Academic Portfolio

presenting the Author's scientific achievements in connection with applying for obtaining a scientific degree of habilitated doctor

Structural analysis of glycosides by theoretical and experimental methods

by

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Contents

1. Scientific diploma and scientific degree

Master of Science (M.Sc.), Faculty of Chemistry, University of Warsaw, Warsaw 2002
Title of M.Sc. thesis: *An attempt at a synthesis of the derivatives of ureido acids*
Thesis supervisor: Prof. Dr. hab. Jan Izdebski

Doctor of Chemical Sciences (Ph.D.), Faculty of Chemistry, University of Warsaw, Warsaw 2007
Title of Ph.D. dissertation: *Studies on the structure and interaction of nitrophenyl derivatives of saccharides with cyclodextrins in selected physicochemical processes*
Dissertation supervisor: Prof. Dr. hab. Andrzej Temeriusz

2. Employment in scientific institutions

October 2007 – January 2010 scientific-technical specialist, Faculty of Chemistry, University of Warsaw

February 2010 – September 2010 assistant professor, Faculty of Chemistry, University of Warsaw

October 2010 – until present time assistant professor, Faculty of Pharmacy with Division of Laboratory Medicine, Medical University of Warsaw

3. Presentation of the scientific achievement in connection with applying for obtaining a scientific degree of habilitated doctor

3.1. The title of the scientific achievement

Structural analysis of glycosides by theoretical and experimental methods

This scientific achievement consists of eight monothematic original articles published in scientific journals from ISI Master Journal List (known in Poland as the Philadelphia List) of total impact factor IF = **16.553**.

3.2. List of articles forming a monothematic series of publications, with estimation of the habilitant's individual contribution

H.1. K. Paradowska, **T. Gubica**, A. Temeriusz*****, M.K. Cyrański, I. Wawer. "^{13}C CP MAS NMR and crystal structure of methyl glycopyranosides" *Carbohydrate Research* **2008**, *343*, 2299-2307. **IF**$_{2008}$ **1.960**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- interpretation of the results obtained from single-crystal (XRD) and powder (PXRD) X-ray diffraction measurements
- editing of the whole manuscript of publication
I estimate my individual contribution to the authorship at 60%.

H.2. **T. Gubica**, A. Temeriusz*, K. Paradowska, A. Ostrowski, P. Klimentowska, M.K. Cyrański. "Single-crystal and powder X-ray diffraction and solid-state ^{13}C NMR of *p*-nitrophenyl glycopyranosides, the derivatives of D-galactose, D-glucose, and D-mannose" *Carbohydrate Research* **2009**, *344*, 1734-1744. **IF**$_{2009}$ **2.025**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- participation in interpretation of the results performed by XRD and PXRD as well as solid-state NMR spectroscopy (ssNMR)
- editing of the whole manuscript of publication
I estimate my individual contribution to the authorship at 60%.

H.3. **T. Gubica***, D.K. Stępień, A. Temeriusz, K. Paradowska, E. Głowacka, M.K. Cyrański, A. Ostrowski. "Solid-state structure of *N*-*o*-, *N*-*m*-, and *N*-*p*-nitrophenyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylamines" *Carbohydrate Research* **2011**, *346*, 2491-2498. **IF**$_{2011}$ **2.332**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- participation in the interpretation of results obtained by XRD, PXRD and ssNMR techniques

- performing theoretical calculations and their interpretation (optimization of the structures and evaluation of the shielding constants)
- editing of the whole manuscript of publication

I estimate my individual contribution to the authorship at 55%.

H.4. **T. Gubica***, D.K. Stępień, A. Ostrowski, D.M. Pisklak, A. Temeriusz, E. Głowacka, K. Paradowska, M.K. Cyrański. "Crystal and molecular structure of nitrophenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosides" *Journal of Molecular Structure* **2012**, *1007*, 227-234. **IF**$_{2012}$ **1.404**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- performing theoretical calculations and their interpretation (optimization of the structures and evaluation of the shielding constants)
- registering of ^{15}N CP/MAS NMR spectra
- participating in the interpretation of results obtained by XRD, PXRD, ssNMR and differential scanning calorimetry (DSC) techniques
- editing the whole manuscript of publication

I estimate my individual contribution to the authorship at 55%.

H.5. **T. Gubica***, D.K. Stępień, D.M. Pisklak, A. Ostrowski, M.K. Cyrański. "Single-crystal and powder X-ray diffraction, ^{13}C CP/MAS NMR, and DFT-GIAO calculations of methyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-gluco-pyranoside and methyl 2,4,6-tri-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-α-D-glucopyranoside" *Journal of Molecular Structure* **2013**, *1036*, 407-413. **IF**$_{2013}$ **1.599**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- performing theoretical calculations and their interpretation (optimization of the structures and evaluation of the shielding constants)
- participating in the interpretation of results obtained by XRD, PXRD and ssNMR

- editing the whole manuscript of publication

I estimate my individual contribution to the authorship at 75%.

H.6. **T. Gubica***, J. Bukowicki, D.K. Stępień, A. Ostrowski, D.M. Pisklak, M.K. Cyrański. "Solid-state structure of methyl 2,4,6-tri-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside and methyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside" *Journal of Molecular Structure* **2013**, *1037*, 49-56. **IF**$_{2013}$ **1.599**

My contribution to this publication consisted in:

- determination of scientific aim and planning the investigations
- performing the organic synthesis
- participating in the interpretation of results obtained by XRD, PXRD and ssNMR techniques
- participating in the interpretation of theoretical calculations (conformational analysis and structure optimization)
- editing the whole manuscript of publication

I estimate my individual contribution to the authorship at 60%.

H.7. **T. Gubica***, Ł. Szeleszczuk, D.M. Pisklak, D.K. Stępień, M.K. Cyrański, M. Kańska. "Reliable evaluation of molecular structure of methyl 3-*O*-nitro-α-D-glucopyranoside and its intermediates by means of solid-state NMR spectroscopy and DFT optimization in the absence of appropriate crystallographic data" *Tetrahedron* **2014**, *70*, 1910-1917. **IF**$_{2013}$ **2.817**

My contribution to this publication consisted in:

- determination of scientific aim and planning the investigations
- performing the organic synthesis
- participating in theoretical calculations (structure optimization and evaluation of the shielding constant)
- interpretation of all obtained results (ssNMR, XRD and optimization by DFT methods)
- editing the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

H.8. J. Bukowicki, **T. Gubica***, Ł. Szeleszczuk. "Time-effective and reliable solid-state structure evaluation of selected peracetylated β-maltose derivatives by means of grid search, genetic algorithm and DFT calculations" *Tetrahedron* **2014**, *70*, 4008-4016. **IF**$_{2013}$ **2.817**

