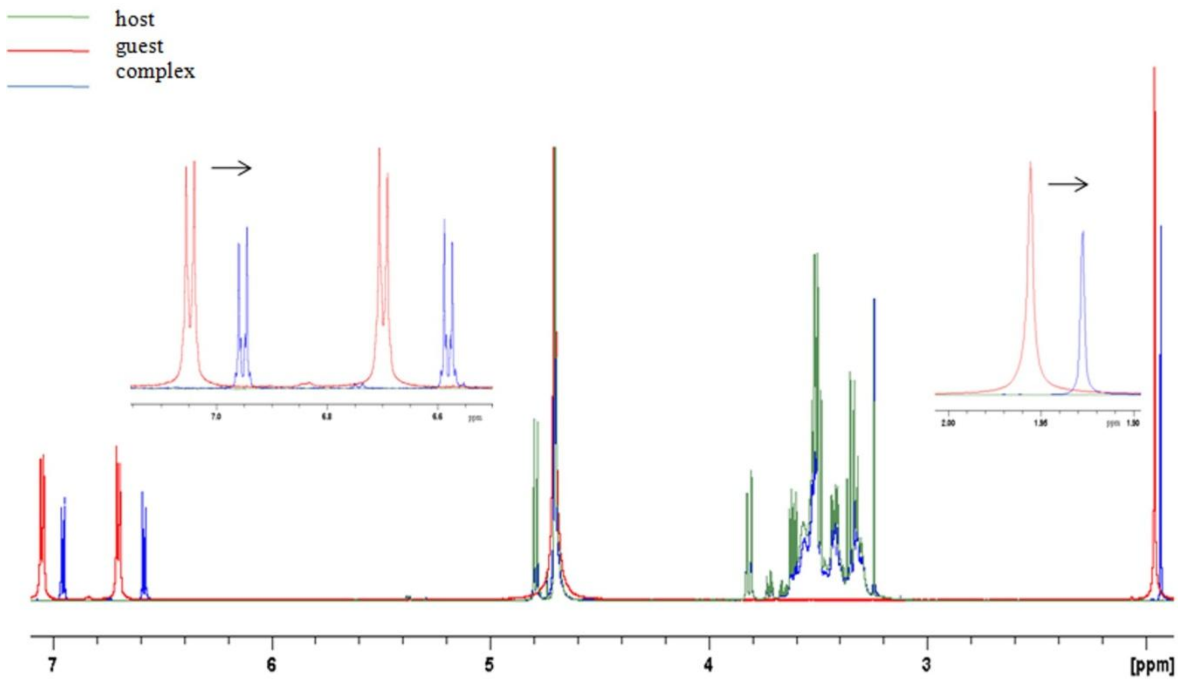


Figure 5. Overlapped ^{1}H NMR spectrums of the complex [**7**/paracetamol] [1:1] and free paracetamol and host **7** at 600 MHz. Zoom views of aromatic protons and methyl protons of the guest (paracetamol).

The signals of both, aromatic and methyl protons of the acetyl group are upfield shifted (-0.10 ppm) and (-0.03 ppm), respectively for complex [**57**/paracetamol] as shown in Figure 5.

The stoichiometries of the complexes were established on the basis of the Job plots (continuous variation method), as illustrated in Figure 6.

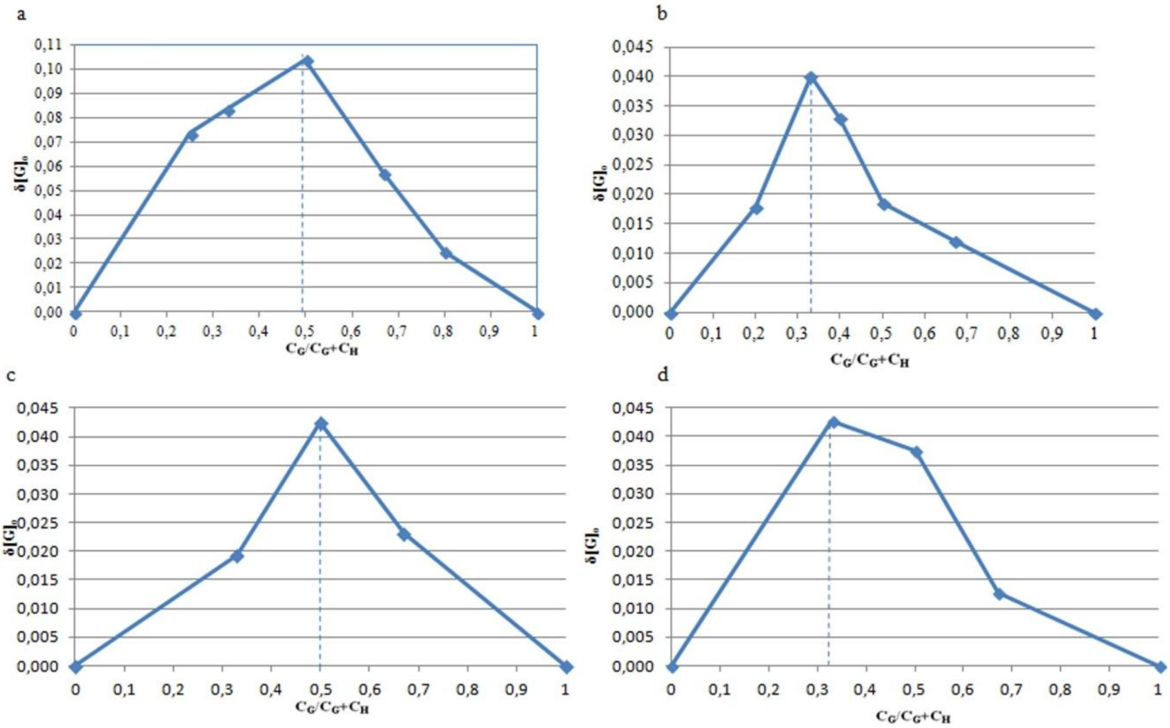


Figure 6. Job plots for the complexes between receptors **6** and **7** and paracetamol or aspirin, respectively: (a) [**7**/paracetamol], (b) [**7**/aspirin], (c) [**6**/aspirin] and (d) [**6**/paracetamol] in D_2O/Pyridine-d_5 at 293 K. (▪ = signal for protons on aromatic ring from the guest).

The values of R 0.5 were reached at the maximum, which ascertains the 1:1 stoichiometry of the complexes [**57**/paracetamol] and [**56**/aspirin], of *R* 0.33 the 2:1 of complexes. Complexation constant (K_a) for the complexes showing the observed 1:1 stoichiometry was determined using Schaeppi–Treadwell method[33] and found to be ca. 3.3 x 10^3 M^{-1} for complex [**57**/paracetamol] and 2.5 x10^3 M^{-1} for complex [**56**/aspirin].

