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# SUMMARY OF PROFESSIONAL ACCOMPLISHMENTS SUBMITTED FOR THE HABILITATION PROCEDURE

**„Harnessing amino acids as molecular platforms in the design of ion pair receptors"**

Warsaw, 22.08.2016

## Table of contents

1. Name and Surname: **Jan Romański**

2. Scientific diploma and degrees:

**Ph.D. in chemistry** – cum laude 2006r., University of Warsaw, Faculty of Chemistry, thesis entitled: *„Synthesis of the heterocyclic compounds using enantio- and diastereoselective 1,3-dipolar cycloaddition reaction"*, supervisor: prof. dr hab. Janusz Jurczak.

**M.Sc.** – 2001r., University of Warsaw, Faculty of Chemistry, thesis entitled: *„Chiral imines – synthesis and properties"*, supervisor: prof. dr hab. Janusz Jurczak.

3. Employment:

**adjunct**, University of Warsaw, Faculty of Chemistry, February 2007 r. – presently

**assistant,** University of Warsaw, Faculty of Chemistry, June 2006 – February 2007.

4. Indication of achievement resulting from Article 16 Section 2 of the Act on University Degrees and the University Title and on University Degrees and the University Title in the Field of Fine Arts of March 14, 2003 (Journal of Laws No. 65, item 595, with later amendments):

a) Title of scientific achievement

**Harnessing amino acids as molecular platforms in the design of ion pair receptors**

b) List of publications constituting the scientific achievement

**[H1] J. Romański**, P. Piątek;

"Tuning the binding properties of a new heteroditopic salt receptor through embedding in a polymeric system",

**Chemical Communications**, 2012, 48, 11346-11348, IF=6.567

**[H2] J. Romański**, B. Trzaskowski, P. Piątek;

"Selective NaNO2 recognition by a simple heteroditopic salt receptor based on L-ornithine molecular scaffold",

**Dalton Transactions,** 2013, 42, 15271-15274, IF=4.177

**[H3]** P. Piątek, M. Karbarz, J. **Romański**;

"Boosting the salt recognition abilities of L-ornithine based multitopic molecular receptors by harnessing a double cooperative effect",

**Dalton Transactions,** 2014, 43, 8515-8522, IF=4.177

**[H4]** P. Piątek, S. Zdanowski, **J. Romański**;

"Cooperative ion pair recognition by multitopic L-ornithine based salt receptors",

**New Journal of Chemistry,** 2015, 39, 2090-2095, IF=3.277

**[H5]** S. Zdanowski, **J. Romański**;

"Ion pair binding by an L-tyrosine-based polymerizable molecular receptor",

**New Journal of Chemistry**, 2015, 39, 6216-6222, IF=3.277

**[H6]** M. Karbarz, **J. Romański**;

"Dual Sensing by Simple Heteroditopic Salt Receptors Containing an Anthraquinone Unit",

**Inorganic Chemistry,** 2016, 55, 3616-3623, IF=4.82

**[H7]** S. Zdanowski, P. Piątek, **J. Romański**;

"An ion pair receptor facilitating extraction of chloride salt from aqueous to organic phase",

**New Journal of Chemistry,** 2016, 40, 7190-7196, IF=3.277

**[H8]** K. Ziach, M. Karbarz, **J. Romański**;

"Cooperative binding and extraction of sodium nitrite by a ditopic receptor incorporated into a polymeric resin",

**Dalton Transactions,** 2016, 45, 11639-11643, IF=4.177

**[H9]** P. Cios, **J. Romański**;

"Enantioselective recognition of sodium carboxylates by an 1,8-diaminoanthracene based ion pair receptor containing amino acid units",

**Tetrahedron Letters,** 2016, 57, 3866-3869, IF=2.347

**Sum of IF (publications H1-H9)= 36.096**

**Average IF 4.011** (the scientometric data taken from Web of Science at 18th of July 2016)

a) Description of the scientific goal and the results described in the publications constituting scientific achievement:

Studying the abilities of molecular receptors to form complexes with ions is one of the main trends of research in contemporary supramolecular chemistry. Taking advantage of noncovalent interactions, this line of work strives to achieve strong and selective binding between receptors and ions. However, while the study of cation complexation is quite well established, the design of receptors capable effectively complexing anions still poses a serious problem. Anions are characterized by varied geometry and more diffused charge than cations, making receptors capable of complexing them is much more difficult to design. When we further consider the optical properties (chirality) of anions, their enantioselective complexation becomes even more difficult.

To resolve these problems, many research efforts strive to design monotopic receptors capable of interacting with cations or anions in particular ways. Such laboratory studies make use of the respective salts containing charge diffuse counterions, which are treated as having negligible influence on the binding of ions by the receptor (tetrabutylammonium or hexafluorophosphate salts). In nature, such salts do not occur, and cations and anions are generally strongly bound with their counterions; monotopic receptors dedicated to binding cations or anions are therefore generally ineffective for such ion pairs, having to compete with the counterion. This problem may be resolved through the design of ditopic receptors, capable of binding cations and anions simultaneously.

Unfortunately, the simple combination of effective cation and anions receptors does not always yield effective ion pair receptors. In designing such receptors, it is very important to ensure the proper positioning of the binding domains. If they are properly attached to the receptor platform, the binding of one of the ions by the receptor may facilitate the binding of the corresponding counterion (e.g. by changing the conformation). In particular, this property may be utilized in the case of complexing weakly interacting ions ($Br^-$, $NO_3^-$, $ClO_4^-$ ). The receptor's binding of ion pairs may proceed in several ways. One way is for the ion pair to be bound to the receptor while its constituent ions are not in direct contact with one another. The most desired property for such receptors, however, is the ability to bind a salt in the form of a contact ion pair. In such situations, there is a very strong electrostatic interaction between the cation and anion, which additionally stabilizes the complex of the receptor and salt.

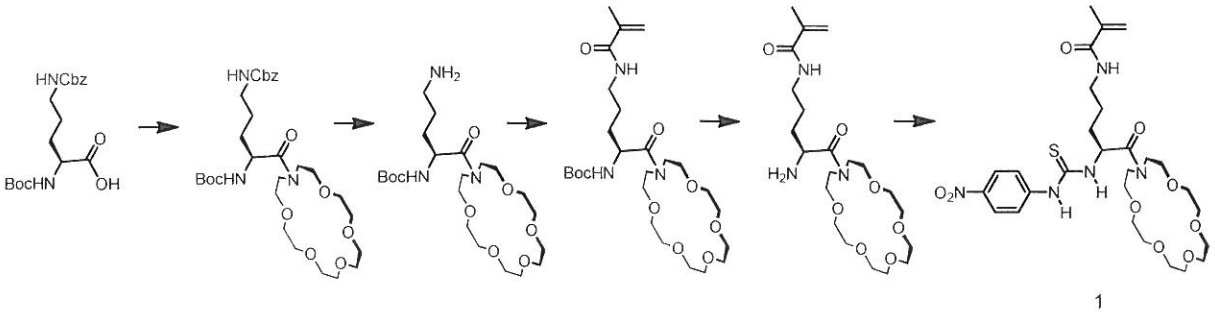
Receptors with such properties are frequently macrocyclic compounds obtained by combining domains capable of binding both cations and anions. However, obtaining such compounds is very difficult because macrocyclic reactions are characterized by low efficiency. Macrocyclic receptors are usually structures not equipped with functional groups that might be utilized for further modification. An alternative to such receptors is offered by open-chain ion-pair receptors. The proper spatial arrangement of binding domains on properly chosen molecular platforms may lead to effective salt receptors. Such receptors are easier to synthesize and more amenable to further modification with the aim of introducing new binding domains, adding additional functional groups (facilitating complexation studies, such as chromophores or fluorophores), or incorporating receptors into polymer networks.

Amino acids are one type of unit frequently utilized in designing monotopic, chiral receptors. They have been used to obtain a range of open-chain or macrocyclic receptors capable of interacting with anions or cations, utilizing amide or carbonyl groups. I also decided to use amino acids in designing receptors, but used them as molecular platforms for synthesizing receptors capable of simultaneously binding cations and anions. To this end, I introduced the respective binding domains to the amino acids. In my research I used simple amino acids as well as ones possessing additional functional groups (e.g. basic α-amino acids). The use of basic amino acids made it easier for me to introduce additional binding domains, as well as to incorporate the receptors into polymer networks.

My research can be divided into three main lines of work, differentiated in terms of the receptor platform forming the skeleton of the amino acid: the first strand deals with ion pair receptors derived from L-ornithine, the second involves receptors derived from other α-amino acids (L-tyrosine and 4-nitro-L-phenylalanine), whereas the third deals with receptors based on an amino benzoic acid skeleton. Each of these I will now describe in turn.

**Ion-pair receptors – L-ornithine derivatives**

My research in this regard began with work on designing and obtaining a new molecular receptor using the amino acid L-ornithine, capable of simultaneous binding of cations and anions. This work was inspired by earlier studies in which I was involved, dealing with a different topic, namely the modification of polymer materials with amino acid units. In that previous work, I obtained L-ornithine derivatives modified with acrylamide or metacrylamide groups, and next showed that such derivatives can be successfully used as monomers in free radical polymerization reactions. In studying ion pair receptors, I decided to modify this structure and to utilize the L-ornithine platform to introduce additional functions, namely domains capable of interacting with cations and anions. I resolved to use a receptor designed in this way to synthesize a new functional polymer material capable of salt extraction (Scheme 1). The findings of this research were reported in publication **H1**.