My contribution to this publication consisted in:
- determination of scientific aim and planning the investigations
- performing the organic synthesis
- interpretation of theoretical calculations (conformational analysis and structure optimization) and of the ssNMR measurements
- editing the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

3.3. Discussion of the habilitant's scientific achievement

3.3.1. Introduction

The chemist's work does not finish with performing the synthesis and purification of the end product. No less significant than compound synthesis and isolation is the confirmation of the purity and composition of the obtained compounds. The next stage of the characteristics of organic compounds is the determination of molecular structure. The organic chemist who wants to determine the structure of a molecule usually makes use of NMR spectroscopy and the information obtained on the basis of the reaction mechanism. An ideal situation occurs when it is possible to determine the spatial structure of a molecule (bond lengths, plane and torsion angles) by single-crystal X-ray diffraction (XRD). Thanks to this technique one can "see" the molecule and the crystal lattice, so it is the best possible way to confirm the molecular structure.

Unfortunately, the XRD technique is very demanding and can be used for few substances only. The first criterion which a substance must fulfill in order to take into account the possibility of XRD measurement is its crystal form. Another, equally important condition is the preparation of a suitable single crystal.

In spite of its undoubtable advantages, the XRD technique is limited as it enables the analysis of only one single crystal, the choice of which is often accidental. The organic compounds in solid state frequently occur in various polymorphic forms which can form

different crystals. Not all the polymorphic forms must be crystalline, some of them appear in amorphous form.

Polymorphism is a particularly important phenomenon in pharmaceutical science because of different bioavailability (due to differentiated solubility) of particular forms of organic compounds possessing the biological properties. In order to confirm or exclude the existence of polymorphic variations one can use the powder X-ray diffraction (PXRD) as well as solid-state NMR spectroscopy (ssNMR). In both PXRD and ssNMR measurements, unlike in the XRD measurements, the macroscopic samples are examined. This means that the use of all those three methods jointly guarantees obtaining full structural characteristics of organic compounds.

It is worth adding here that the PXRD and ssNMR techniques are not as demanding as the XRD method. The basic condition which a substance must fulfill in order to perform its powder analysis or to register its ssNMR spectrum, is the solid state.

In original research works all three above-mentioned measurement methods (XRD and PXRD X-ray diffraction as well as ssNMR spectroscopy) are very rarely used to obtain the full characteristics of organic compounds. Moreover, the fact that these research methods are complementary is often ignored. For instance, in the case when it is not possible to perform XRD measurements one can use the generally available PXRD and ssNMR techniques, or else the molecular modeling in order to obtain the spatial molecular structure.

In my scientific achievement I showed different ways of jointly using the XRD, PXRD, ssNMR and molecular modeling methods. I also made use of the complementarity of these experimental and theoretical techniques in situations when it was impossible to use them at the same time. Such an approach to the description of structural properties of organic compounds is the novelty in research work.

3.3.2. The habilitant's individual investigations

All the publications which constitute my scientific achievement are interrelated thematically. However, in each article I posed different research aims, so each publication is a separate and complete whole. That is why I decided to present and discuss each of them separately.

H.1. K. Paradowska, **T. Gubica**, A. Temeriusz*, M.K. Cyrański, I. Wawer. "^{13}C CP MAS NMR and crystal structure of methyl glycopyranosides" *Carbohydr. Res.* **2008**, *343*, 2299-2307.

In this work my aim was to perform a complete structural analysis of all aldopentoses, i.e. lyxose, arabinose, xylose and ribose. As it is well known, these monosaccharides undergo mutarotation. That is why I decided to block the hemiacetal hydroxyl group of native aldopentoses thus forming the simplest acetals, i.e. methyl glycosides. In this way I was certain about the molecular structure of the examined compounds. Luckily enough, the molecular structure of these glycosides was very similar to the initial compounds. So I examined the following compounds: α-D-lyxopyranoside (**1**), β-D-lyxopyranoside (**2**), α-L-arabinopyranoside (**3**), β-L-arabinopyranoside (**4**), α-D-xylopyranoside (**5**), β-D-xylo-pyranoside (**6**) and β-D-ribopyranoside (**7**). I excluded methyl α-D-ribopyranoside from the investigations because this compound occurs in the form of oil.

The crystal unit cells of compounds **1-4** and **6-7** contained one independent molecule. Only the unit cell of compounds **5** was composed of two independent structures. On the basis of these data (obtained from XRD measurements) it should be expected that in the first case the number of signals in ^{13}C CP/MAS NMR spectra would correspond to the number of carbon atoms in a molecule. Only in the case of compound **5** one should observe double signals in the ssNMR spectrum. However, the above prediction was not true for compounds **4** and **7**. The signals in the ^{13}C CP/MAS NMR spectra for compounds **4** and **7** occurred in the form of doublets and triplets, respectively. At this stage of investigations it would be difficult to explain this phenomenon unequivocally, in particular for compound **7**. If this sample contained three magnetically inequivalent molecules, then compound **7** might consist of three polymorphs, each of which would have one independent molecule in the crystal unit cell. This problem was solved by using PXRD. Thanks to the use of this technique I was able to find out that: (*i*) compound **4** consists of two polymorphs, each of which has one independent molecule in the crystal unit cell; (*ii*) compound **5** forms only one crystal form according to the PXRD measurement; and (*iii*) compound **7** occurs in two crystal forms, one of which (not measured by XRD) contains two independent molecules in the unit cell.

A comparison of chemical shifts in the NMR spectra in solution with the ^{13}C CP/MAS NMR spectra for compounds **1-7** confirmed that the methoxyl group is much more mobile in solution than in the crystal lattice. It should be added here that the difference between chemical shifts in solution and in solid state are also affected, apart from conformational effects, by intermolecular interactions in the crystal lattice. If the data from XRD measurements are available, it is very easy to show the position of intermolecular hydrogen bonds. In this work I proved that on the basis of a correlation between the calculated shielding

constants and the experimental chemical shifts (^{13}C CP/MAS NMR) it is possible to determine the position of hydrogen bonds without necessarily using XRD technique.

H.2. **T. Gubica**, A. Temeriusz*, K. Paradowska, A. Ostrowski, P. Klimentowska, M.K. Cyrański. "Single-crystal and powder X-ray diffraction and solid-state ^{13}C NMR of *p*-nitrophenyl glycopyranosides, the derivatives of D-galactose, D-glucose, and D-mannose" *Carbohydr. Res.* **2009**, *344*, 1734-1744.