In conclusion, two new water-soluble pseudocryptands were synthesised in high yields by the tandem Staudinger/aza-Wittig/one-pot coupling reaction. The binding studies allowed us to establish experimentally that the new hosts interact with paracetamol and aspirin to form [1:1] and [1:2] supramolecular species.

Publication P8

"New ureas containing glycosyl and diphenylphosphinyl scaffolds: synthesis and the first attempts to use them in asymmetric synthesis"
Carbohydr. Res., **2014**, *DOI 10.1016/j,carres.1014.04.015*

The paper presents the synthesis of new ureas containing glycosyl and diphenylphosphinyl scaffolds and the first attempts to use them in asymmetric synthesis.
Among the organic compounds provided by nature, carbohydrates are those which contain the highest density of stereochemical information. Carbohydrates derivatives have some distinct

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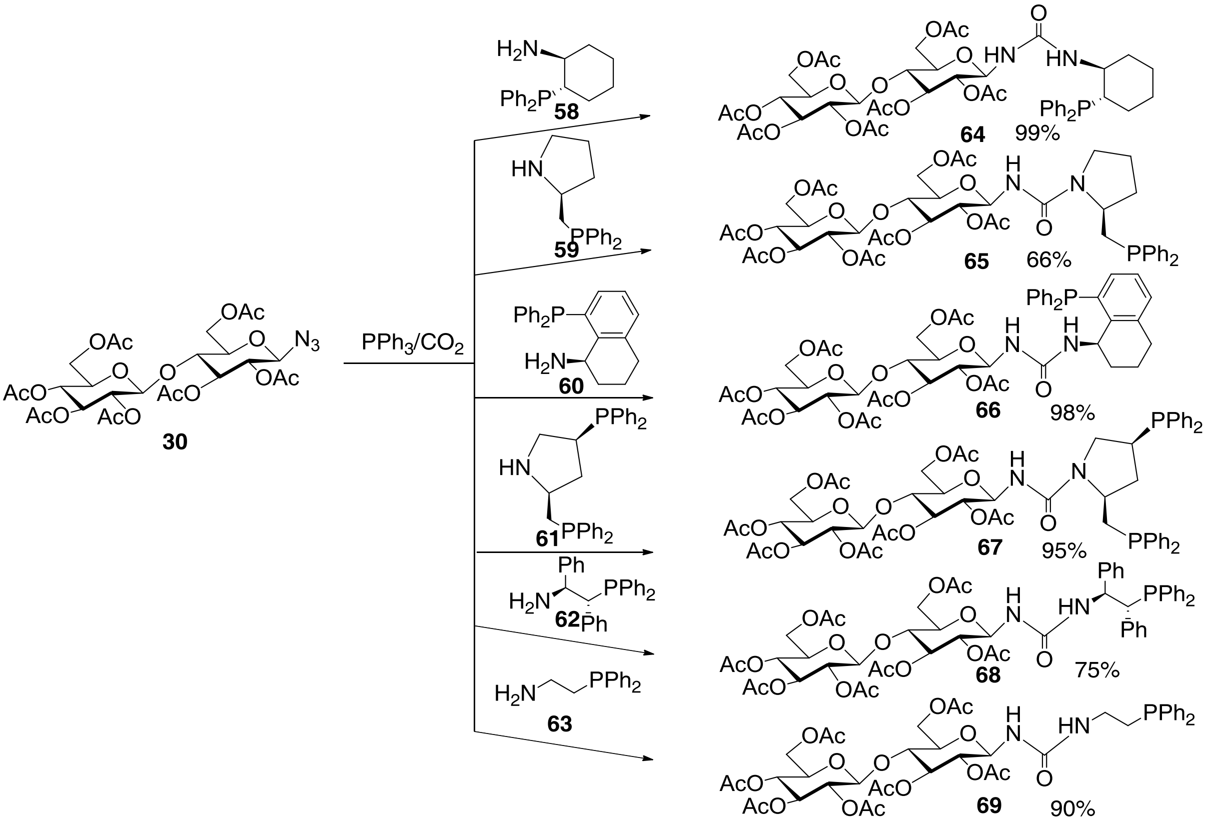
[33] Schaeppi, Y.; Treadwell, W. D. *Helv. Chim. Acta* **1948**, *31*, 577.

advantages as ligands: the starting materials are cheap and available in bulk quantities and the ligands can be easily constructed in models.

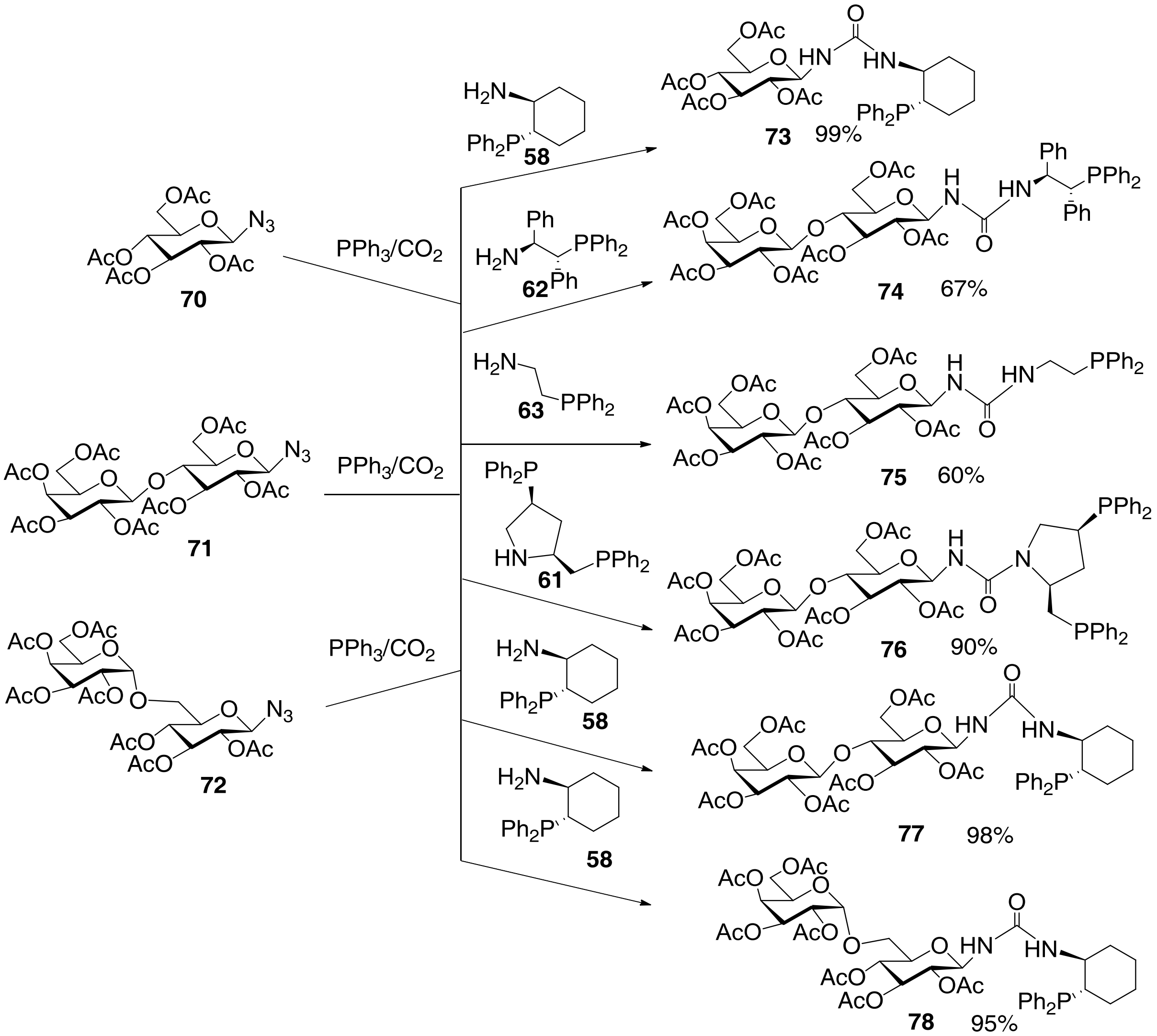
I proposed synthesis new ureas containing glycosyl and diphenylphosphinyl scaffolds present Scheme 12.