**Scheme 1.** Synthesis of receptor **1**

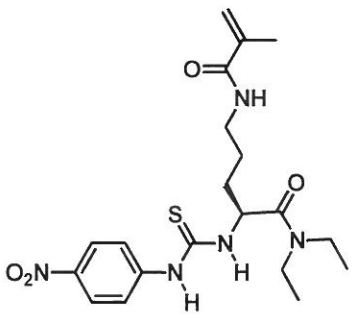
I began synthesis of receptor **1** from an L-ornithine derivative with selectively protected amino groups. First I introduced a crown ether unit into the structure, treating this functional group as a cation-binding domain. I attached 1-aza-18-crown-6 to the amino acid platform *via* the amide bond, carrying out the reaction in the presence of dicyclohexylcarbodiimide. Next, after deprotecting the δ-amine group, I carried out an acylation reaction using methacrylic

anhydride. The final stage in the receptor's synthesis involved deprotecting the α-amine group and reacting it with 4-nitrophenyl isothiocyanate. This reaction led to the introduction of a thiourea unit intro the receptor structure, which I decided to use for anion binding. This group was additionally modified with a chromophore in order to facilitate the study of anion interactions using UV-Vis. However, I carried out complexation studies using the technique of $^1$HNMR titration, so as to be able to identify the association constants for complexes with cations, anions, and ion pairs. I performed those studies in acetonitrile, utilizing the respective tetrabutylammonium salts for studying anions, hexafluorophosphate salts for studying cations, and mixtures thereof for studying ion pairs. I first checked the receptor's affinity for cations by carrying out titration using sodium and potassium hexafluorophosphates. These studies showed that attaching the crown ether unit to the receptor via the amide bond leads to stronger binding of sodium cations than potassium cations (Ka= 6040 $M^{-1}$ for complexation with sodium cation and Ka= 195 $M^{-1}$ with potassium cations).

**Table 1.** Association constants for complexes of receptor **1** ($K_a$ [$M^{-1}$])

| | **$TBA^+$** | **$Na^+$** |
|---|---|---|
| $AcO^-$ | >50 000 | 1940 |
| $Cl^-$ | 13 990 | 4520 |
| $NO_3^-$ | 160 | 410 |

Next I studied the complexation properties of receptor 1 with respect to selected anions (Table 1), finding that its binds nitrate ions weakly, chloride anions more strongly, and acetate anions most strongly. Acetate anion is bound so strongly that identifying the association constant by means of $^1$H NMR titration proved impossible. A series of titrations carried out in the presence of one equivalent of sodium cations (added as $NaPF_6$) for chloride and acetate showed that those anions are bound much more weakly. On this basis we can conclude that for these structures, the formation of ion pairs outside the receptor is privileged (i.e. the cation competes with the receptor in interacting with the anion). Unlike for chloride and acetate, in the case of nitrates I observed a higher association constant for complexes formed when titration was carried out in the presence of sodium cation.

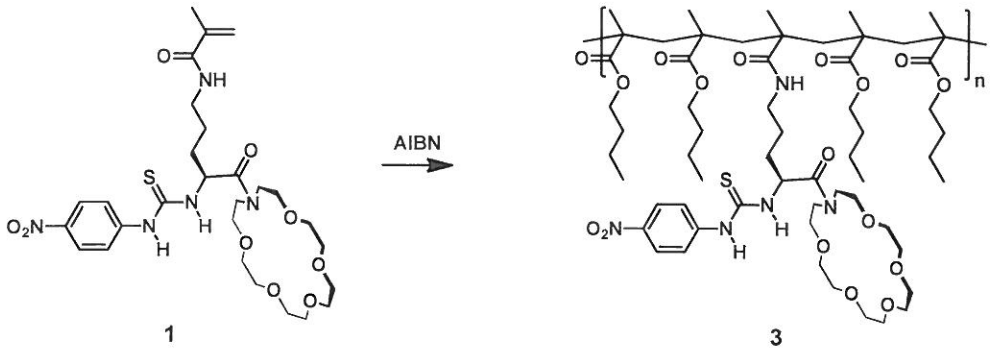



2

**Figure 1.** The structure of receptor **2**

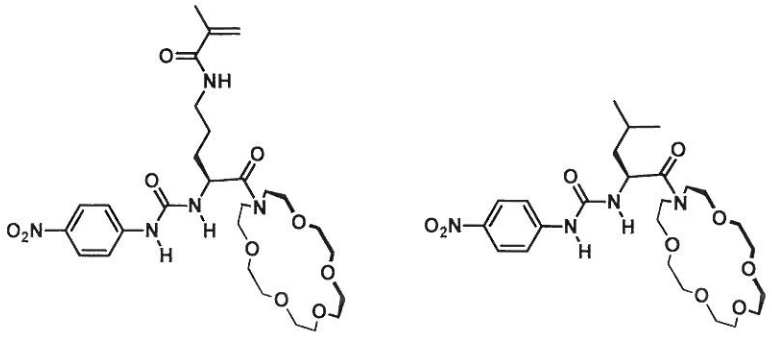
To rule out the possibility that the crown ether unit might be playing a key role in reinforcing the nitrate anion bonding, I synthesized anion receptor **2**, analogous to receptor **1** but lacking the cation binding domain (Figure 1). Comparative studies showed a weakening, rather than strengthening, of nitrate anion bonding in the case of the monotopic receptor **2** in the presence of sodium cations ($K_{NO3^-}$= 95 $M^{-1}$ in the presence of sodium cations). Thereby I demonstrated that the presence of the cation binding domain in receptor **1** is responsible for reinforcing the receptor's interaction with ion pairs, as compared to anion binding.

I designed receptor **1** so that, apart from the groups binding cations and anions, it could also be utilized as a monomer in polymerization reactions. As such, I decided to obtain a functional copolymer chain containing units of the receptor. Unfortunately, copolymerization carried out using methyl methacrylate yielded only polymethyl methacrylate, with the receptor not being incorporated into the chain this reaction, instead remaining in the solution. I resolved this problem by changing the comonomer to *n*-butyl methacrylate, thereby obtaining a functional copolymer under the conditions of free-radical polymerization (Scheme 2). I identified its molecular mass, 96.1 KDa (polydispersity index PDI=2.8) by means of gel chromatography. I ascertained the receptor content in the polymer (8%) using $^1$HNMR analysis and confirmed it using combustion analysis, taking the sulfur content into account.




**Scheme 2.** Synthesis of polymer **3**

I used chloroform solutions of receptor **1** and copolymer **3** to examine their ability to extract sodium nitrate from aqueous media. To evaluate the efficiency of salt extraction from aqueous phase to organic phase, I measured the sodium cation content in the organic phase using the atomic emission spectroscopy technique. This research confirmed that the use of the copolymer allowed for the extraction of $NaNO_2$ from the aqueous to organic phase with efficiency of 44%, whereas receptor **1** is ineffective under the same conditions (extraction efficiency of 2.9%). Thereby I proved that the complex-forming properties of receptor **1** may be modified by incorporation into a polymer chain.



4 5

**Figure 2.** Structures of receptors **4** and **5**

The next step in my research, described in publication **H2**, involved synthesizing and studying the complexation properties of receptor **4**, which is the urea analog to receptor **1** (Figure 2). According to reports in the literature, such a modification should represent a step backwards, as we should expect weaker interaction with anions. This is due to the lower acidity of the urea protons as compared to thiourea protons (pKa = 21.1 and 26.9 for thiourea and urea, respectively, in DMSO, pKa = 13.4 and 18.7 for diphenylurea and diphenylthiourea, respectively, in DMSO). However, my complexation studies of receptor **4** with selected ions showed that in this case the above property is only half true (Table 2). Comparative studies with receptor **1** confirmed receptor **4**'s much lower affinity for all the anions previously studied. For instance, nitrate anions were bound by receptor **1** with the association constant Ka=160 $M^{-1}$, whereas receptor **4** interacts with the same anions with the association constant Ka=110 $M^{-1}$.

**Table 2.** Association constants for complexes of receptor **4** ($K_a$ [$M^{-1}$])

| | $TBA^+$ | $Na^+$ | $K_{Na}/K_{TBA}$ |
|---|---|---|---|
| $AcO^-$ | 10 700 | 2 340 | 0.22 |
| $Cl^-$ | 2 040 | 930 | 0.46 |
| $Br^-$ | 320 | 3 310 | 10.34 |
| $NO_2^-$ | 1 180 | 7 590 | 6.43 |
| $NO_3^-$ | 110 | 850 | 7.73 |
| $HSO_4^-$ | 490 | 690 | 1.41 |

I observed a completely different situation when I carried out complexation studies of receptor **4** in the presence of sodium cations. Under such conditions, receptor **4** is able to interact with anions much stronger than its thiourea analog **1**. For instance, nitrate anions were bound by receptor **1** in the presence of sodium cations with the association constant Ka=410 $M^{-1}$, whereas receptor **4** interacts with sodium nitrate with the association constant

Ka=850 $M^{-1}$, more than two times more strongly than receptor **1**. I observed reinforced anion binding in the presence of sodium cations also for anions $Br^-$, $NO_2^-$ and $HSO_4^-$. On the other hand, strong complexes of receptor **4** with acetate anions and chloride anions undergo significant weakening when sodium cations are in the solution. As a result of these changes, the presence of sodium cation significantly affects the selectivity of receptor **4** by strengthening and weakening anions. I showed that receptor **4** binds acetate anions most strongly, whereas in the presence of sodium anions the most strongly bound anion is nitrite (Figure 3).