In this work the *p*-nitrophenyl glycosides: α-D-galactopyranoside (**1**), β-D-galactopyranoside (**2**), α-D-glucopyranoside (**3**), β-D-glucopyranoside (**4**), α-D-mannopyranoside (**5**) and β-D-mannopyranoside (**6**) were taken as the subject for structural studies. These compounds are used as markers in the investigations into the activity of certain enzymes (glycosidases) which hydrolyze glycosidic bonds. *p*-Nitrophenyl glycosides are colorless. Whereas *p*-nitrophenol, which is released as a result of hydrolysis due to glycosidases, has an intensive color. That is why this process can be observed spectrophotometrically.

The crystal structures (XRD) for compounds **3** and **5** were already described in the literature. In this study we managed to measure the crystals of compounds **1** and **2**. The crystal unit cells for compounds **1**, **3** and the hemihydrate **5** were found to contain two independent molecules. On the other hand, the crystal unit cells for compound **2** and the ethanol solvate **5** had one independent molecule. In the ^{13}C CP/MAS NMR spectra for compounds **1-6**, only in the case of compound **2** the signals occurred in the form of singlets. Hence it was supposed that compound **2** should occur in only one crystal form, including the single crystal which was taken for crystallographic studies. However, the results of PXRD measurements showed that compound **2** contains two crystal forms. One of them was in agreement with XRD measurements, but the other unknown polymorth occurred in very small quantities, that is why it was not detected by ssNMR measurements.

The number of resonance lines in the ^{13}C CP/MAS NMR spectra for compounds **1** and **3-6** was greater than the number of carbon atoms in the molecules of those compounds. However, it was difficult to state unequivocally (because of poor quality of the ssNMR spectra for these compounds) how many magnetically inequivalent molecules occurred in each sample. This problem was solved with the help of PXRD measurements. Thanks to those measurements I was able to confirm that the macroscopic samples consist of one crystal form to which belong the single crystals of compounds **1**, **3** and hemihydrate **5** which were taken to XRD measurements. So each of these samples contained two magnetically inequivalent

molecules. In addition, the ssNMR measurements showed that compound **4** occurs as an ethanol solvate.

H.3. **T. Gubica***, D.K. Stępień, A. Temeriusz, K. Paradowska, E. Głowacka, M.K. Cyrański, A. Ostrowski. "Solid-state structure of *N*-*o*-, *N*-*m*-, and *N*-*p*-nitrophenyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylamines" *Carbohydr. Res.* **2011**, *346*, 2491-2498.

The derivatives of *N*-phenyl-β-D-xylopyranosylamine are the inhibitors of enzymatic processes and are frequently used as fungicides. Certainly, not all the derivatives of this compound are known yet. I performed the synthesis of new nitro derivatives of phenylxylosylamine in order to determine their biological activity. I obtained three isomers: *ortho* (**1**), *meta* (**2**) and *para* (**3**) of *N*-nitrophenyl-2,3,4-tri-*O*-acetyl-β-D-xylopyranosylamine.

I performed detailed characteristics of structural properties of compounds **1**-**3** by the XRD, PXRD and ^{13}C CP/MAS NMR techniques. I obtained the most interesting results for compound **1**. This derivative showed polymorphic transitions together with the change of temperature. The phase transformations occurred at the temperature of 180K and 210K. I was able to determine the crystal structures of three polymorphs (at three different temperatures). The XRD method showed that the unit cell of compound **1** can consist of four or three molecules, or even one independent molecule depending on the temperature at which the measurement was performed. Unfortunately, I had no possibility to register the ssNMR spectra or to perform PXRD measurement at the temperature below 210K. These measurements were performed at room temperature.

H.4. **T. Gubica***, D.K. Stępień, A. Ostrowski, D.M. Pisklak, A. Temeriusz, E. Głowacka, K. Paradowska, M.K. Cyrański. "Crystal and molecular structure of nitrophenyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranosides" *J. Mol. Struct.* **2012**, *1007*, 227-234.

In this work, apart from standard experimental methods that I usually applied for my investigations, I also used the differential scanning calorimetry (DSC) and ^{15}N CP/MAS NMR spectroscopy. The xylosides that I examined in this work are oxygen analogs of xylosylamines which were described in the previous article. As the molecular structures of both these groups of compounds (xylosides and xylosylamines) are similar, I expected that also in this case a change of crystal form depending on temperature would be observed. That

is why first of all I performed DSC measurements of all nitrophenyl xylosides. Only for the *meta* isomer did I observe a single signal at the temperature of about 127K. A small intensity of that signal suggested that both polymorphs have similar energy. In fact, the XRD measurements performed for the *meta* isomer confirmed similar packing in the crystal lattice of both crystal forms. The unit cell of the *meta* isomer contained, respectively, four independent molecules and one independent molecule at the temperature of 100K and 295K.

The nitro group, which is present in all isomers (*ortho*, *meta* and *para*) of nitrophenyl xylosides, and the benzene ring plane were not coplanar. The nitro group was most strongly twisted in the case of the *ortho* isomer (by an angle of about 45°), and least twisted for the *meta* isomer (by an angle of about 3-5°). I decided to find out if the twist angle of the nitro group correlates with chemical shift values in the ^{15}N CP/MAS NMR spectra. However, I did not observe any correlation. I also decided to calculate the theoretical shielding constants (σ) for the nitrogen atom of the isolated molecules. In this case I observed a clear correlation between the twist angle of the nitro group and the σ values. Thus I can suppose that the interactions in the crystal lattice affect much more the chemical shift value for the nitrogen atoms in the nitro group than the coupling of this group with the benzene ring. The coupling of the nitro group with the benzene ring is most effective when this group is coplanar with the plane formed by the aromatic system.

H.5. **T. Gubica***, D.K. Stępień, D.M. Pisklak, A. Ostrowski, M.K. Cyrański. "Single-crystal and powder X-ray diffraction, ^{13}C CP/MAS NMR, and DFT-GIAO calculations of methyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-gluco-pyranoside and methyl 2,4,6-tri-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-α-D-glucopyranoside" *J. Mol. Struct.* **2013**, *1036*, 407-413.

This investigation was concerned with two rare disaccharides made up of galactose and glucose. These two monosaccharide units were connected by atypical glycosidic bonds: β-(1→2) (compound **1**) and β-(1→3) (compound **2**). The disaccharides of this type can be a valuable dietary product, such as isomaltulose (palatinose). This compound is also an atypical disaccharide, the isomer of sucrose in which glucose and fructose are connected by an α-(1→6) glycosidic bond. Thanks to the atypical composition of monosaccharide units in palatinose, it undergoes a much slower hydrolysis in comparison with sucrose. That is why palatinose has a much lower glycemic index than sucrose. The addition of palatinose to the drinks for sportspeople ensures a slow and constant supply of glucose.