Scheme 12

The synthetic route for the preparation of the chiral, sterically congested, bifunctional urea-phosphine organocatalysts is straightforward (Scheme 12). Bifunctional ureas 64-69 were synthesised in high yields by coupling of the corresponding azido-cellobiose 30 with chiral amines 58-62 and achiral amine 63 in the presence of PPh_3 and $CO_{2.}$

Next the aza-Wittig, simple and efficient reaction of other mono- and disaccharides was investigated (Scheme 13).

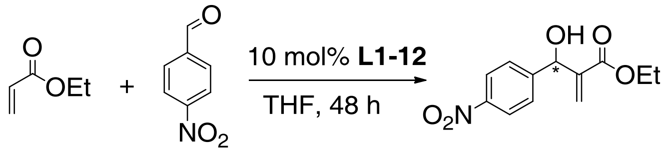


Scheme 13

Organocatalyst **73** was obtained in a high 99% yield from azido-glucose **73** and the aminocyclohexane **58**. The yields of ligands **74-78** from azido-lactose **71** and azido-melibiose **72** were also satisfactory (60 to 98%).

Initially, we chose the reaction of ethyl acrylate with *p*-nitrobenzaldehyde as a model transformation in which organocatalysts **64-78** were evaluated. The reaction was performed for 48 hours in THF using 10 mol% of the organocatalysts.The results are summarised in Table 3.

Table 3. Screening of the catalysts in the Morita-Baylis-Hillman reaction of ethyl acrylate and *p*-nitrobenzaldehyde.



Entry	Catalysts	Yield (%)[a]	ee (%)[b]
1	**64**	30	58
2	**69**	28	4
3	**73**	33	61
4	**75**	21	2
5	**77**	60	80
6	**78**	36	72

[a] Yield refers to isolated pure product after column chromatography.
[b] Enantioselectivity was measured by HPLC.

The best result was obtained in the presence of **77** as the organocatalyst at room temperature (Table 1, entry 5). Under the same conditions **78** gave a product with a lower yield and a slightly lower enantioselectivity (Table 1**,** entry 6).

Proposed transition state of this asymmetric MBH reaction is illustrated in Figure 6.

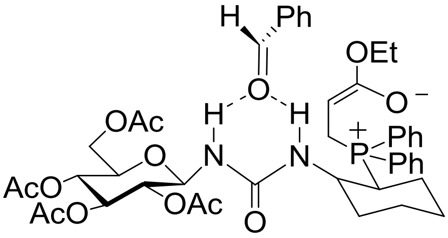


Figure 6

The urea hydrogens forms a hydrogen-bond with the aldehyde carbonyl group, and the alkoxy enolate was formed *via* an phosphinoyl attack on an activated carbonyl group from *si*-face and give *R*-product.

The best disaccharide organocatalysts **64**, **77** and **77** were also tested in the aza-Henry reaction. In present of the derivative **64** and **77** products of aza-Henry reaction were synthesised with high yield but with low enantioselectivity.

In conclusion, we have prepared a new chiral bifunctional phosphinoureas derived from saccharides and in high yields using simple procedure. Organocatalysts **77** and **78** were efficient for the asymmetric Morita-Baylis-Hillman reaction of an acrylate with an aldehyde. This reaction requires the optimization of conditions, which is currently underway.

Conclusions and future perspectives:

- I developed effective transacetalisation reaction of sucrose with aldehydes and ketone dimethylacetals in the presence of lanthanide cations supported on resin. The catalyst can be recovered and reused.
- I perfected the synthesis of isocyanates, isothiocyanates, and di- and polysaccharide urea derivatives obtained in phosphineimide reaction.
- I developed effective synthesis of cryptands, di- and polysaccharides, as hosts in the complexation of drugs and aminoacids (guests),
- I developed effective synthesis of new ureas containing glycosyl and diphenylphosphinyl scaffolds as chiral ligands and organocatalysts.
- I would like to expand the cryptands group and verifying their as host in complexes with other guests both inorganic and organic anions and cations.
- Further refinement of the MBH reaction and other asymmetric reactions is also under active investigation in aqueous media.
- Verification of the effectiveness of phosphine derivatives of sugars in an aqueous medium.

3 Other publications and achievements

3.1 Publications

Below the list of publications not included in the **P1-P8** list.

<u>Before obtaining the degree of doctor</u>

<u>Original publications</u>

1. R. Bartnik, Z. Cebulska, B. Kryczka, S. Leśniak, **S. Porwański,** T. Zieliński

" New cation dyes by the condensation of 1-hydroxyethyl or 1-chloroethyl-2-formylmethyleneindoline with aromatic amines. **I**. Hemicyaninic salts".

Pol. J. of Appl. Chem., **1994,** 189-198. **(4 pt. MSHE)**

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 70%.

2. R. Bartnik, Z. Cebulska, B. Kryczka, S. Leśniak, **S. Porwański,** T. Zieliński

"New cation dyes by the condensation of 1-hydroxyethyl or

1-chlotoethyl-2-formylmethyleneindoline with aromatic amines.

II. Free bases and their methylation".

Pol. J. of Appl. Chem., **1994,** 199-207. **(4 pt. MSHE)**

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 70%.

3. I. Frappa, P. Lhoste, **S. Porwański,** B. Kryczka, D. Sinou

"Stereoselective palladium(0)-mediated synthesis of 1,4-disaccharides".

Tetrahedron Letters, **1995**, 36**,** 1251-1254. IF=2,257 (25 pt**.** MSHE)

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 70%.