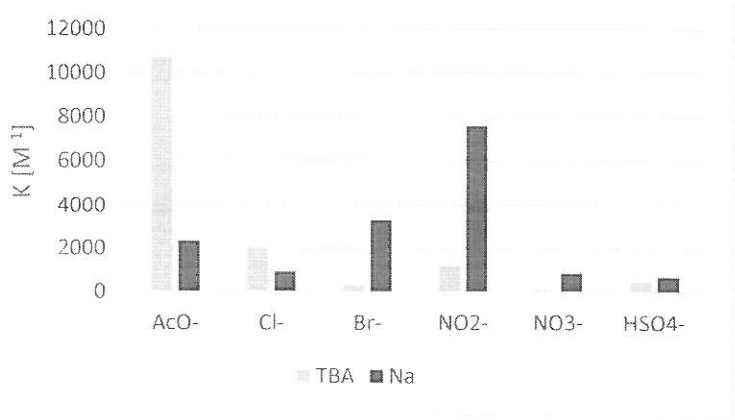



**Figure 3.** Change in selectivity of receptor **4** caused by the addition of sodium cations

To explain the difference in the interaction of sodium salts with receptors **1** and **4,** I decided to ascertain the stability constant for receptor **4** complexing with sodium cation. Applying the $^1H$ NMR titration technique, I showed that receptor **4** binds sodium cation with a very high association constant (>50000 M-1). Greater affinity for sodium cation in the case of the urea analog of the receptor is caused by the interaction of the cation with the crown ether unit and with the lone electron pairs of the oxygen atom of the urea group. This complexation manifests itself in shifts in the $^1$HNMR spectral position of signals belonging to the crown ether protons and protons of the urea group, observed during titration of receptor **4** with sodium hexafluorophosphate. Receptor **4**'s greater affinity for sodium cations, as compared to receptor **1** (thiourea analog), which complexes sodium anions with association constant 6460 $M^{-1}$, may be explained in terms of the theory of hard and soft bases and acids: a hard acid (sodium cation) interacts more strongly with a hard base (the oxygen of the urea group).

I also resolved to check whether the methacrylamide group present in the receptor structure, dedicated to the polymerization reaction, may also be involved in anion binding. Comparative study with a receptor that lacks an additional binding site on the lateral arm of the amino acid (leucine derivative **5**, Figure 2), indicates that when lacking this group the receptor binds $NO_2^-$ salts much more weakly. Moreover, this points to the involvement of the methacrylamide group in receptors **1** and **4** in binding anions and salts (Figure 4). Receptor **5**, without a methacrylamide group, binds nitrite anions with the association constant $K_{NO2^-}$= 790 $M^{-1}$ and sodium nitrite with the association constant $K_{NaNO2}$=4170 $M^{-1}$. These constants are nearly half those found for complexes of receptor **4** with $NO_2^-$. From this comparison I drew a very

important conclusion, which became the basis for further research described in publication **H3**. Namely, the methacrylamide group situated on the side arm of the amino acid has a large effect on the receptor's binding of anions and salts.

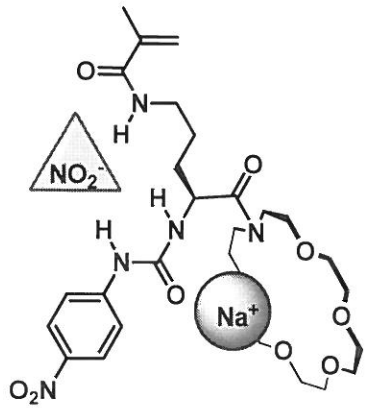
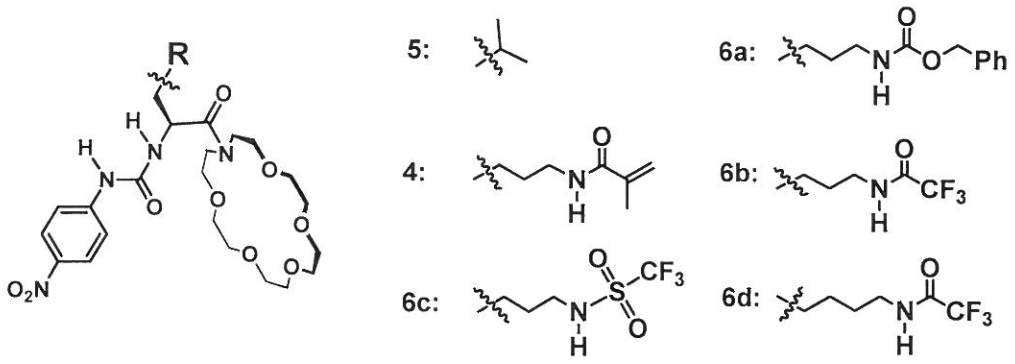



**Figure 4**. Proposed model for the binding of salts by receptor **4**

For the above reasons I decided to synthesize a series of L-ornithine derived receptors containing a cation binding domain (crown ether), an anion binding domain (a 4-nitro-L-phenylalanine group in the $\alpha$ position of the amino acid), and an additional anion binding group situated on the side arm of the amino acid (position $\delta$). The additional binding groups were variable elements and I selected them so as to be able to trace out the influence of the increasing strength of these groups' interaction with anions on the binding strength of the receptor (Scheme 3).




**Scheme 3.** The structures of receptors **4**, **5** and **6a-d**

Bearing in mind the high affinity of such receptors towards sodium cations, I performed studies with respect to selected anions and their sodium salts. I resolved to identify the correlations between the binding strength of the variable anion binding domain and the binding strength of the receptor by utilizing nitrite anions and sodium nitrate (generated *in situ*). In line with expectations, observed a trend of increasing complexation strength for receptors containing amide groups characterized by greater acidity. This trend is moderately visible for complexes with $NO_2^-$ anions, but very distinct for studies out in the presence of sodium cations (Table 3). For receptor **6b**, equipped with an additional trifluoroacetamide

group, I obtained the strongest complexes with nitrite. I showed that it is capable of binding nitrite anions over 13 times more strongly when sodium cations are in the solution. In systems of this sort, an important role is also played by the proper positioning of the binding domains. Complexation studies with receptor **6d** (derived from lysine), an analog of receptor **6b** with a lengthened side chain, showed that it is capable of binding nitrite anions with a strength comparable to receptor **6b**, but is not as effective in binding sodium salts (cooperative factors of 5.9 for **6d** vs. 13.1 for **6b**). Moreover, the principle of introducing amide groups of increasing acidity into the side chains of amide groups does have certain limits: introducing an excessively acidic amide (trifluorosulfonamide derivative **6d**) causes the deprotonation of the receptor, even by weakly basic anions like nitrite.

**Tabela 3.** Association constants for complexes of receptors **4**, **5** and **6a-d** with nitrite salts ($K_a$ [$M^{-1}$])

| $NO_2^-$ | $TBA^+$ | $Na^+$ | $K_{Na+}/K_{TBA+}$ |
|---|---|---|---|
| 5 | 790 | 4170 | 5.28 |
| 6a | 795 | 4250 | 5.35 |
| 4 | 1180 | 7590 | 6.43 |
| 6b | 1450 | 19000 | 13.10 |
| 6c | 1400 | 8300 | 5.93 |
| 6d | deprotonation | | - |

Complexation studies with receptor **6b**, expanded to include other salts, showed that it most strongly binds the sodium salts of nitrite. In the case of fluorides, receptor **6b** showed deprotonation, whereas for chlorides there was a preference for the formation of ion pairs (sodium choride) outside the receptor. I therefore decided to check whether those results would be consistent with extraction studies (solid/liquid) of the salts studied, using a solution of receptor **6b** in chloroform as extraction solvent. I monitored the sodium salt content in the organic phase by means of atomic emission spectroscopy, showing that receptor **6b** is capable of extracting sodium salts with efficiency of 26-47%, in accordance with the selectivity: NaCl<NaBr<$NaNO_3$<$NaNO_2$. Moreover, I showed that a solution of receptor **6b** may be utilized as a bulky liquid membrane in studying the transport of $NaNO_2$.

As previously, drawing conclusions from the research presented above paved the way for further research, as a result of which I published another article (publication **H4**) concerning L-ornithine derived receptors. Knowing that introducing an excessively acidic amide into the receptor structure leads to its deprotonation, I decided to replace the group with ones that possess not one but rather two protons capable of interacting with anions. I selected urea and thiourea derivatives for this purpose and introduced them into the L-ornithine platform to obtain receptors **7** and **8** (Figure 5). I obtained receptor **8** by the procedure presented for

receptor **1**, utilizing L-ornithine with selectively protected amine groups. The synthesis of receptor **7**, on the other hand, is easier; I obtained it by introducing a crown ether unit into the amino acid platform, next after the removal of two protective groups, I reacted it with 4-nitrophenyl isocyanate to obtain the desired compound. Given that the receptors are constructed in such a way that they possess chromophores in close proximity to the anion binding groups, they were investigated mainly by means of UV-Vis spectroscopy with supplementary $^1$HNMR spectroscopy.

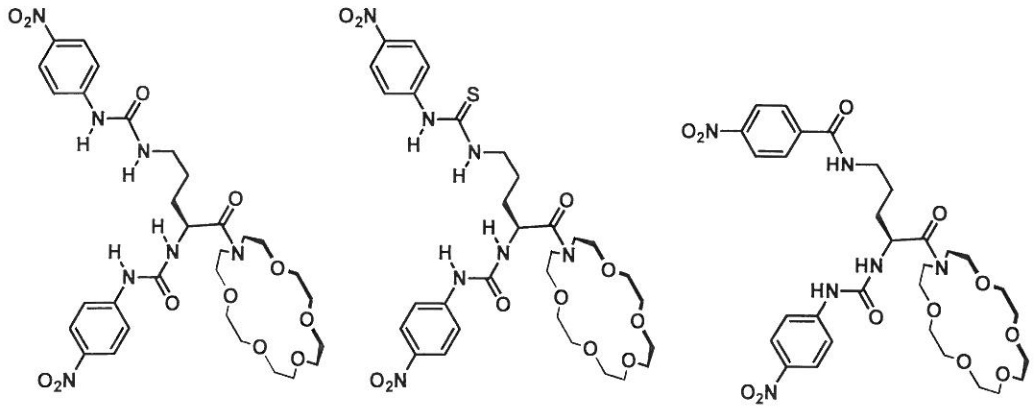



**Figure 5.** Structures and association constants for receptors **7-9**

Complexation studies of **7** and **8**, carried out with respect to choride anions and sodium chloride (generated *in situ*), confirm the much better binding properties of receptors containing urea and thiourea groups on the side arm of L-ornithine than in the case of amide groups. Comparison of the association constants of these receptors' complexes with those of the structurally similar receptor **9**, possessing an amide group on the side arm, indicates that the latter is capable of forming much weaker complexes with choride salts than receptors **7** and **8** (Figure 5). As for the previously studied structures, removal of the crown ether unit from the receptor structure eliminates the reinforcement of anion binding in the presence of sodium cations. To confirm that receptors **7** and **8** are equally selective with respect to sodium cations as their previously discussed analogs, I used the UV-Vis technique in an indirect way, as adding cations to solutions of the receptors in acetonitrile did not cause any changes in the spectrum of the receptor. As such, I decided to carry out a series of titrations of receptors **7** and **8** using chloride anion, in the presence of tetrabutylammonium, sodium, potassium, and ammonium cations. The results confirmed that the greatest reinforcement of receptors **7** and **8**'s binding of chloric anion is observed when the experiments are carried out in the presence of sodium cations. That is why I also carried out an expanded complexation analysis of receptors **7** and **8** with respect to selected anions using tetrabutylammonium salts, in the presence of sodium perchlorate as a source of sodium cations. The results indicate that receptor **8,** supported with a thiourea anion-binding domain, is much more effective at binding both sodium anions and sodium salts, than receptor **7**, equipped with two urea

domains (Table 4). For chloride anions and sodium chloride, the strength of interaction with receptor **8** was more than twice that for receptor **7**. Both receptors bind carboxylate anions most strongly, but in the presence of sodium cations there is an increased tendency for the formation of ion pairs outside the receptor. In the case of the interaction of receptor **8** with acetate anions, deprotonation of the thiourea domain is observed.