Before starting the biological investigations, I decided first to describe thoroughly the structural properties of compounds **1** and **2**. As concerns compound **1**, I managed to solve its structure by XRD. The situation was more complicated for compound **2** because of its twin crystals. In spite of numerous attempts, I was unable to determine the structure of compound **2** by XRD. Only the unit cell parameters were established. The unit cell of compound **2** consists of two independent molecules, whereas the unit cell of compound **1** is composed of three independent molecules. The PXRD measurements showed that sample **1** forms one crystal form corresponding to the data obtained from XRD, whereas sample **2** consists of two or three polymorphs. The same intensity of multiplet components in the ^{13}C CP/MAS NMR spectrum for compound **2** suggests that the content of particular crystal forms is similar in this sample.

At the C-6 carbon atom of glucose in one of the independent molecules of compound **1**, the lack of ordering was observed (on the basis of XRD). This was confirmed by the ssNMR spectroscopy. Namely, the theoretically calculated chemical shift for this atom was clearly greater than the analogical experimental value. The remaining theoretical and experimental chemical shift values correlated with each other very well ($R^2 > 0.99$).

H.6. **T. Gubica***, J. Bukowicki, D.K. Stępień, A. Ostrowski, D.M. Pisklak, M.K. Cyrański. "Solid-state structure of methyl 2,4,6-tri-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside and methyl 3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-galactopyranoside" *J. Mol. Struct.* **2013**, *1037*, 49-56.

In this work I also dealt with atypical disaccharides made up of glucose and galactose, which were connected by glycosidic bonds β-(1→3) (compound **1**) and β-(1→2) (compound **2**). The difference in structure between those two rare disaccharides, in comparison with the previous article, consisted in a reverse position of both monosaccharide units.

The aim of this work was to assess if the theoretical calculations can predict the structural properties of compounds **1** and **2**. Using the molecular mechanism (the MM3 force field) assisted by the genetic algorithm and DFT calculations I created the so-called adiabatic maps. These maps presented the energy of particular conformations (in the form of iso-lines) against two torsion angles (φ and ψ) around the glycosidic bond which connects glucose to galactose. It should be added here that in this article for the first time we used the genetic algorithm for searching conformational space of functionalized disaccharides. The use of a genetic algorithm as a calculation tool enabled a very effective shortening of the time of

calculations. On the adiabatic map of compound **1** there was one deep energetic minimum visible as well as three local minima. Similarly, for compound **2** I obtained four energetic minima, of which two deepest minima had a similar energy but differed considerably in conformation. This observation can explain why the molecules of compound **2** are unable to form the crystal lattice and that is why this compound occurs in amorphous form (this result was confirmed by PXRD and ssNMR investigations).

The position of a global energetic minimum on the adiabatic map of compound **1** did not much differ from the φ and ψ angles determined in the XRD measurement. The lowest energy conformation and the structure obtained on the basis of XRD differed only slightly by the position of exocyclic groups.

A comparison of chemical shifts in the ^{13}C NMR spectra registered in solution and in solid state for compound **1** allowed me to conclude that the rest of glucose, unlike galactose, has a greater conformational liability in the crystal. This hypothesis is also confirmed by the XRD structure, because the atoms in the rest of glucose have larger ellipsoids of vibrations than it is in the case of galactose.

H.7. **T. Gubica***, Ł. Szeleszczuk, D.M. Pisklak, D.K. Stępień, M.K. Cyrański, M. Kańska. "Reliable evaluation of molecular structure of methyl 3-*O*-nitro-α-D-glucopyranoside and its intermediates by means of solid-state NMR spectroscopy and DFT optimization in the absence of appropriate crystallographic data" *Tetrahedron* **2014**, *70*, 1910-1917.

In this work I described among other things the synthesis of a new glucose nitrate (methyl 3-*O*-nitro-α-D-glucopyranoside (**5**)), which can be used as a new potent drug for the treatment of cardiovascular diseases. I obtained this compound in a four-step synthesis starting from methyl α-D-glucopyranoside (**1**). First I introduced protection of two hydroxyl groups at the C-4 and C-6 carbon atoms in compound **1** and in this way I obtained methyl 4,6-*O*-ethylidene-α-D-glucopyranoside (**2**). Then I performed esterification of the remaining two free hydroxyl groups at the C-2 and C-3 carbon atoms in compound **2** and I obtained methyl 2,3-di-*O*-nitro-4,6-*O*-ethylidene-α-D-glucopyranoside (**3**). Next I hydrolyzed selectively the ester grouping at the C-2 carbon atom in compound **3** and I obtained methyl 3-*O*-nitro-4,6-*O*-ethylidene-α-D-glucopyranoside (**4**). As the final step of the synthesis I removed protection of the hydroxyl groups at the C-4 and C-6 carbon atoms in compound **4**.

I will now try to explain why compound **5**, which was obtained by me for the first time, deserves special attention. Namely, all organic nitrates used in pharmacotherapy possess

the same mechanism of action, irrespectively of the kind of organic grouping. The key problem here is the formation of nitric oxide (NO) which is an active metabolite of all drugs of this type. Even though a lot of various organic nitrates are used in medicine, it is still sensible to introduce new representatives of this kind of drugs on the market. Many patients with chronic heart failure require prolonged use of organic nitrates, as a result of which the effect of these drugs is weakened. An increase in dosage usually does not solve the problem because then the side effects increase too. The best way to avoid organic nitrate tolerance in therapy is to change the currently applied drug to a different one. As I mentioned above, the organic nitrates as such do not possess therapeutic properties, it is the nitric oxide (NO) that is responsible for biological activity. In my opinion the organic rest which remains after NO is formed from a respective nitrate, should be at least little toxic. This condition is fulfilled for instance for nitroglycerin, because the organic rest (glycerin) is not a toxic substance. A similar situation would occur in the case of the glucose nitrate discussed here (**5**). Compound **1**, which would probably form after NO release from compound **5**, is harmless. And most importantly, because of great similarity of compound **5** to glucose, I would expect that this compound could be recognized by glucose transporters. In such a case the bioavailability of compound **5** would be very high.

Apart from performing a synthesis of compound **5**, I was also going to carry out XRD measurements for compounds **2-5**. (The XRD measurement for compound **1** was already published earlier.) Unfortunately, in spite of numerous attempts, I did not manage to obtain the appropriate single crystal of compound **5**. Moreover, compound **2** is a very hygroscopic compound, so the XRD measurement would be very difficult to perform, if possible at all. However, I was able to obtain high quality single crystals of compounds **3** and **4**, for which the XRD measurements were performed.