4. I. Frappa, P. Lhoste, **S. Porwański,** B. Kryczka, D. Sinou

"Stereoselective palladium(0)-mediated synthesis of 1,4-disaccharides".

J. Carbohydr. Chem. **1997**.16(6), 891-910. IF=1,079 (20 pt**.** MSHE)

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 60%.

<u>After obtaining the degree of doctor</u>

<u>Original publications</u>

1. I. Frappa, P. Lhoste, **S. Porwanski**, B. Kryczka, D. Sinou, A. Zawisza

Palladium(0)-mediated synthesis of acetylated unsaturated 1,4-disaccharides

J. Carbohydr. Chem. **1998**, *17*, 1117-1130, IF=1,033 (20 pt**.** MSHE)

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 60%.

2. A. Zawisza, B. Kryczka, P. Lhoste, **S. Porwański**, D. Sinou

Efficient palladium(0)-catalyzed synthesis of alkenyl 1-thioglycosides and thiodisaccharides

J.Carbohydr. Chem. **2000**, *19*, 795-804 IF=0,855 (20 pt. MSHE)

My contribution consisted in: perform all experiments, registration of the NMR spectra, description of the results. I estimate my participation at 35%.

3. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański**, D. Sinou, A. Zawisza

An easy and efficient access to bis-allyloxy-arenes

Synth.Commun. **2000**, *30*, 3955-3961 IF=0,828 (20 pt. MSHE)

My contribution consisted in: the reaction of 1,2 -dihydroxybenzene with allyl methyl carbonate, registration of the NMR spectra, description of the results. I estimate my participation at 25%.

4. R. Kolodziuk, B. Kryczka, P. Lhoste, **S. Porwanński**, D. Sinou, A. Zawisza
Palladium(0)-catalysed access to bis-glycosyloxy-arenes
Synth. Commun. **2001**, *31*, 3863-3870 IF=0,912 (20 pt**.** MSHE)
My contribution consisted in: the reaction of 1,4-dihydroxybenzene with 6-O-(tert-butyldiphenylosilil)-4-O-methokxycarbonyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside, registration of the NMR spectra, description of the results. I estimate my participation at 25%.

5. D. Sinou, P. Lhoste, N. Pichon, B. Kryczka, **S. Porwański**, A. Zawisza
Palladium-catalyzed synthesis of bis-glycosides of but-2-ene-1,4-diol, butane-1,4-diol and 1,2-bis(propenyl)benzene
J. Carbohydr. Chem. **2002**, *21*, 541-554 IF=0,798 (20 pt**.** MSHE)
My contribution consisted in: the reaction of but-2-ene-1,4-diol with 6-O-(tert-butyldiphenylosilil)-4-O-methokxycarbonyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranoside, registration of the NMR spectra, description of the results. I estimate my participation at 35%.

6. **Stanislaw Porwanski,** Stephane Menuel, Xavier Marsura, Alain Marsura
"The modified 'phosphine imide' reaction: a safe and soft alternative ureas synthesis"
Tetrahedron Letters; **2004;** *45;* 5027-5029. IF=2,484 (25 pt**.** MSHE)
My contribution consisted in: synthesis of aminoacid ureas, registration of the NMR spectra, description and interpretation of the results. I estimate my participation at 60%.

7. B. Kryczka, S. Lesniak, B. Pasternak, **S. Porwanski**
„Reaction of (2-Ethyl-aziridin-2-yl)diphenyl Methanol and Diphenyl-(2-phenyl-aziridin-2-yl)methanol with Phenyl and t-Butyl Isocyanates, Phenyl Isothiocyanate and Thiophosgene"
Polish J. Chem., **2007**, 81, 1927-1934, IF=0,483 (15 pt**.** MSHE)

My contribution consisted in: synthesis of isothiocyanates, registration of the NMR spectra, description and interpretation of the results. I estimate my participation at 35%.

8. B. Olszewska, I. Szulc, B. Kryczka, A. Kubiak, **S. Porwański,** A. Zawisza.
„Asymetric synthesis of optically active vinyltetrahydrofurans via palladium-catalysed cyclisation of bis(hydroxymethyl)allylic carbonates”.
Tetrahedron Asymmetry, **2013**, 24, 212-216. IF=2,115 (25 pt**.** MSHE)
My contribution to this work consisted: of synthesis of carbohydrateurea catalyst registration of the NMR spectra, description and interpretation of the results. I estimate my participation at 20%

<u>Review articles</u>

1. G.Descotes, J.Gagnaire, A.Bouchu, S.Thervent, N.Giry-Panaud, P.Salanski, S.Bielniak, A.Wernicke, **S.Porwanski** and Y.Queneau**.**
“Preparation of esters, ethers and acetals from unprotected sucrose”.
Polish J. Chem., **1999**, 73, 1069-1077. IF=0,595 (15 pt**.** MSHE)
My contribution consisted in: description of sucrose 4,6-O-acetal (method synthesis and applications in organic synthesis). I estimate my participation at 20%.

2. B. Kryczka, **S. Porwański,**
“Synteza glikozydów, disacharydów i pseudodisacharydów w reakcjach z udziałem związków palladu”
Wiadomości Chemiczne; **2002;** *56*, 627-660. (8 pt**.** MSHE)
My contribution consisted in the joint editing of the manuscript. I estimate my participation at 50%.

3.2 Communications

<u>Before obtaining the degree of doctor:</u>

<u>Posters:</u>

1. B. Kryczka, R. Bartnik, **S. Porwański.**
“Reakcje azirydynokarbinoli z tiofosgenem”.
Zjazd P.T.Chem. Toruń **1993**, S-1, P-19.

2. B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou.
"Nowa metoda syntezy tioglikozydów alkenylowych w reakcjach katalizowanych kompleksami palladu(0)".
IV Ogólnopolskie Sympozjum Chemii Organicznej Łódź 22-24 styczeń **1997**.

3. B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou.
" Synteza disacharydów pochodnych acetylowych w reakcjach katalizowanych kompleksami palladu(0)".
XL Zjazd naukowy PTCH i SITP Gdańsk 22-26.10.**1997**.M-1, P-7.

4. B.Kryczka, **S.Porwański,** A.Zawisza.
"Zastosowanie węglanów pochodnych glikozydów w reakcjach katalizowanych kompleksami palladu(0)".
XL Zjazd naukowy PTCH i SITP Gdańsk 22-26.10.**1997**.M-1, P-8.

Oral communications:

1. R. Bartnik, Z. Cebulska, A. Galindo, **S. Porwański**
"Synthese et etude des spectres d'une serie des aza-1-bicyclobutanes deuteres".
Colloque Spała **1987**.

2. B. Kryczka, R. Bartnik, **S. Porwański**
"Reactions des aziridines alcools avec le thiophosgene".
Colloque Lyon **1993**, Resumes des Conferences et Communications **5**.