**Table 4.** Association constants for receptors **7** and **8** ($K_a$ [$M^{-1}$])

| | **7** | | | **8** | | |
|---|---|---|---|---|---|---|
| | $TBA^+$ | $Na^+$ | $K_{Na}/K_{TBA}$ | $TBA^+$ | $Na^+$ | $K_{Na}/K_{TBA}$ |
| $NO_2^-$ | 3 800 | 7 800 | 2.05 | 7 200 | 18 500 | 1.82 |
| $Br^-$ | 3 400 | 5 100 | 1.50 | 3 700 | 4 700 | 1.27 |
| $Cl^-$ | 18 200 | 33 500 | 1.84 | 46 800 | 85 500 | 2.57 |
| $PhCOO^-$ | 460 000 | 161 000 | 0.35 | $1.19 \cdot 10^6$ | 526 000 | 0.44 |
| $Ac^-$ | $3.5 \cdot 10^6$ | 280 000 | - | deprotonation | deprotonation | - |

Summarizing this research, I would like to point out that unlike the previously presented work, here I observed a significantly smaller increase in anion binding strength in the presence of sodium cations. On the other hand, the presented receptors **7** are **8** capable of binding anions and ion pairs more strongly. Based on the studies described here, one can draw the conclusion that effective salt receptors can be obtained in two ways: one involves harnessing the effect of stronger anion binding through cation interaction, while the other involves introducing an additional, strongly interacting anion-binding domain and the simultaneous action of these domains, at the expense of lesser cooperativity in cation and anion binding.

The final stage of my research on the development of receptors based on the L-ornithine platform which I would like to present in this report looked at receptors derived from squaramide (publication **H8**). Unlike for monotopic anion receptors, the literature offers only a few reports dealing with ditopic salt receptors in which squamide is responsible for interaction with anions. I therefore resolved to examine how the complexation properties would be influenced by replacing the urea and thiourea units in L-ornithine derived receptors and how the binding domains (situated at the carbon atoms $\alpha$ i $\delta$) in the structure of receptor **10** influenced salt binding (Figure 6).

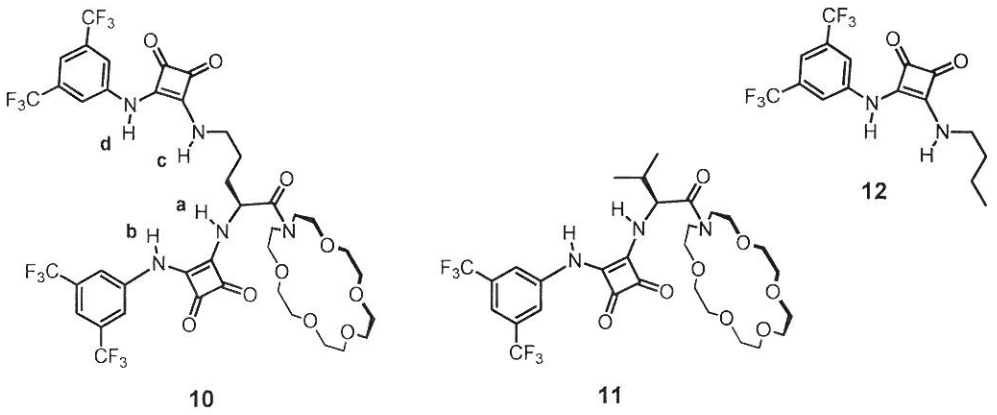



**Figure 6.** The structures of receptors **10-12**

I obtained the receptors through simple transformations and already during their synthesis I noticed a major difference in the behavior of these receptors (intermediate compounds derived from squaric acid), involving their poor solubility. On the one hand, I took advantage of this phenomenon to easily purify the individual derivatives through crystallization, yet on the other hand it hampered the study of certain structures in view of their insufficient solubility in acetonitrile. Receptor **10** is poorly soluble in acetonitrile, but soluble enough to enable titration to be carried out using the UV-Vis technique.

**Table 5.** Association constants for complexes of **9** ($K_a$ [$M^{-1}$])

| | **9** | **9 + 1 eq. $Na^+$** |
|---|---|---|
| $Br^-$ | $5.37\times10^4$ | $5.12\times10^4$ |
| $NO_2^-$ | $1.04\times10^5$ | $1.07\times10^5$ |
| $Cl^-$ | $1.62\times10^6$ | $1.58\times10^6$ |
| $PhCOO^-$ | $6.31\times10^5$ | $6.30\times10^5$ |
| $CH_3COO^-$ | $2.95\times10^6$ | $2.90\times10^6$ |

The results confirm that receptor **10** binds the anions studied very strongly (Table 5). This binding is so strong that the complexation properties of the receptor do not differ very much in the presence of sodium cations. Interestingly, the receptor binds chloride salts very strongly, forming stronger complexes with this halide than with benzoates. As such, I performed further comparative studies aimed at identifying the influence of the individual domains on ion-pair binding using chloride salts. For this I used receptors **11** and **12**, which are structural elements of receptor **9** (Figure 6).

**Tabela 6.** Comparison of the association constants for complexes of receptors **10-12** ($K_a$ [$M^{-1}$])

| | **10** | **11** | **12** |
|---|---|---|---|
| TBACl | $1.62\times10^6$ | $3.23\times10^4$ | $2.17\times10^5$ |
| NaCl | $1.58\times10^6$ | $5.25\times10^4$ | $2.06\times10^5$ |

Analysis of the association constants for complexes with chloride anions and sodium chloride (generated *in situ*) leads to several conclusions (Table 6). Firstly, the monotopic receptor **12** forms complexes with chlorides an order of magnitude more weakly than the ditopic receptor **10** and, as should be expected, I did not observe stronger anion binding in the presence of sodium cations (given the absence of a cation binding domain). Secondly, the ditopic receptor **11** binds chloride anions more strongly in the presence of sodium cations, but two orders of magnitude more weakly than receptor **9** and one order of magnitude more weakly than the monotopic receptor **12**. Combining receptors **11** and **12** into a single structure, in turn, permits for stronger salt binding and the formation of more stable complexes as compared to each of these receptors considered separately. On this basis one can conclude that the two amide domains in the structure of receptor **10** operate cooperatively, but the domain situated in position δ makes a greater contribution. To confirm this conclusion, I carried out a $^1$HNMR study. Unfortunately, the poor solubility of receptor **10** precluded titration in pure acetonitrile, so I performed the experiment with the addition of 10% dimethyl sulfoxide. In line with the above conclusion, this confirmed the greater involvement of the domain situated in position δ of the receptor in complex formation (Figure 7).

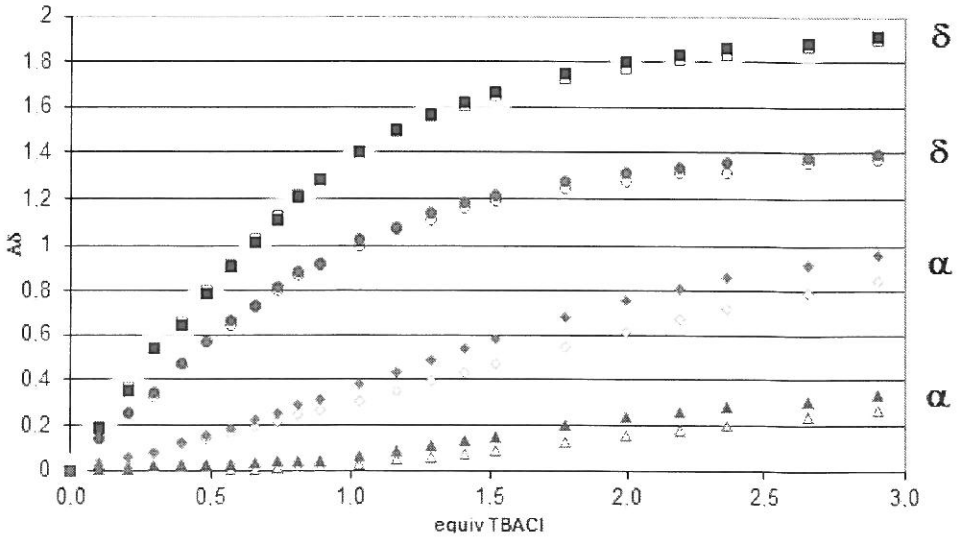
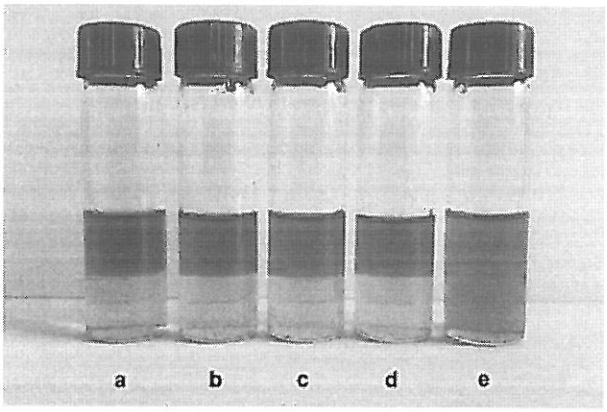