The only difference in molecular structure between compounds **5** and **1** as well as compounds **2** and **4** consists in, respectively, the presence and the absence of the nitrate group. So I decided to make use of crystal structures of compounds **1** and **4** by adding and removing the nitrate group, respectively. I treated the structures obtained in this way as starting geometries for further optimization by the DFT methods. Certainly, such an approach did not guarantee obtaining reliable structures of compounds **5** and **2**. In order to verify the newly obtained spatial structures I used ^{13}C CP/MAS NMR spectroscopy. I calculated the theoretical chemical shifts for the structures of compounds **5** and **2** and then compared them with the experimental shifts. R^2 for these correlations was equal to 0.984 and 0.998, respectively. In view of the above I assumed that the obtained structures are reliable. The

spatial structure of compound **5** is important because it notably expands structural information about this promising glucose derivative. Moreover, the molecular structure of compound **2** resembles that of a very important hydro- and organogelator, i.e. methyl 4,6-*O*-benzylidene-α-D-glucopyranoside. The gelating properties of this compound are due to a specific hydroxyl groups position at the C-2 and C-3 carbon atoms thanks to which cross-linkings can form in hydrogel structure. It turns out that in compound **2** there is the same positioning of the above-mentioned hydroxyl groups. So it is not surprising that compound **2**, similarly as methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, exhibits very high affinity for water.

H.8. J. Bukowicki, **T. Gubica***, Ł. Szeleszczuk. "Time-effective and reliable solid-state structure evaluation of selected peracetylated β-maltose derivatives by means of grid search, genetic algorithm and DFT calculations" *Tetrahedron* **2014**, *70*, 4008-4016.

In this work I aimed to improve the method of conformation analysis, as described in the article H.6., in a way that would maximally shorten the computation time and also in order to obtain better agreement between the theoretical and experimental (XRD) structure. To this aim I applied the force field with better parameters (MMFF94 instead of MM3) and I used different values of dielectric constants. Besides, I did not attempt to obtain full adiabatic maps, I only thoroughly analyzed the lower energy areas. As a result of these efforts, after a relatively short time of calculations, I obtained an almost ideal agreement between the theoretical conformation and XRD structure for peracetylated β-maltose (**1**).

I was also planning to obtain reliable conformations for the other two peracetylated β-maltose derivatives, methyl glycoside (**2**) and ethyl thioglycoside (**3**) for which however I did not manage to obtain appropriate single crystals. In order to confirm the reliability of the obtained structures I used the ^{13}C CP/MAS NMR spectroscopy. The correlations between the theoretical and experimental chemical shifts were even better than in the case of compound **1**. So I succeeded in replacing the XRD measurement for compounds **2** and **3** by theoretical methods.

3.3.3. Summing up

The molecular structure determination by XRD is now the best method to establish the spatial arrangement of the particular atoms. Data of molecular structure confirm unequivocally the chemical structure of the newly obtained compound. The knowledge of the most stable

conformation of a molecule is particularly important for molecular docking, i.e. the computations the aim of which is to determine the best molecular fit between ligand and receptor, the enzyme or other protein molecules. The role of docking in *in silico* pharmacology can hardly be overestimated at present. So the knowledge of appropriate molecular structures, including the most stable conformations, is highly desirable.

Among the compounds which I synthesized while working for my habilitation procedure, there are potential enzyme inhibitors and dietary components and also a very promising glucose nitrate. The knowledge of the structure and conformation of the molecules of these substances is necessary for preliminary assessment of their activities. Unfortunately, in several cases I encountered difficulties in performing the XRD analyses. However, I worked out a very effective methodology which enables replacement of XRD measurements by DFT calculations and ssNMR spectroscopy.

The scope of my investigations which are the subject of habilitation included: organic synthesis, physicochemical measurements and theoretical computations. My scientific achievement consisted in performing multi-step syntheses and obtaining 27 glycosides. Besides, I established in a novel way the structural properties of 31 glycosides. Another aim of my habilitation procedure was to show that the experimental methods (XRD, PXRD, ssNMR and DSC) as well as theoretical ones (molecular modeling and genetic algorithm) are complementary and allow one to obtain reliable structural information even in experimentally difficult cases. In the habilitation publications I studied the derivatives of saccharides. However, in my opinion the methods of investigations that I applied are not limited to sugars only and are of a more general character.

In my scientific achievement I presented a new approach in the field of structural studies. In the literature I have not found a research aim that would be posed in this way.

4. Discussion of the other scientific achievements

My Ph.D. dissertation was of interdisciplinary character, as I dealt with the synthesis of nitrophenyl derivatives of saccharides of a differentiated molecular complexity, and also performed structural and electrochemical investigations of the obtained compounds. The synthesized compounds were the derivatives of mono-, di- and oligosaccharides which were coupled with the isomers of nitrophenol and nitroaniline.

Although the majority of the compounds that I obtained were already described in the literature, yet in each case I attempted to improve the method of synthesis or to apply new

methods of the compounds preparation. It is worth adding here that during realization of my Ph.D. dissertation I obtained six new compounds, including three cyclodextrin derivatives.

After obtaining a considerable number of saccharide derivatives, I turned to performing structural studies of the obtained compounds. For twelve synthesized glycosides and glycosylamines the single-crystal X-ray diffraction measurements were performed and the solid-state NMR spectra were registered. The obtained results of structural studies allowed me to accurately interpret the results of electrochemical measurements that I performed for most of the obtained compounds.

As a result of electrochemical investigations performed by me (cyclic voltammetry and chronocoulometry) I was able to establish the effect of the structure of a non-electroactive fragment of the molecule on electrochemical properties of the whole electroactive molecule. The nitrophenyl group, which is present in each of the compounds I obtained, occurred to be a good electrochemical marker for assessment of the effect of the structure of a molecule on the electrochemical properties of that molecule.

In the course of realization of my Ph.D. dissertation I also undertook an additional research activity which I have been continuing until today. Namely, I have been engaged in investigations concerned with the effect of native and modified cyclodextrins on chemical reactions with participation of amino acids catalyzed by respective enzymes. These studies were not included in my Ph.D. dissertation, and are not included as part of the presented scientific achievement.