3. I. Frappa, B. Kryczka, P. Lhoste, **S. Porwański**, D. Sinou
"Synthese de O-glycosides et d'oligosaccharides catalysee par les complexes du palladium(0) ***I****.*
Congres de la Societé Française de Chimie S.F.C. 26-30.10.**1994** Lyon.

4. B. Kryczka, **S. Porwański**
"*Recherches sur les carbonates et les thiocarbonates".*
VI^{čme} Colloque Université Lyon I - Université de Łódź 19-20.05.**1995** Łódź.

5. I. Frappa, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou
"Synthese de O-glycosides et d'oligosaccharides catalysee par les complexes du palladium(0) ***II****.*
VI^{čme} Colloque Université Lyon I - Université de Łódź 19-20.05.**1995** Łódź.

6. I. Frappa, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou
"Synthese de disaccharides catalysee par les complexes du palladium(0)".
SECO XXXII, 28 Mai-3Juin **1995** ŕ St. Germain-aux-Monts d'Or.

7. I. Frappa, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou
"Synthese de disaccharides catalysee par les complexes du palladium(0)".
SPISY'S Sympopzjum on Asymetric Catalisis, 22-23 juin **1995** a Paris.

8. B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou
"Synthese de disaccharides catalysee par les complexes du palladium(0)".
S.F.C.-J^{ees} region. Centre-Est 96, Lyon, 19-20.09.**1996**.

9. B.Kryczka, P.Lhoste, **S.Porwański**, D.Sinou.
Utilisation du palladium(0) en serie glucidique".

VII^{eme} Colloque Franco-Polonaise Lyon 11-16 mai **1997**.

10. B.Kryczka, P.Lhoste, **S.Porwański**, D.Sinou
"Synthese de S-glucopyranosides d'alcenyles catalysee par les complexes du palladium(0)".
VII^{eme} Colloque Franco-Polonaise Lyon 11-16 mai **1997**.

<u>After obtaining the degree of doctor:</u>

<u>Posters:</u>

1. B.Kryczka, R. Kołodziuk, **S.Porwański,** A.Zawisza
"Reakcje nukleofili z węglanami allilowymi w obecności kompleksów palladu(0)"
XLI Zjazd naukowy PTCH i SITPCH, Wrocław 14-18.09.**1998**. S-1, P-119.

2. A. Felcenloben, B. Kryczka, **S. Porwański**
„Alkenylowanie hydroksylowych pochodnych amin kompleksami π-(allilowo-palladowymi)"
I Sesja Posterowa Tematów Prac Dyplomowych Środowiska Chemików Łódzkich; Łódź; 22.06.**1998;** P-39.

3. R.Kołodziuk,B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou, A.Zawisza
"Synteza Alkenylowych eterów i N-Alkenylowych Pochodnych Amin w Reakcjach Katalizowanych Kompleksami Palladu(0)"
XLII Zjazd naukowy PTCH i SITPCH, Rzeszów, 6-10.09.**1998**. S-3, P-16

4. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Synteza molekuł typu bolaamfifile w warunkach katalizy homogenicznej kompleksami palladu(0)"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź; 10-15.09.**2000;** M-3, P-14.

5. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Nowa metoda syntezy 2,3-nienasyconych β-glikozydów aromatycznych"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź, 10-15.09.**2000;** M-3, P-15.

6. **S. Porwański,** G. Descotes, B. Kryczka, M. Łuczynska, Y. Queneau
„Zastosowanie Lantanowców osadzonych na żywicach w chemii cukrów"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź; 10-15.09.**2000;** M-3, P-16.

7. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Reakcja bis-hydroksyarenów z węglanem cukrowym katalizowana kompleksami palladu(0)"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź; 10-15.09.**2000;** M-3, P-17.

8. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Reakcja bis-hydroksyarenów z węglanami allilowymi katalizowana kompleksami palladu(0)"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź; 10-15.09.**2000;** S-1, P-108.

9. R. Kołodziuk, B. Kryczka, **S. Porwański,** A. Zawisza
„Reakcje związków dihydroksylowych z węglanami allilowymi katalizowane kompleksami palladu(0)”
XLIV Zjazd Naukowy PTCh i SITPCh; Katowice; 9-13.09.**2001;** S-6, P-28.

10. S. Porwański, R. Kołodziuk, B. Kryczka, A. Zawisza
„Reakcje węglanu pochodnej cukru z nukleofilami siarkowymi i tlenowymi”
XLIV Zjazd Naukowy PTCh i SITPCh; Katowice; 9-13.09.**2001;** S-6, P-68.

11. A. Zawisza, R. Kołodziuk, B. Kryczka, **S. Porwański**
„Nieoczekiwany przebieg reakcji węglanów allilowych z aminami w warunkach katalizy kompleksami palladu(0)”
XLIV Zjazd Naukowy PTCh i SITPCh; Katowice; 9-13.09.**2001;** S-6, P-84.

12. I. Sobalska, **S. Porwański,** A. Zawisza
„Próby funkcjonalizowania polihydroksyzwiązków reagentami allilowymi”.
V Sesja Posterowa Prac Dyplomowych Łódzkiego Środowiska Chemicznego;
Łódź; 14.06.**2002;** P-110.

13. A. Gruda, **S. Porwański,** A. Zawisza
„Zastosowanie katalizatorów lantanowcowych w reakcjach trans-O-glikozylowania”.
V Sesja Posterowa Prac Dyplomowych Łódzkiego Środowiska Chemicznego;
Łódź; 14.06.**2002;** P-111.

14. B. Kryczka, **S. Porwański,** A. Marsura
„A triphenylphosphine polymer-supported assisted „phospine imide” reaction”.
XLV Zjazd Naukowy PTCh i SITPCh; Kraków; 9-13.09.**2002;** S-1, P-80.

15. R. Kołodziuk, B. Kryczka, **S. Porwański,** A. Zawisza
“Synteza glikozydów alkenylowych z wykorzystaniem węglanów allilowych w reakcjach katalizowanych kompleksami palladu(0)”
Ogólnopolskie Sympozjum dedykowane Prof.dr hab. Marii Michalskiej,
Łódź, 17. 06. **2003,** P-10.

16. N. Domińczak, R. Kołodziuk, B. Kryczka, **S. Porwański,** A. Zawisza
“Synteza glikozydów przy udziale 3-O-izobutyloksykarbonylo-D-glukalu katalizowana kompleksami palladu(0)”
Ogólnopolskie Sympozjum dedykowane Prof. dr hab. Marii Michalskiej
Łódź, 17. 06. **2003,** P-11.

17. B. Kryczka, R. Kołodziuk, **S. Porwański,** A. Zawisza
„Reakcje katalizowane kompleksami palladu(0) w syntezach pochodnych cukrów”
XLVI Zjazd Naukowy PTCh i SITPCh; Lublin; 15-18.09.**2003;** S-1, K-2.