**Figure 7**. Changes in chemical shifts for selected signals of receptor **10**

Bearing in mind that receptor **10** binds chloride salts so strongly, I decided to utilize it in the extraction of chloride dye (toluidine) from aqueous to organic phase. I controlled the dye

content in the aqueous phase using UV-Vis analysis, identifying the extraction efficiency on that basis. I performed the extraction of $5x10^{-5}$ M aqueous solution of toluidine by means of 1, 10 and 50 equivalents of receptor **10,** suspended in a mixture of organic solvents. The suspension underwent clarification after the process of extraction (better solubility for the receptor **10** complex with the dye than for the complex itself). I showed that as receptor content increased, the dye could be extracted with 20%, 30%, and 68% efficiency, respectively. I also showed that unlike for receptor **10**, the use of 50 equivalents of reference receptors **7**, **11**, **12** and also 15-crown-5 did not allow for effective extraction of the dye from the aqueous phase to the organic phase (Figure 8). Unfortunately, none of the receptors is capable of extracting sodium chloride from its aqueous solution.




**Rysunek 8**. Extraction of aqueous solution of toluidine by means of:

a) 15-crown-5; b) receptor **7**; c) receptor **11**; d) receptor **12**; e) receptor **10**

To sum up the strand of research described so far, dealing with receptors using the L-ornithine platform, below I present a schematic representation of the complex association constants for chloride anion and sodium chloride together with the receptors described above. This table, summarizing the findings of the studies described in this section, graphically depicts both the development of the L-ornithine derived receptors through time and the increasing capacity for complexation attained with each successive modification. Each of the successive studies was based on results obtained from previous analysis and previously published experiments.

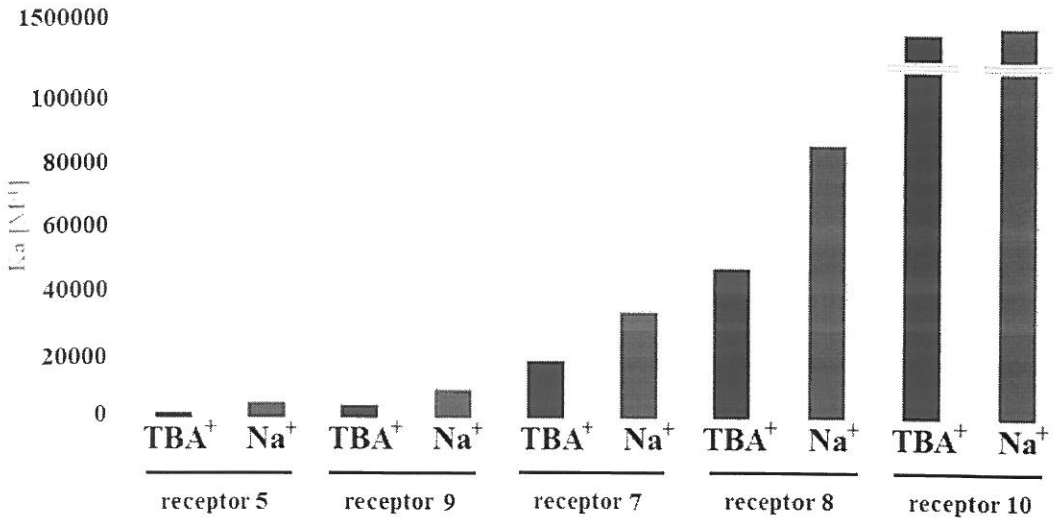
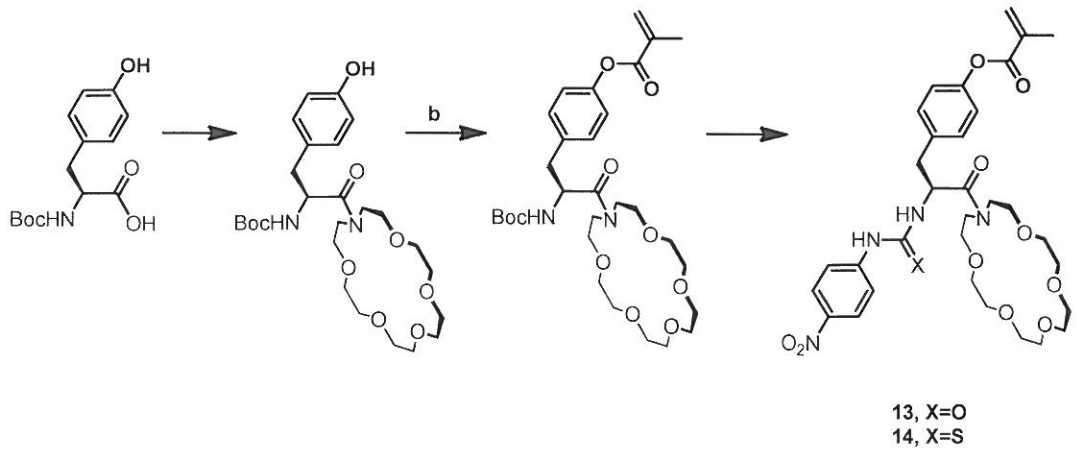



**Figure 9**. Comparison of association constants for successive receptors

**Ion pair receptors: derivatives of L-tyrosine and 4-nitro-L-phenylalanine**

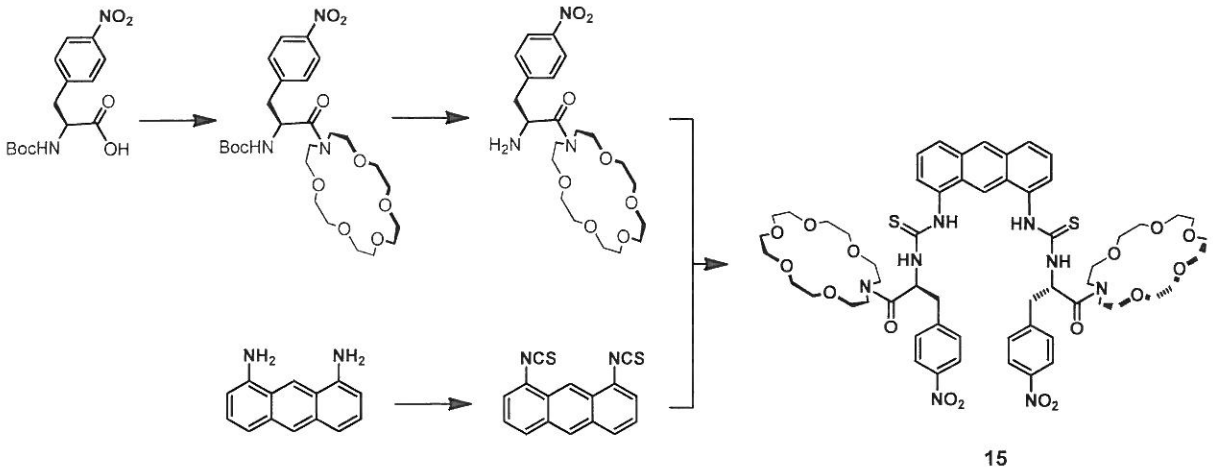
During the course of research on obtaining functional polymer materials, I encountered a few difficulties. One of them was the low reactivity of receptor **1**, containing a methacrylamide functional group, in the copolymerization reaction. I therefore decided to try to resolve this problem by obtaining an analogous receptor containing a crown ether as a cation-binding site and a urea or thiourea anion-binding domain. I decided to modify the phenyl group, in turn, by means of a methacrylate function to obtain the corresponding ester, hoping that it would show better copolymerization reactivity with other methacrylate comonomers. This research was reported in publication **H5**. I obtained the receptor in a similar way as its L-ornithine analog, but unlike in the previously described synthesis, in this case as the substrate I used an amino acid derivative with one protecting group, namely N-(tert-butoxycarbonyl)-L-tyrosine. First I introduced a cation-binding domain into the amino acid (a crown ether), then I obtained the corresponding methacrylate and, after deprotection of the amine group, I carried out a reaction with 4-nitrophenyl isocyanate or 4-nitrophenyl isothiocyanate, obtaining the intended receptors **13** and **14** (Scheme 4).




**Scheme 4.** Synthesis of receptors **13** i **14**

I carried out complexation studies of both receptors, finding that they are capable of effective ion-pair binding, in particular for sodium salts. I also obtained the respective functional copolymers, employing one of the living polymerization techniques (RAFT). The molecular mass of the copolymers was much lower than for the previously described structure, but I attained a favorable mass distribution. I obtained polymers with masses of 24.8 and 17.1 kDa and PDI 1.65 and 2.30, respectively, for the urea and thiourea receptor. I used the polymers so obtained in extraction experiments on aqueous salt solutions. However, both copolymers proved to be much less effective than the previously studied polymer material, characterized by much higher molecular mass.

Given that each of the receptors described above were obtained from optically active amino acids, I decided to harness that property in constructing a receptor capable of enantioselective recognition of chiral anions and salts (publication **H9**). Examples of such receptors can be found in the literature, usually utilizing optical information from easily available chiral amino acids or sugars. I decided to design a receptor that would be capable of effectively binding salts (ion pairs) and discriminating between chiral salts (tetrabutylamonium and sodium salts). With this objective, I optimized the synthesis of 1,8-diaminoanthracene found in the literature, then utilized this compound to react with amines, amino acid derivatives containing an ether crown in their structure. The purpose of this reaction was not only to connect the optically active amino acid units but also to generate anion-binding domains (thiourea group). By this means I obtained receptor **15,** possessing a stereogenic center in close proximity to the anion-binding domain (Scheme 5).