Both the native and the modified cyclodextrins are able to form inclusion complexes with amino acids. They can also form complexes with enzymatic amino acid decomposition products. Moreover, cyclodextrins also interact with the enzymes themselves, leading to an increase or a weakening of their catalytic activity. The determination of the effect of cyclodextrins on the course of enzymatic reactions can contribute, for example, to the development of new methods for the treatment of phenylketonuria. Phenylketonuria is a rare inherited disorder for which no effective drugs are known. The only available method of treatment is a special diet, low in phenylalanine. However, such a diet is very uncomfortable for patients, hence alternative methods of treatment are being searched for. It was reported in the literature [R.M. Shah, A.P. D'mello. *Int. J. Pharm.* 2007, *331*, 107-115] that the enzyme phenylalanine ammonia lyase (PAL), when reacted with selected cyclodextrins, is much more resistant to hydrolysis during oral dosage. This enzyme decomposes phenylalanine to cinnamic acid, which is much less toxic than the phenylpirogronic acid which is also formed from phenylalanine but in the organisms of ill people. Hence the oral administration of the

thus prepared PAL enzyme (which is more resistant to decomposition than the same enzyme in its native form) can hopefully result in better comfort for people suffering from phenylketonuria.

In my investigations I found out that the promising cyclodextrins to be applied in phenylketonuria are native β-cyclodextrin and hexakis(2,3-di-*O*-methyl)-α-cyclodextrin. In the presence of those two cyclodextrins I observed an increased activity of the PAL enzyme.

4.1. List of articles published before obtaining Ph.D. degree, with estimation of the habilitant's individual contribution

1. A. Temeriusz*, **T. Gubica**, P. Rogowska, K. Paradowska, M.K. Cyrański. "Crystal structure and solid state ^{13}C NMR analysis of nitrophenyl 2,3,4,6-tetra-*O*-acetyl-β-D-gluco- and D-galactopyranosides" *Carbohydrate Research* **2005**, *340*, 1175-1184. **IF**$_{2005}$ **1.669**

My contribution to this publication consisted in:
- performing organic synthesis
- preparing full analytical characteristics of the obtained compounds
- editing of part of the manuscript for publication

I estimate my individual contribution to the authorship at 45%.

2. A. Temeriusz*, **T. Gubica**, P. Rogowska, K. Paradowska, M.K. Cyrański. "Crystal structure and solid state ^{13}C NMR analysis of *N*-*p*-nitrophenyl-α-D-ribopyranosylamine, *N*-*p*-nitrophenyl-α-D-xylopyranosylamine, and solid state ^{13}C NMR analysis of *N*-*p*-nitrophenyl-2,3,4-tri-*O*-acetyl-β-D-lyxopyranosylamine and *N*-*p*-nitrophenyl-2,3,4-tri-*O*-acetyl-α-L-arabinopyranosylamine" *Carbohydrate Research* **2005**, *340*, 2645-2653. **IF**$_{2005}$ **1.669**

My contribution to this publication consisted in:
- performing organic synthesis
- preparing full analytical characteristics of the obtained compounds
- editing of part of the manuscript for publication

I estimate my individual contribution to the authorship at 45%.

3. **T. Gubica**, E. Boroda, A. Temeriusz*, M. Kańska. "Effects of Native and Permethylated Cyclodextrins on the Catalytic Activity of L-Tryptophan Indole Lyase" *Journal of Inclusion Phenomena and Macrocyclic Chemistry* **2006**, *54*, 283-288. **IF**$_{2006}$ **1.251**

My contribution to this publication consisted in:
- participation in determining the research aim and planning the investigations
- performing organic synthesis
- participation in performing the measurements of enzymatic kinetics
- interpretation of the results
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

4. A. Temeriusz*, **T. Gubica**, P. Rogowska, K. Paradowska, M.K. Cyrański. "Crystal structure and solid-state ^{13}C NMR analysis of *N*-*o*-, *N*-*m*- and *N*-*p*-nitrophenyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamines, and their *N*-acetyl derivatives" *Carbohydrate Research* **2006**, *341*, 2581-2590. **IF**$_{2006}$ **1.703**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations
- performing organic synthesis
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

5. **T. Gubica**, J. Stroka, A. Temeriusz*. "Synthesis and electrochemical study of nitrophenyl derivatives of β-cyclodextrin" *Journal of Physical Organic Chemistry* **2007**, *20*, 375-383. **IF**$_{2007}$ **1.594**

My contribution to this publication consisted in:
- participation in determining the research aim and planning the investigations
- performing organic synthesis
- performing electrochemical investigations
- editing of part of the manuscript for publication

I estimate my individual contribution to the authorship at 70%.

4.2. List of articles published after obtaining Ph.D. degree which are not the subject of habilitation procedure, with estimation of the habilitant's individual contribution

1. **T. Gubica**, E. Winnicka, A. Temeriusz*, M. Kańska. "The influence of selected *O*-alkyl derivatives of cyclodextrins on the enzymatic decomposition of L-tryptophan by L-tryptophan indole-lyase" *Carbohydrate Research* **2009**, *344*, 304-310. **IF**$_{2009}$ **2.025**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations
- performing organic synthesis
- participation in performing the measurements of enzyme kinetics
- interpretation of the results
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

2. **T. Gubica**, A. Temeriusz*, P. Pawłowski, J. Stroka. "Molecular structure of nitrophenyl *O*-glycosides in relation to their redox potentials" *Journal of Physical Organic Chemistry* **2010**, *23*, 853-858. **IF**$_{2010}$ **1.478**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations
- performing organic synthesis
- participation in performing electrochemical investigations
- interpretation of the results
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 75%.

3. **T. Gubica***, A. Pełka, K. Pałka, A. Temeriusz, M. Kańska. "The influence of cyclomaltooligosaccharides (cyclodextrins) on the enzymatic decomposition of L-phenyl-alanine catalyzed by phenylalanine ammonia-lyase" *Carbohydrate Research* **2011**, *346*, 1855-1859. **IF**$_{2011}$ **2.332**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations

- participation in performing organic synthesis
- participation in performing the measurements of enzyme kinetics
- interpretation of the results
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 70%.

4. **T. Gubica***, J. Stroka, A. Temeriusz, M. Kańska. "Cyclic voltammetry of nitrophenyl *N*-glycosides on mercury electrode" *Journal of Physical Organic Chemistry* **2011**, *24*, 1229-1234. **IF**$_{2011}$ **1.963**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations
- performing organic synthesis
- performing electrochemical investigations
- participation in interpretation of the results
- editing of the whole manuscript for publication

I estimate my individual contribution to the authorship at 80%.

5. **T. Gubica***, M. Mazur, Ł. Szeleszczuk, A. Temeriusz, M. Kańska. "The influence of native and methylated β-cyclodextrin on the electroreduction of nitrophenyl glycosides" *Journal of Electroanalytical Chemistry* **2013**, *699*, 40-47. **IF**$_{2013}$ **2.871**

My contribution to this publication consisted in:
- determining the research aim and planning the investigations
- performing organic synthesis
- performing electrochemical investigations
- participation in interpretation of the results
- editing of part of the manuscript for publication

I estimate my individual contribution to the authorship at 60%.