18. A. Zawisza, N. Domińczak, B. Kryczka, R. Kołodziuk, **S. Porwański**
„Synteza węglanów allilu i ich zastosowanie jako prekursorów układu -(allilo)palladu”.
XLVI Zjazd Naukowy PTCh i SITPCh; Lublin; 15-18.09.**2003;** S-1, P-98.

19. A. Miazek, **S. Porwański**
„Próby selektywnego wprowadzania grup azotowych w sacharydach”.
VII Sesja Posterowa Prac Dyplomowych Środowiska Chemików Łódzkich;
Łódź; 17 .06.**2004;** P-90.

20. S. Porwański, B. Kryczka, A. Marsura
“Zastosowanie trifenylofosfiny osadzonej na polimerze w fosfinoimidowej reakcji benzyloaminy z β-cyklodekstryną oraz próby jej regeneracji”.
VII Ogólnopolskie Sympozjum Chemii Organicznej; Warszawa; 18-20.11.**2004**; P-46

21. K. Trzeciak, **S. Porwański**
„Próby syntezy niektórych azydopochodnych cukrów nienasyconych”
VIII Sesja Posterowa Prac Dyplomowych Łódzkiego Środowiska Chemicznego;
Łódź; 16.06.**2005;** P-36

22. S. Kozłowska, **S. Porwański**
„Synteza niektórych azydopochodnych cukrów nienasyconych”
VIIISesja Posterowa Prac Dyplomowych Łódzkiego Środowiska Chemicznego;
Łódź; 16.06.**2005;** P-46

23. K. Kołakowska, **S. Porwański**
„Znane i nieznane zastosowania pochodnych sacharozy”
X Sesja Posterowa Prac Dyplomowych Łódzkiego Środowiska Chemicznego;
Łódź; 20.04.**2007;** P-52 (nagrodzony).

24. S. Porwański, B. Kryczka, A. Marsura
„ Funkcjonalizowanie sacharozy i celobiozy”
52 Zjazd PTChem oraz SITPChem Łódź 12-16.09.**2009**, S01-PC-01-89.

25. M. Pintal, **S. Porwański**
„Synteza kryptandów cukrowych”
II Sesja Magistrantów i Doktorantów Łódzkiego Środowiska Chemików;
Łódź; 20.06.**2011;** P-35

26. J. Imielska, **S. Porwański**
„Synteza mocznikowych i tiomocznikowych organokatalizatorów cukrowych”
II Sesja Magistrantów i Doktorantów Łódzkiego Środowiska Chemików;
Łódź; 20.06.**2011;** P-16.

27. J. Imielska, B. Kryczka, M. Pintal, **S. Porwański**
„Synteza mocznikowych pochodnych disacharydów”.
54 Zjazd PTChem i SITPChem, 18-22 wrzesień **2011**, S04-p 76, Lublin

28. J. Imielska, B. Kryczka, **S. Porwański,** M. Pintal
„Mocznikowe i tiomocznikowe pochodne disacharydów”
XIV Ogólnopolskie sympozium sekcji chemii heteroorganicznej PTChem.,
Łódź, 18. 11. **2011**; P 34.

29. B. Kryczka, R. Kołodziuk, B. Olszewska, **S. Porwański,** A. Zawisza
„Synteza i wykorzystanie katalizatorów pochodnych cukrów w reakcjach cyklizacji i addycji”.
IX Ogólnopolskie Sympozium Chemii Organicznej,
Warszawa, 6-9. 0.4. **2011**, K-POIG, 11,12.

30. M. Urbańczyk**, S. Porwański,** B. Kryczka
„Otrzymywanie Organokatalizatorów Disacharydów”
III Sesja Magistrantów i Doktorantów Łódzkiego Środowiska Chemików;
Łódź; 12.06.**2012;** P-21

31. A. Zawisza, B. Kryczka, R. Kołodziuk, B. Olszewska, **S. Porwański,** I. Wiśniewska
„Synteza ligandów pochodnych cukrów i ich wykorzystanie w katalizowanych palladem reakcjach substytucji allilowej”,
55 Zjazd PTChem i SITPChem, Białystok, 16-20.09. **2012**. S06-P-61

32. M. Pintal, B. Kryczka, **S. Porwański,** J. Robak
„Synteza i właściwości kompleksujące makrocyklicznych pochodnych glukozy i celobiozy”,
56 Zjazd PTChem i SITPChem, Siedlce, 16-20.09. **2013**. S01-P29

33. J. Robak, B. Kryczka, M. Pintal, **S. Porwański**
„Synteza mocznikowych organokatalizatorów pochodnych glukozy”,
56 Zjazd PTChem i SITPChem, Siedlce, 16-20.09. **2013**. S01-P31

34. M. Pintal, B. Kryczka, **S. Porwański,** J. Robak
„Synteza i właściwości kompleksujące makrocyklicznych pochodnych celobiozy i glukozy”
II Łódzkie Sympozjum Doktorantów Chemii, Łódź, 7-8.05. **2014**; P38.

35. J. Robak, B. Kryczka, M. Pintal, **S. Porwański**
„Synteza mocznikowych organokatalizatorów cukrowych”
II Łódzkie Sympozjum Doktorantów Chemii, Łódź, 7-8.05. **2014**; P39.

Oral communications:

1. R. Kołodziuk, B.Kryczka, **S.Porwański,** A.Zawisza
"*Alkenylowanie nukleofili tlenowych, azotowych i siarkowych w reakcjach katalizowanych kompleksami palladu(0)*"
V Ogólnopolskie Sympozium Chemii Organicznej, Konstancin-Jeziorna,
11-14.11.**1998**, K-5

2. B. Kryczka, R. Kołodziuk, **S. Porwański,** A. Zawisza
“*Nieoczekiwany przebieg reakcji węglanów allilowych z nukleofilami azotowymi i tlenowymi w obecności palladu(0)*”
Postępy w Laboratoryjnej i Przemysłowej Syntezie Organicznej; Ustroń 07-10.11.**1999**; K-9.

3. R. Kołodziuk, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Nowa metoda syntezy 1-tioglikozydów alkenylowych i tiodisacharydów"
Jubileuszowy Zjazd Naukowy PTCh i SITPCh; Łódź; 10-15.09.**2000;** M-3, K-3.

4. B. Kryczka, R. Kołodziuk, **S. Porwański,** A. Zawisza
„Homogeniczna kataliza kompleksami palladu(0) w reakcjach glikozylowania".
XLV Zjazd Naukowy PTCh i SITPCh; Kraków; 9-13.09.**2002;** S-1, K-1.

5. B. Kryczka, R. Kołodziuk**, S. Porwański,** A. Zawisza
„Reakcje katalizowane kompleksami palladu(0) w syntezach pochodnych cukrów"
XLVI Zjazd Naukowy PTCh i SITPCh; Lublin; 15-18.09.**2003;** S-1, K-2.