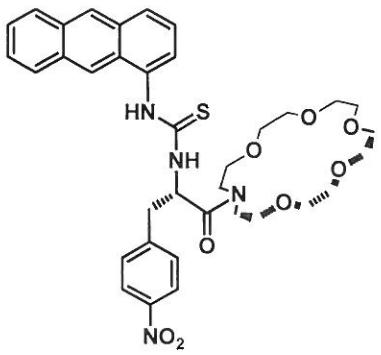

**Scheme 5.** Synthesis of receptor **15**

First I performed complexation studies on receptor **15** with respect to achiral anions (TBA salts) and their sodium salts; this was performed in acetonitrile, using the UV-Vis and $^{1}$HNMR titration techniques.

**Table 7.** Association constants for complexes of receptor **15** ($K_a$ [$M^{-1}$])

| | **15** | **15 + 1 eq. $Na^+$** | **$K_{Na}/K_{TBA}$** |
|---|---|---|---|
| $Br^-$ | 110 | 565 | 5.14 |
| $NO_2^-$ | 200 | 295 | 1.48 |
| $Cl^-$ | 1510 | 7070 | 4.68 |
| $PhCOO^-$ | 89100 | 28800 | 0.32 |
| $CH_3COO^-$ | 144500 | -[b] | - |

I showed that receptor **15** forms the strongest complexes with carboxylate anions, but in the presence of sodium cations I observed the preferred formation of ion pairs outside the receptor, manifesting itself in the precipitation of sodium acetate. Unlike for carboxylates, for the weaker associated anion such as nitrites or halides I observed stronger binding in the presence of sodium cations. I noted the strongest, nearly fivefold increase for binding of sodium chloride (generated *in situ*, Table 7). Next I obtained a series of optically pure, protected tetrabutylammonium amino acids derived from D- and L-valine, phenylalanine, and tryptophan, as well as R- and S- acids of 2-phenylbutyric acid and mandelic acid, and used them in titration experiments with receptor **15**. Analysis of the association constants for receptor **15** with optically active anions and their sodium salts led to several very important conclusions. The presence of sodium did not affect enantioselection. Anions and their sodium salts are bound in the same D:L and R:S ratios, whereas the presence of cations modulates the association constants for the complexes. Weakly binding anions, such as derivatives of mandelic acid, are complexed more strongly in the presence of sodium cations, whereas strongly complexed anions, such as derivatives of 2-phenylbutyric acid, are bound significantly more weakly when receptor **15** is precomplexed with sodium cation. I obtained the greatest enantioselectivity, $K_L/K_D$= 1.66 for sodium anions and salts derived from tryptophan, and I used this set of chiral salts for further comparative studies with receptor **16**, containing one amino acid unit in its structure (Figure 10).




**16**

**Figure 10.** The structure of receptor **16**

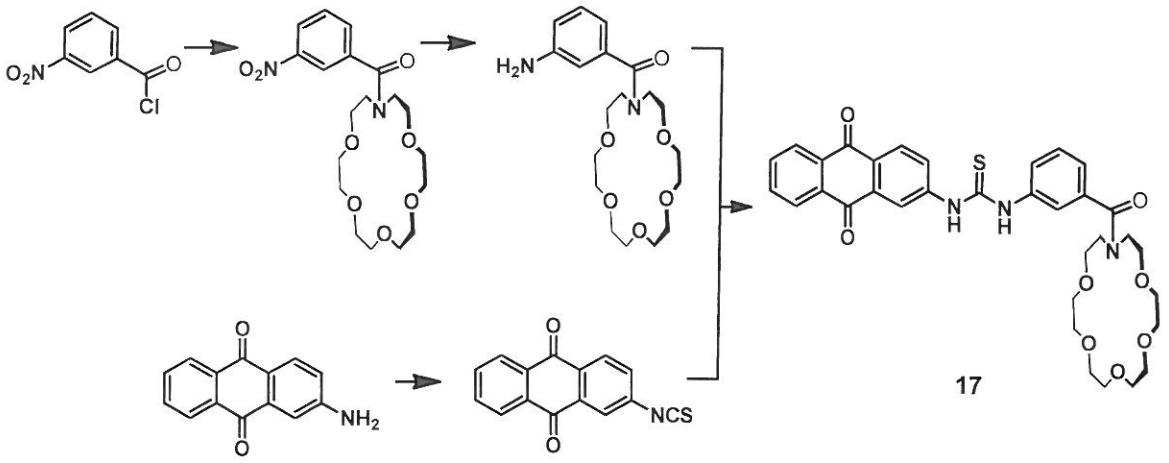
**Table 8.** Comparison of the association constants for complexes of receptors **15** and **16** ($K_a$ [$M^{-1}$])

| [$M^{-1}$] | 15 | | | | 16 | | | |
|---|---|---|---|---|---|---|---|---|
| | $K_{TBA}$ | $K_{Na}$ | $K_{Na}/K_{TBA}$ | $K_{L/D}$ | $K_{TBA}$ | $K_{Na}$ | $K_{Na}/K_{TBA}$ | $K_{L/D}$ |
| L-TrpCOO$^-$ | 2630 | 5250 | 1.99 | 1,20 | 128800 | 97700 | 0.76 | 1.66 |
| D-TrpCOO$^-$ | 2200 | 4360 | 1.98 | | 77620 | 60250 | 0.78 | |

These studies indicate that the two amino acid units present in receptor **15** are responsible for greater enantioselectivity as compared to receptor **16**. Moreover, receptor **16** binds sodium anions and salts of tryptophan much more weakly than receptor **15**, possessing a double number of domains. Based on the gathered results, one may conclude that the two amino acid units in receptor **15** are needed for the effective and enantioselective binding of anions and salts.

**Ion pair receptors: derivatives of 3-aminobenzoic and 4-aminobenzoic acid**

I also decided to investigate whether 3-aminobenzoic acid would be an equally good platform for synthesizing an ion pair receptors. First I will present the study described in publication **H6**. I designed a receptor so that it would act as an electrochemical sensor of anions and ion pairs, by modifying the anion-binding domain with a unit of anthraquinone, acting as a reporter. Moreover, I decided to introduce the crown ether in a way that reduces the electron density on the aromatic ring (amide binding), and thereby strengthens the action of the anion-binding domain. I obtained the receptor through simple synthesis, starting with 3-nitrobenzoyl chloride. Reacting this chloride with 1-aza-18-crown-6 allowed for the introduction of a cation-binding domain into the receptor platform. Next, through the reduction of a nitro group I obtained the respective amine derivative, which I reacted with previously obtained 2-isothiocyanoanthraquinone, obtaining the desired receptor **17** (Scheme 6).




**Scheme 6.** Synthesis of receptor **17**

I carried out complexation studies for the receptor in acetonitrile and showed that of the salts tested, receptor **17** binds chloride anions the most strongly, followed by nitrite, bromide, and nitrate ions. More basic anions, such as carboxylates, caused the deprotonation of the receptor. In the presence of sodium cations, receptor **17** is capable of creating much stronger complexes with anions than in the presence of tetrabutylammonium cation. I observed the greatest reinforcement of anion binding in the presence of sodium cations for bromides, $K_{Na}/K_{TBA} = 4.28$ (Table 9). I also showed that such a reinforcement is possible exclusively in the presence of sodium cations, whereas the presence of potassium or ammonium cations decreases the affinity of receptor **17** to form complexes with anions.

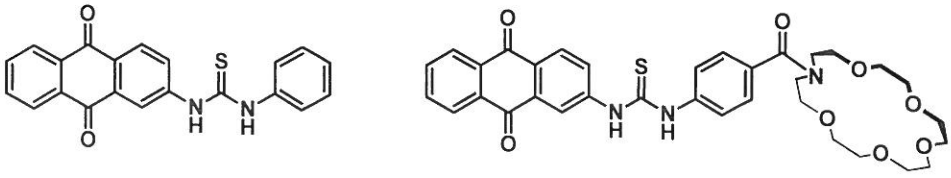
**Table 9.** Stability constants for complexes of receptor **17** ($K_a$ [$M^{-1}$])

| | **17** | **17+$Na^+$** | **$K_{Na}/K_{TBA}$** |
|---|---|---|---|
| $Cl^-$ | 10000 | 30900 | 3.09 |
| $NO_2^-$ | 4300 | 5600 | 1.30 |
| $Br^-$ | 630 | 2700 | 4.28 |
| $NO_3^-$ | 230 | 600 | 2.61 |

To prove that the crown ether unit linked to receptor **17** through an amide bond reinforces anion binding (as an electron-withdrawing group), I synthesized and tested the simple anion receptor **18**, lacking such a crown ether unit (Figure 11). Comparison of the complexing properties of the monotopic receptor **18** to data obtained for the ditopic receptor **17** led to two very important conclusions. Firstly, receptor **18**'s lack of an electron-withdrawing configuration makes it unable to interact with anions as strongly as its ditopic analog **17**. Secondly, studies carried out in the presence of sodium cations confirm that unlike receptor **17**, receptor **18** is unable to form stronger complexes with sodium chloride (generated *in situ*) than with tetrabutylammonium chloride.

In designing receptor **17**, I assumed a salt binding mechanism similar to that of ion pair receptors derived from α-amino acids. I assumed that sodium cation will be complexed by the crown ether while at the same time interacting with the sulfur atom of the thiourea, changing the conformation of the receptor and increasing the acidity of the urea protons. To confirm this assumption I synthesized and studied receptor **19**, an analog of receptor **17** possessing binding domains in *para* position (Figure 11), which rules out the possibility of such simultaneous interaction with the crown ether and thiourea group. My studies nevertheless showed that receptor **19** is also an effective ion pair receptor and also binds salts effectively. On this basis, and after additional $^1$HNMR studies, I modified the above-presented assumption concerning how ion pairs are bound by such receptors. I showed that complexation of the crown ether by sodium cation further diminishes the electron density in the aromatic ring of receptor **17**, thereby reinforcing the thiourea group's ability to form hydrogen bonds.