5. Active participation in scientific conferences

1. XLVI Convention of PTChem and SITPChem, Lublin **2003**
   P. Rogowska, **T. Gubica**, M.K. Cyrański, T.M. Krygowski, A. Temeriusz, K. Paradowska. „Synteza i badania strukturalne *N*-glikopiranozydów" [Synthesis and structural studies of *N*-glycopyranosides] *poster*
2. International Conference on Electrode Processes, Szczyrk **2004**
   T. Gubica, P. Pawłowski, J. Stroka, A. Temeriusz. "Electrochemical Study of Nitrophenyl *O*-Glycopyranosides Reduction on the Mercury Electrode" *poster*
3. 13th European Carbohydrate Symposium, Bratislava, Slovakia **2005**
   T. Gubica, E. Boroda, A. Temeriusz, M. Kańska. "Effects of Native and Permethylated Cyclodextrins on the Catalytic Activity of L-Tryptophan Indole Lyase" *poster*
4. 13th International Cyclodextrin Symposium, Torino, Italy **2006**
   T. Gubica, J. Stroka, A. Temeriusz. "Synthesis and Study of Electrochemical Behaviour of New Nitrophenyl Derivatives of β-Cyclodextrin" *poster*
5. 3rd ERA Chemistry "Flash" Conference, Killarney, Ireland **2008**
   E. Winnicka, **T. Gubica**, M. Kańska, A. Temeriusz. "The Influence of Selected Alkyl Derivatives of Cyclodextrins on the Catalytic Activity of L-Tryptophan Indole Lyase" *poster*
6. 19th IUPAC Conference on Physical Organic Chemistry, Santiago de Compostela, Spain **2008**
   T. Gubica, P. Pawłowski, J. Stroka, A. Temeriusz, Z. Galus. "The Influence of Molecular Structure of Nitrophenyl *O*-Glycopyranosides on their Electrochemical Properties" *oral report*
7. 51. Convention of PTChem and SITPChem, Opole **2008**
   T. Gubica, J. Stroka, A. Temeriusz. „Woltamperometria cykliczna na elektrodzie rtęciowej (WKER) nitrofenylowych glikozyloamin" [Cyclic voltammetry on mercury electrode of nitrophenyl glycosylamines] *oral report*
8. 10th Latin American Conference on Physical Organic Chemistry, Florianópolis, Brazil **2009**
   T. Gubica, A. Temeriusz, K. Paradowska, A. Ostrowski, P. Klimentowska, M.K. Cyrański. "Structural analysis of *p*-nitrophenyl glycosides" *lecture*
9. 26th International Carbohydrate Symposium, Madrid, Spain **2012**

T. Gubica, A. Temeriusz, D.K. Stępień, J. Bukowicki, A. Ostrowski, D.M. Pisklak, M.K. Cyrański. "Comprehensive structural analyses of disaccharides with unusual linkage" *oral report*

10. 17th European Carbohydrate Symposium, Tel-Aviv, Israel **2013**
    T. Gubica, M. Mazur, Ł. Szeleszczuk, A. Temeriusz, M. Kańska. "The influence of native and methylated β-cyclodextrin on the electroreduction of nitrophenyl glycosides" *oral report*
11. 27th International Carbohydrate Symposium, Bangalore, India **2014**
    T. Gubica, Ł. Szeleszczuk, D.M. Pisklak, D.K. Stępień, M.K. Cyrański. "Reliable evaluation of molecular structure of carbohydrates by CP/MAS NMR spectroscopy and DFT optimization in the absence of crystallographic data" *oral report*

6. Cooperation with scientific institutions

1. The team of Prof. Dr. hab. Michał K. Cyrański. Laboratory of Crystallochemistry, Faculty of Chemistry, University of Warsaw. Single-crystal X-ray diffraction measurements.
2. The team of Prof. Dr. hab. Marianna Kańska. Laboratory of Chemistry of Biomolecules, Faculty of Chemistry, University of Warsaw. The investigations on catalytic activity of enzymes in the presence of cyclodextrins.
3. Dr. hab. Maciej Mazur. Laboratory of Electrochemistry, Faculty of Chemistry, University of Warsaw. Electrochemical measurements.
4. Dr. Andrzej Ostrowski. Chemistry Department, Warsaw Technical University. Powder X-ray diffraction measurements.

7. Obtained research grants

1. Promotor grant from KBN (Committee for Scientific Research) (1 T09A 001 30) „Synteza i badania elektrochemiczne nitrofenylowych pochodnych sacharydów w obecności natywnej i permetylowanej β-cyklodekstryny" [The synthesis and electrochemical investigations of nitrophenyl derivatives of saccharides in the presence of native and permethylated β-cyclodextrin]. The granting period: 18 months (2006-2007). Grant manager: Prof. Dr. hab. Andrzej Temeriusz. In this grant I performed the role of the chief scientist.
2. Research grant from the Medical University of Warsaw entitled "Young Scientists" (FW28/PM1/11) „Synteza i kompleksowe badania strukturalne pochodnych sacharydów

stosowanych w enzymologii" [The synthesis and complex structural studies of saccharide derivatives applied in enzymology]. The granting period: 2 years (2011-2012). In this grant I performed the role of the manager and chief scientist.

8. Reviews of publications in international and national journals

In the period from 2009 until the present time I reviewed: 7 original articles, 5 review articles and 2 academic textbooks in the following journals: *Carbohydrate Research* (IF_{2013} 1.966) (3×), *Biuletyn Wydziału Farmaceutycznego WUM* [Bulletin of Faculty of Pharmacy of the Medical University of Warsaw] (4×), *Przemysł Chemiczny* [Chemical Industry] (IF_{2013} 0.367) (2×), *Trends in Food Science and Technology* (IF_{2013} 4.651) (1×), *Monatshefte für Chemie* (IF_{2013} 1.347) (1×), *Current Pharmaceutical Analysis* (IF_{2013} 0.771) (1×), *Molbank* (1×) and *Nutrition and Dietary Supplements* (1×).