6. B. Kryczka, R. Kołodziuk, A. Kubiak, **S. Porwański,** K. Wawrynko, A.Zawisza
„Reakcje podstawienia nukleofilowego w warunkach reakcji Trosta-Tsuji na przykładach pochodnych cukrów".
Postępy w Syntezie Związków Nieracemicznych; Szklarska Poręba, 14-16.10.**2004;** K-7.

7. **Stanisław Porwański,** Bogusław Kryczka, Alain Marsura
„Disacharydy z elementami eterów azakoronowych"
51 Zjazd PTChem oraz SITPChem, 7-11 wrzesień **2008**, S01-KS-11, Opole

8. **Stanisław Porwański**, Bogusław Kryczka
„Co łatwiej funkcjonalizować, sacharozę czy celobiozę"
IV Seminarium Sekcji Chemii Organicznej PTChem.,
Szklarska Poręba 16-18 październik **2008**, K-5

9. **S. Porwański,** F. Dumarcay-Charbonnier, A. Marsura
„ Tandem Staudunger-Aza-Wittig Reaction: A versatile strategy for the synthesis of building blocks in supramolecular chemistry" 52 Zjazd PTChem oraz SITPChem Łódź 12-16.09.**2009**, S01-OC-01-14.

10. B. Kryczka, R. Kołodziuk, B. Olszewska, **S. Porwański, A.** Zawisza
„Synteza i wykorzystanie katalizatorów pochodnych cukrów w reakcjach cyklizacji i addycji".
IX Ogólnopolskie Sympozium Chemii Organicznej,
Warszawa, 6-9. 0.4. **2011**, K-POIG, 11,12.

11. B. Kryczka, R. Kołodziuk, **S. Porwański**, A. Zawisza
„Synteza ligandów i organokatalizatorów pochodnych cukrów i ich wykorzystanie w syntezie asymetrycznej",
55 Zjazd PTChem i SITPChem, Białystok, 16-20.09. **2012**. S06-K-11

12. J. Imielska, B. Kryczka, **S. Porwański,** M. Pintal
„Synteza mocznikowych pochodnych cukrów Postępy w Syntezie Związków Nieracemicznych;
Polanica Zdrój, 16-19.10. **2012;** K-33.

13. B. Kryczka, **S. Porwański,** A. Zawisza
Synteza ligandów i organokatalizatorów pochodnych cukrów i ich wykorzystanie w syntezie asymetrycznej
Panel nr V, Sesja sprawozdawcza projektu „ *Cukry jako surowce odnawialne w syntezie produktów o wysokiej wartości dodanej*", Warszawa 12.04.**2014**

Reports at international or foreign conferences

Posters

1. **S.Porwanski**, P Salanski,N.Panaud G.Descotes, A.Bouchu and Y.Queneau.
"Acetals of sucrose: selection of [OH-4;OH-6] or [OH-2;OH-3] diols".
10th European Carbohydrate Symposium, Galway (Irlande), 11-16 juillet **1999,** PA 096.

2. R. Kolodziuk, B. Kryczka, P. Lhoste, **S. Porwanski,** D. Sinou, A. Zawisza
„An easy and efficient access to bis-allyloxyarene"
The Sixth International Conference on Heteroatom Chemistry;
Łódź; 22-27.06.**2001;** P-107

3. S. **Porwański,** B. Kryczka**,** A. Marsura
„Disacharydy z elementami eterów koronowych"
50 Jubileuszowy Zjazd Polskiego Towarzystwa Chemicznego oraz Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, 11th International Conference on Chemistry and the Environment, PCCE-DCE'2007; 9-12 września **2007**, S1-PS1-34, Toruń

4. S. Menuel, J. P. Joly, N. E. Ghermani, **S. Porwanski,** A. Marsura
„Synthesis and Inclusion Ambility of Novel bis β-Cyclodextrin Pseudo-Cryptands and Glyco-Cryptands"
50 Jubileuszowy Zjazd Polskiego Towarzystwa Chemicznego oraz Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, 11th International Conference on Chemistry and the Environment, PCCE-DCE'2007; 9-12 września **2007**, S1-SL-16, Toruń

5. **S. Porwanski**, B.Kryczka
"*Synthesis of Bifunctional Chiral Urea and Thiourea in the Phosphinimide Reaction"*
17th International Symposium on Homogeneous Catalysis
July 4-9, **2010** Poznań, Poland; P-191

6. J. Imielska, B. Kryczka, **S. Porwański**
„Synthesis of urea and thiourea saccharides organocatalysts"
18th International Sympozium on Homogeneneous Catalysis,
July 9-13. **2012**, Toulouse, France, P 081.

7. M. Pintal, B. Kryczka, **S. Porwański**
„Saccharides bonded with azacrown ethers by urea or thiourea bridge as organocatalysts", 18th International Sympozium on Homogeneneous Catalysis,
July 9-13. **2012,** Toulouse, France, P 082.

8. M. Pintal, J. Robak, B. Kryczka**, S. Porwański**
„Synteza kryptandów cukrowych"
XV International Symposium „Advances in the Chemistry of Heteroorganic Compounds
Łódź, November 16, **2012**; P54.

9. J. Robak, B. Kryczka, M. Pintal, **S. Porwański**
„Synteza mocznikowych organokatalizatorów cukrowych"
XV International Symposium „Advances in the Chemistry of Heteroorganic Compounds"
Łódź, November 16, **2012**; P55.

10. M. Pintal, B. Kryczka, **S. Porwański,** J. Robak
„Synthesis and complexation properties of a bis-glucose pseudo-cryptand towards aspirin and paracetamol"
18th European Symposium on Organic Chemistry Marseille, France-July 7-12, **2013**, P2-124

11. J. Robak, B. Kryczka, M. Pintal, **S. Porwański,**
„Synthesis of urea and thiourea saccharides organocatalysts"
18th European Symposium on Organic Chemistry Marseille, France-July 7-12, **2013**, P2-154

<u>Oral communications:</u>

1. **S.Porwanski,** G.Descotes, A.Bouchu et Y.Queneau
"Acetalation du saccharose catalysee par les sels de lanthanides".
3eme Journee des Glycosciences, Villeurbanne, 6 novembre **1998**.

2. S.Dos Santos, B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou, A.Zawisza
„Synthese de molecules de type bolaamphiles par catalyse au palladium(0)"
VIIIeme Colloque Franco-Polonais, Ruciane-Nida 26-30.05.**1999**. K-42.

3. R.Kołodziuk,B.Kryczka, P.Lhoste, **S.Porwański,** D.Sinou, A.Zawisza
„Substitution allylique par un nucleophile oxygene ou azote catalysee par les complexes du palladium(0)"
VIIIeme Colloque Franco-Polonais, Ruciane-Nida 26-30.05.**1999**. K-44.

4. N.Giry-Panaud,**S.Porwanski,** G.Descotes, A.Bouchu and Y.Queneau
"Reversible Functionalization of unprotected sucrose by acetalation with activated carbonyl compounds".
6th Synposium on renewable for the chemical industry, Bonn(Allemagne), 23-25 mars **1999**. 546.