Moreover, I carried out X-ray structural analysis of the complex [**19**·$Na^+$] and showed that the sodium cation fits into the macrocyclic cavity of the crown ether. The sodium cation is linked by this ether by means of five oxygen atoms, analogously to 15-crown-5, whereas the nitrogen atom does not take part in interacting with the sodium cation.



18 19

**Figure 11.** The structures of receptors **18** and **19**

**Tabela 10.** Comparison of association constants for complexes of receptors **17-19** ($K_a$ [$M^{-1}$])

| | **17** | **19** | **18** |
|---|---|---|---|
| $K_{Cl^-}$ | 10000 | 11500 | 7600 |
| $K_{[L+Na+]\cdot Cl^-}$ | 30900 | 25700 | 3550 |

Lastly in this study, I demonstrated that receptor **17** can be used as an electrochemical sensor of anions and ion pairs. Analysis of electrochemical measurements (cyclical voltagrams) indicated that receptor **17** shows two consecutive one-electron reversible waves in acetonitrile solution, corresponding to two single-electron reductions, and that the potentials of the two peaks depend on the addition of anions and sodium salts. Given that the potential changes for the first peak are more distinct, I monitored the behavior of this peak in further analysis. Adding additional anions to the receptor caused the two signals, each derived from single-electron reductions, to shift toward more negative potentials. This shift is more distinct for the first of them, and so I used this shift in further analysis. Upon addition of 1, 3, or 5 equivs. of selected anions (TBA salts), the potential of the first peak shifts gradually toward more negative potentials. The exception was for carboxylate anions, for which no shift in signal caused by anion complexation was observed, but rather one signal disappeared whereas the other emerged (Figure 12). This is consistent with results previously obtained and confirms that receptor deprotonation occurs in the case of carboxylates. Such a disappearance of one signal and appearance of another, as a consequence of the addition of carboxylate anions, reflects the situation involving a change in quantities of the receptor and its deprotonated form. Unlike for anions, when sodium cations are added the potential of the first peak also shifts, albeit this time toward positive potentials. This made it possible to differentiate anions and their sodium salts in terms of their interactions with receptor **17**. In complexation studies performed in the presence of sodium cations, I noted greater changes in potential differences than in those performed for anions, thereby showing that a simple amino benzoic acid skeleton may be successfully used in synthesizing ion pair sensors.

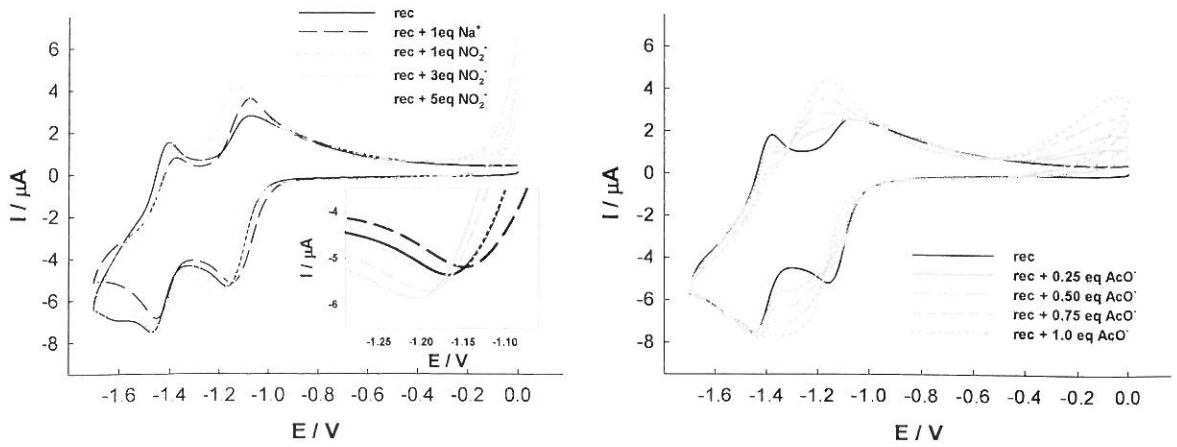
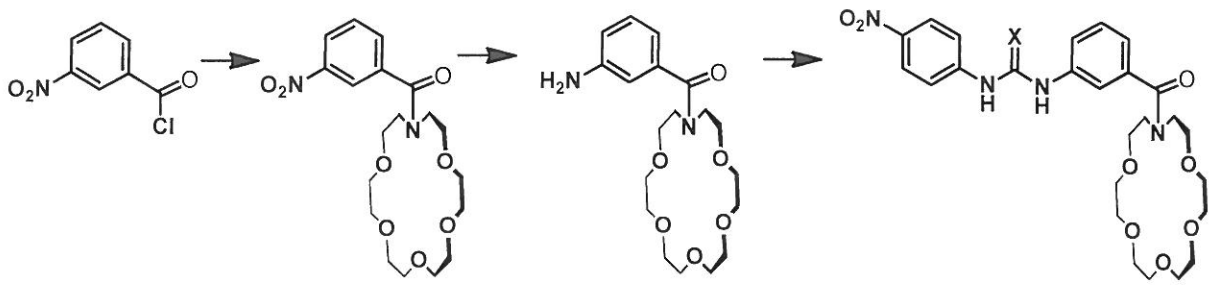



**Figure 12.** Chromatograms for receptor **17** with addition of selected ions

I also decided to synthesize and study simple ion-pair receptors derived from aminobenzoic acid (publication **H8**) following the most widely used approach, i.e. using 4-nitro(thio)urea groups. This reporter, situated by the anion-binding domain, on the one hand contributes to stronger anion binding (as an electron-withdrawing group), while on the other hand allowing complexation studies to be carried out using UV-Vis spectroscopy (Scheme 7). I showed that receptor **20** is capable of binding selected anions more strongly in the presence of sodium cations, although it is highly susceptible to deprotonation (Table 10). I observed this phenomenon during titration even using a base as weak as nitrite anions. To investigate whether such deprotonation could be prevented by reducing the acidity of the anion-binding domain, I synthesized receptor **21** , supported by an urea binding domain, and subjected it to the action of nitrite anions. I found that this modification may be successfully used to modulate the receptor's binding strength and to prevent its deprotonation. Moreover, I confirmed that the absence of the cation binding domain attached as an electron withdrawing group eliminates the effective binding of ion pairs.

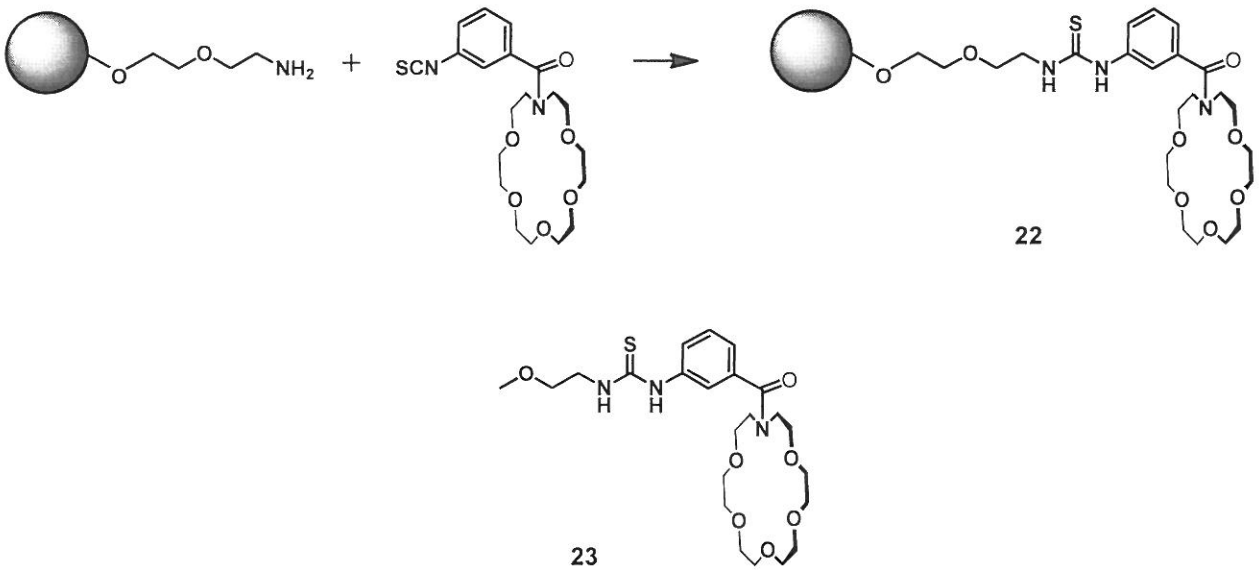



**Scheme 7.** Synthesis of receptors **20 and 21**

**Table 10.** Association constants for complexes of receptor **20** ($K_a$ [$M^{-1}$])

| | **20** | **20+$Na^+$** | **$K_{Na+}/K_{TBA+}$** |
|---|---|---|---|
| $Cl^-$ | 8500 | 12000 | 1.41 |
| $NO_2^-$ | deprotonation | deprotonation | - |
| $Br^-$ | 870 | 1510 | 1.73 |
| $NO_3^-$ | 260 | 430 | 1.65 |

Given the above observations, I decided to obtain polymer material **22**, containing units of the salt receptor in its structure (Scheme 8), with the aim of obtaining a cross-linked polymer so that it could be easily separated from the solution. I used commercially available polymer resin modified with poly(ethylene glycol) chains with terminated amine groups, which I reacted with properly prepared isothiocyanate, possessing a cation-binding domain, generating at the same time an anion-binding domain (the thiourea group). To confirm that the receptor attached to the resin was not susceptible to deprotonation by the nitrite salts that I intended to use in extraction studies, I obtained and structurally studied the similar receptor **23** (Scheme 8). I showed that the ethylene glycol linker which I used to immobilize the receptor may also be utilized to modulate the binding strength of the anion domain, like replacing the thiourea group with a urea group.