9. Didactic achievements

9.1. Managing and supervising of Master (M.Sc.) theses

1. „Synteza pochodnych 6-monoamino-β-cyklodekstryny" [Synthesis of the derivatives of 6-monoamine β-cyclodextrins] A. Bartodziej (academic year 2003/2004)
2. „Elektrochemiczne właściwości nitrofenyloglikopiranozydów" [Electrochemical properties of nitrophenylglycopyranosides] P. Pawłowski (academic year 2003/2004)
3 „Badanie reakcji elektrodowych nitrofenyloglikopiranozydów metodami elektrochemicznymi" [A study of electrode reactions of nitrophenylglycopyranosides by electrochemical methods] M. Stasiewicz (academic year 2004/2005)
4. „Wpływ *per*(2,3,6-tri-*O*-2'-metoksyetylo)-α-cyklodekstryny na katalityczną aktywność L-trypto-fan indol liazy" [The effect of *per*(2,3,6-tri-*O*-2'-mehoxyethyl)-α-cyclodextrin on catalytic activity of L-tryptophan indol lyase] M. Rackiewicz (academic year 2005/2006)
5. „Oddziaływania pomiędzy modyfikowanymi cyklodekstrynami a L-tryptofan indol liazą" A. Minkowska [Interactions between modified cyclodextrins and L-tryptophan indol lyase] (academic year 2006/2007)
6. „Zmiana aktywności L-tryptofan indol liazy w obecności modyfikowanych cyklodekstryn" [The change in activity of L-tryptophan indol lyase in the presence of modified cyclodextrins] K. Ferszt (academic year 2006/2007)

7. „Wpływ pochodnych cyklodekstryn na reologiczne właściwości mikro- i nanoproszków ceramicznych" [The effect of the derivatives of cyclodextrins on reological properties of ceramic micro- and nanopowders] I. Żeglińska (academic year 2007/2008)
8. „Wpływ natywnych i selektywnie *O*-metylowanych pochodnych cyklodekstryn na aktywność katalityczną enzymu liazy fenyloalaninowej" [The effect of native and selectively *O*-methylated derivatives of cyclodextrins on catalytic activity of phenylalanine lyase enzyme] A. Pełka (academic year 2009/2010)
9. „Synteza i rentgenowska analiza strukturalna wybranych pochodnych 2,3,4-tri-*O*-acetylo-β-D-ksylopiranozyloaminy oraz 2,3,4-tri-*O*-acetylo-β-D-ksylopiranozydu" [The synthesis and X-ray structural analysis of selected derivatives of 2,3,4-tri-*O*-acetyl-β-D-xylopyranosylamine and 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside] E. Głowacka (academic year 2011/2012)
10. „Analiza konformacyjna pochodnych maltozy za pomocą algorytmu genetycznego i spektroskopii NMR dla ciała stałego" [Conformational analysis of maltose derivatives using genetic algorithm and solid-state NMR spectroscopy] M. Mądra (academic year 2012/2013)

9.2. Managing and supervising of Bachelor (B.Sc.) theses

1. „Próby syntezy i charakterystyki kompleksów inkluzyjnych L-fenyloalaniny z cyklodekstrynami" [Attempts at the synthesis and characteristics of inclusion complexes of L-phenylalanine with cyclodextrins] K. Szubstarska (academic year 2009/2010)
2. „Próby syntezy i charakterystyki kompleksów inkluzyjnych L-tryptofanu z cyklodekstrynami" [Attempts at the synthesis and characteristics of inclusion complexes of L-tryptophan with cyclodextrins] K. Walicka (academic year 2009/2010)
3. „Próby syntezy i charakterystyki kompleksów inkluzyjnych L-tyrozyny z cyklodekstrynami" [Attempts at the synthesis and characteristics of inclusion complexes of L-tyrosine with cyclodextrins] M. Wajk (academic year 2009/2010)

9.3. Conducting didactic classes

I conducted the following didactic classes at the Faculty of Chemistry, University of Warsaw:
1. Laboratory classes in Organic Chemistry I (academic year 2002/2003)
2. Laboratory classes in Organic Synthesis (academic year 2003/2004)
3. Proseminar of Foundations of Organic Chemistry (academic year 2004/2005)

4. Laboratory classes in Identification of Organic Compounds (from academic year 2007/2008 to 2009/2010)
5. Proseminar of Identification of Organic Compounds (from academic year 2007/2008 to 2009/2010)
6. Laboratory classes in Organic Chemistry taught to students of Biology Department, University of Warsaw (academic year 2007/2008)

I also conducted the following didactic classes at the Faculty of Pharmacy, Medical University of Warsaw:
1. Laboratory classes in Physical Chemistry (field of study: pharmacy) (from the academic year 2010/2011 until today; subject manager from the academic year 2011/2012 until today)
2. Laboratory classes in Physical Chemistry (field of study: medical analysis) (academic year 2010/2011 and from 2013/2014 until today)
3. Calculation classes in Physical Chemistry (field of study: pharmacy) (academic year 2014/2015)

9.4. Authorship of didactic materials

I am the editor and co-author of a course book for students of pharmacy and medical analysis: **T. Gubica**, K. Gulik, M.K. Jamróz, S. Kaźmierski, K. Łastawska, K. Paradowska, D.M. Pisklak, Ł. Szeleszczuk, S. Warycha, K. Zawada, A. Zimniak: Ćwiczenia laboratoryjne z chemii fizycznej.[Laboratory classes in physical chemistry], 5th edition. Warszawa: Oficyna Wydawnicza Warszawskiego Uniwersytetu Medycznego, 2012, ISBN-978-83-7637-212-9.

10. Achievements in popularization of science

1. I prepared a demonstration of interesting chemical experiments at the Laboratory of Teaching Chemistry (Faculty of Chemistry, University of Warsaw) for secondary school students (2001).
2. I prepared a demonstration of chemical experiments during the 5th Festival of Science organized at Faculty of Chemistry, University of Warsaw (2001)
3. I conducted the workshops for talented young people within the National Children's Fund (Faculty of Chemistry, University of Warsaw, 2010).

4. I delivered a lecture entitled „Wykorzystanie spektroskopii NMR do badań strukturalnych pochodnych sacharydów" [The use of NMR spectroscopy for structural studies of the derivatives of saccharides] for the Students' Scientific Circle "Free Radical" at Faculty of Pharmacy of the Medical University of Warsaw (2012).
5. I delivered a lecture entitled „Mariaż cyklodekstryn z amoniakoliazą fenyloalaninową nadzieją dla chorych na fenyloketonurię" [The union of cyclodextrins with phenylalanine ammonia lyase as new hope for people suffering from phenylketonuria] during the seminar for Warsaw school teachers "Co wspomaga nasze zdrowie, czyli o suplementach diety" [What improves our health – about diet supplements] organized at Faculty of Pharmacy of the Medical University of Warsaw (2014).

11. Summing up of scientific achievements

Number of all published articles: **18**
Number of articles published after obtaining Ph.D. degree: **13**
(I was the first author in 13 articles, the corresponding author in 9 articles)
The total impact factor IF (according to the year of publishing): **35.108**
Number of all/independent citations: **57/32** (according to Web of Science®)
H-Index: **5** (according to Web of Science®)