5. **S.Porwanski,** P Salanski, G.Descotes, A.Bouchu and Y.Queneau
"Lanthanide(III) cations exchanged resins as heterogeneous catalysts for the acetalation of carbohydrates".
5 th International Symposium on Heterogeneous Catalysis and Fine Chemicals, Lyon, 30 aout-3 septembre **1999**.

6. S. Dos Santos, B. Kryczka, P. Lhoste, **S. Porwański,** D. Sinou, A. Zawisza
„Synthese de molecules de type bolaamphiles par catalyse au palladium(0)”
IV^{eme} Journee du Groupe Lyonais des Glyco-Sciences; Lyon; 05.11.1999; K-2.

7. **S. Porwański,** P. Sałański, N. Giry-Panaud, G. Descotes, A. Bouchu, Y. Queneau
„Acetals du saccharose: selection des diols [OH-4 ; OH-6] au [OH-2 ; OH-3]”
IV^{eme} Journee du Groupe Lyonais des Glyco-Sciences; Lyon; 05.11.**1999;** K-12.

8. **S. Porwanski**
“Synthese de disaccharides catalysee par les complexes du palladium(0)”
Seminaire des enseignants chercheurs invites, 19 juin **2002**, Nancy (France)

9. **S. Porwanski**
“Fonctionnalisation en position 6 des oligosaccharides et polysaccharides”
Seminaire enseignants invites, 25 juin **2003**, Nancy (France)

10. S. Menuel, J. P. Joly, N. E. Ghermani, **S. Porwanski,** A. Marsura
„Synthesis and Inclusion Ambility of Novel bis β-Cyclodextrin Pseudo-Cryptands and Glyco-Cryptands”
50 Jubileuszowy Zjazd Polskiego Towarzystwa Chemicznego oraz Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, 11th International Conference on Chemistry and the Environment, PCCE-DCE’2007; 9-12 września **2007**, S1-SL-16, Toruń

11. Dumarcay-Charbonnier, Florence, **Porwanski Stanislaw,** Manuel Stephane, Joly, Jean-Pierre, Marsura Alain,
“Bis-β-Cyclodextrin and Bis-Cellobiosyl Pseudo Cryptands. Synthese et Complexation”
XI-emes Journees Cyclodextrines, 26-28 novembre **2008** Rouen, France, O-4

3.3 Awards, distinctions, scholarships

- Award of the President of the Uniwersity of Łódź (first degree) for a series of works *Application of Pd(0)-catalysed reaction in the synthesis of carbohydrate derivatives,*
- Award of the President of the Uniwersity of Łódź (three degree) for achieve organizational,
- Scholarship Region Ron-Alp (Lyon France)
- Gold badge UŁ.

3.4 Research fellowships

1993-1994 (9 months)
1995 (3 months) Universite Claude Bernard Lyon I
Laboratoire de Synthese Asymetrique
Prof. Denis Sinou

- Pos-doc at the Unite Mixte de Sucrochimie CNRS-Beghin-Say(UMR143), c/o Eridania Beghin-Say, Villeurbanne, France (prof. Gerard Descotes et Yves Queneau), 1998/1999 (11 months);
- **2002** (5 months), **2003** (3 months**)**, **2004** (3 months), **2005** (5 months), **2006** (5 months), **2007** (2 months), **2008** (2 months), **2009** (2 months). Universite Henri-Poincare Nancy 1, Laboratoire de Chimie Therapeutique Professor Alain Marsura (Maitre de conference invite).

3.5 Research projects

- Grant of Rector University of Łódź (Chemical waste management at the University of Łódź), place of project implementation: University of Łódź, Faculty of Chemistry, Department of Organic and Applied Chemistry, nature of contribution: project manager (2002-2011).
- The "Sugars as raw materials in the synthesis of products with high added value," co-financed by the European Union from the European Regional Development Fund under the Operational Programme Innovative Economy 2007-2013, (UDA-POIG.01.01.02-14-102/09-03), place of project implementation: University of Łódź, Faculty of Chemistry, Department of Organic and Applied Chemistry, the nature of participation: project manager – 11 task, (2010-2014).

  This project is realized within a consortium concluded between: Institute of Organic Chemistry and Institute of Physical Chemistry Polish Academy of Sciences in Warsaw, Warsaw University of Technology, University of Gdansk, Silesian University of Technology and the University of Lodz.

3.6 Activity concerning scientific, educational and organizational work

- Teaching classes:

  Organic Chemistry - seminar, first year of biology
  Organic Chemistry - laboratory, first year of biology
  Organic Chemistry I - laboratory, second year of chemistry
  Organic Chemistry II - laboratory, third year of chemistry
  Chemistry of sugars - Monographic Lecture, fifth year of chemistry
  Spectroscopy - the laboratory, first year of chemistry, second-cycle

Spectroscopy - seminar, first year of chemistry, second-cycle
Applied chemistry and management of chemicals - lecture, third year of chemistry

- Number of teaching hours:
  in the academic year 2007/2008 : **271 (+31)**
  in the academic year 2008/2009 : **320 (+90)**
  in the academic year 2009/2010 : **327**
  in the academic year 2010/2011 : **324**
  in the academic year 2011/2012 : **338**
  in the academic year 2012/20123 :**344**
- Number of completed master's thesis: **18**
- Number of completed diploma's thesis: **17**
- Scientific take care of PhD student: **2**
- Achievements and initiatives to improve the educational process:
  - I prepared a monographic lecture (Chemistry of sugars),
  - I prepared a new lecture "Applied chemistry and management of chemicals" in all directions chemical
- Achievements in the popularization of science:
  - I led a lectures at the Akademia Ciekawej Chemii at the Faculty of Chemistry of the University of Lodz.
- Participation in committees:
  - selection committee,
  - Rector's Residential Committee
- Reviews:
  - *Synthetic Communication*,
  - diploma theses.
  - National Defense grants
- Assistance in the organization of conferences:
  - VI$^{\text{čme}}$ Colloque Université Lyon I - Université de Łódź 19-20.05.1995 Łódź
  - VIII$^{\text{eme}}$ Colloque Franco-Polonais, Ruciane-Nida 26-30.05.1999
  - Jubilee Scientific Congress Polish Chemical Society, Łódź 10-15.09.2000 (Office manager congress)
  - The Sixth International Conference on Heteroatom Chemistry, Lódź 22-27.06.2001

- 52 Scientific Congress Polish Chemical Society, Łódź 12-16.09.2009

3.7 Memberships

- member of the Polish Chemical Society

3.8 Other activities

- Expert MSHE
- Member of the committee of defending Ph.D. thesis (Stephane Menuel, University of Nancy I)
- One of the main initiators (together with prof. Kryczka), direct cooperation between the Universite of Łódź and Universite of Nancy I (France).

St. Porwański