**Scheme 8.** Synthesis of resin **22** and the structure of receptor **23**.

I carried out extraction studies using the polymeric resin so obtained to examine its cooperative ability to extract sodium nitrite from acetonitrile solution. I showed that its extraction efficiency was 2% for $TBANO_2$, 10% for sodium perchlorate, but 50% for a mixture of these salts. Unfortunately, even a small addition of water to the salt solution causes resin **22** to be ineffective at extraction. I took advantage of this property to regenerate the resin and showed that the regenerated material did not lose its salt binding properties.

**Summarizing all three of these strands of research, I consider my main achievements to be as follows:**

- Designing a new type of ion pair receptors using the basic amino acid L-ornithine as a platform. I obtained a receptor containing a crown ether unit as a cation binding site and a thiourea capable of interacting with anions. I showed that this receptor is capable of binding anions in the presence of sodium cations.

- Obtaining functionalized polymer materials and using them in aqueous to organic phase salt extraction. I used the ion pair receptor to synthesize a functional copolymer. I showed that unlike the receptor itself, a polymer containing its units effectively extracts sodium nitrite from the aqueous to organic phase.

- Showing that ion pair receptors containing urea based anion binding domains are effective at binding ion pairs. I compared the complexation properties of analogous receptors differing solely in terms of their anion binding domains (thiourea and urea groups), showing that the receptor containing a urea group shows high affinity for sodium cations due to this cation's interaction with the crown ether unit and the oxygen atom of the urea group. The receptor containing a urea binding domain therefore showed stronger ion pair binding than its thiourea analog.

- Demonstrating that there is a correlation between the strength of additional binding domains and the receptor's complexation properties. I obtained a series of receptors by introducing a series of additional binding domains to the platform, with increasing binding strength. The introduction of strong hydrogen bond donors led to stronger ion pair complexation. I obtained a receptor showing a major (13-fold) reinforcement in anion binding in the presence of sodium cations. I confirmed that the distance between the binding domains on the L-ornithine platform is optimal and allows for effective cooperation.

- The use of urea and thiourea groups as additional binding domains. To avoid receptor deprotonation, I introduced additional binding domains into the L-ornithine platform, possessing two protons capable of forming hydrogen bonds (urea and thiourea groups). I showed that the anion binding domains act in cooperative fashion and that a receptor equipped with an additional, thiourea based anion binding domain is characterized by better complexation properties.

- Obtaining ion pair receptors utilizing a squaramide unit as an anion binding domain. I showed that this receptor forms complexes so strong that it can be used for salt extraction from the

aqueous to organic phase. I showed how individual receptor binding domains affect the salt-binding ability.

- Using amino acid units to construct an ion pair receptor capable of salt enantioselection. I showed that attaching optically active amino acid units to a rigid anthracene platform leads to an effective ion pair receptor that can be used for the enantioselective complexation of chiral anions and their sodium salts. I demonstrated that removing one of the amino acid units from the structure of the receptor significantly weakens its binding strength and boosts its enantioselectivity.

- Obtaining ion pair receptors derived from L-tyrosine and utilizing them as comonomers in a polymerization reaction. I demonstrated that the L-tyrosine platform can also be used for synthesizing receptors and polymer materials. I used the copolymers so obtained to study the extraction and transport of salt through bulky liquid membranes.

- Using aminobenzoic acid derivatives to synthesize electrochemical salt sensors. I designed a new salt receptor using a simple platform of 3-aminobenzoic acid. I showed that attaching an cation binding domain to the receptor platform through the respective linker is responsible for stronger binding of anions and ion pairs. Introducing an anthraquinone unit into the receptor structure, acting as a reporter, enabled complexation studies to be carried out using cyclic voltammetry.

- Obtaining a polymer resin modified with receptor units. I designed an isothiocyanate module containing a cation binding domain, which through reaction with amines yielded to ion pair receptors. Starting from commercially available resin, I obtained a polymer material that I used in the extraction of nitrite salts, demonstrating that sodium nitrite is extracted by the resin in a cooperative fashion.

5. Other scientific publications and achievements

a) Bibliographic summary of scientific achievements

| | |
|---|---|
| Total number of publications: | 24 |
| Total number of publications after Ph.D. degree | 22 |
| Total impact factor | 79.25 |

Citation report based on Web of Science at 18.08.2016 (last publications **H7**-**H9** not included):

Total number of citations: 151

Total number of citations (without self-citations): 105

Hirsch index: 9

b) List of publications before Ph.D. degree (except these listed in chapter 4)

**[M1]** I. Kudyba, J. Jóźwik, J. Romański, J. Raczko, J. Jurczak;

"The synthesis of oximes and nitroalkanes bearing a chiral auxiliary unit: convenient substrates for the preparation of enantiomerically pure nitrile oxides"

**Tetrahedron Asymmetry,** 2005, 16, 2257-2262, IF=2.108.

**[M2]** A. Kulesza, A. Mieczkowski, J. Romański, J. Jurczak;

"Asymmetric addition of titanium and sodium alkoxides to chiral imines"

**Tetrahedron Asymmetry,** 2003, 14, 1161-1166, IF=2.108.

a) List of publications after Ph.D. degree (except these listed in chapter 4)

In respect to my research projects to date, I have focused an two main areas: asymmetric synthesis and synthesis of new functional materials containing amino acid units. Within the field of asymmetric synthesis, I focused on 1,3-dipolar cycloaddition witch chiral auxiliaries. I conducted experiments in two approaches: using optically pure dipoles (nitrile oxides) and optically pure dipolarophiles (fumaric acid derivatives) consisting of a chiral auxiliary unit. I explored an easy way to generate nitrile oxides from their stable precursors – oximes. As a result of these studies I have demonstrated that distereoselectivity of 1,3-dipolar cycloaddition is more dependent on the electron density of dipolarophiles than on the electron density of dipoles (publication **P1, P2, P3, P10**). For some cycloadducts I encountered difficulties in the recovery of chiral auxiliaries. The resolution of this problem resulted in a publication concerning high-pressure transesterification (publication **P8**). These studies have shown that the sterically hindered esters can be converted to methyl esters under high pressure (10 kbar) in methanol in the presence of base. This work is cited as one of the methods for removal of protecting groups in the handbook *Greene's Protective Groups in Organic Synthesis* (Fifth Edition). Lastly I decided to use the reaction of 1,3-dipolar cycloaddition in the total synthesis of natural compounds. I have shown that (5*S*)-dihydroyashabushiketol can be obtained in a four-step reaction sequence involving 1,3-dopolar cycloaddiction reaction as a key step.

In terms of the synthesis of functional polymeric materials containing amino acid units in their structure, I have proposed new method for the synthesis of ornithine and lysine derivatives of (meth)acrylic acid. These compounds were used as monomers in the copolymerization reaction and we found that the gels so obtained (crosslinked polymers) are environmentally sensitive. These compounds we used to synthesize gels and microgels capable of volume change upon the addition of divalent metal ions as well as upon change of pH and temperature. I have also proposed synthesis of cystine derivative of acrylic acid and found that this compound can be used as a degradable cross linker. The presence of cystine linkers in the gel structures allowed ferrocene units to be incorporated. We have shown that oxidation and reduction of ferrocene in the gel structure influence its volume phase transition. In addition,

we used an acrylic derivative of cysteine as a biodegradable linker and obtained polymeric gels, the degradation of which is capable of releasing the active substances. These studies are described in detail in the publications **P4, P5, P7, P9, P12, P13.**

**[P1]** J. Romański, J. Jóźwik, C. Chapuis, J. Jurczak;

"Diastereoselective 1,3-dipolar cycloadditions of chiral derivatives of 2-oxoethanenitrile oxide to noncyclic conjugated symmetrical alkenes",

**Helvetica Chimica Acta,** 2007, 90, 2116-2131, IF=1.087.

**[P2]** J. Romański, J. Jóźwik, C. Chapuis, M. Asztemborska, J. Jurczak;

"Asymmetric 1,3-dipolar cycloadditions of chiral carboxyloyl nitrile oxides to cycloalkenes",

**Tetrahedron Asymmetry,** 2007, 18, 865-872, IF=2.108.

**[P3]** J. Romański, C. Christian, J. Jurczak;

"1,3-Dipolar Cycloadditions of a 2-Oxoethanenitrile Oxide Derived from (2R)-Bornane-10,2-sultam to Electronically Modified 4,4 '-Disubstituted Stilbenes",

**Helvetica Chimica Acta,** 2009, 92, 1056-1069, IF=1.087.

**[P4]** M. Karbarz, J. Romański, K. Michniewicz, J. Jurczak, Z. Stojek;

"Influence of polymer network-metal ion complexation on the swelling behaviour of new gels with incorporated alpha-amino acid groups",

**Soft Matter,** 2010, 6, 1336-1342, IF=3.798.

**[P5]** M. Karbarz, K. Pyrzyńska, J. Romański, J. Jurczak, Z. Stojek;

"New poly(N-delta-acryloyl ornithine) gels cross-linked with N,N '-methylenebisacrylamide. Sorption properties",

**Polymer,** 2010, 51, 2959-2964, IF=3.586.

**[P6]** J. Romański, P. Nowak, C. Chapuis, J. Jurczak;

"Total synthesis of (5S)-dihydroyashabushiketol",

**Tetrahedron Asymmetry,** 2011, 22, 787-790, IF=2.108.

**[P7]** J. Romański, M. Karbarz, K. Pyrzyńska, J. Jurczak, Z. Stojek;

"Polymeric hydrogels modified with ornithine and lysine: Sorption and release of metal cations and amino acids",

**Journal of Polymer Science Part A** – Polymer Chemistry, 2012, 50, 542-550, IF 3.113.

**[P8]** J. Romański, P. Nowak, K. Kosiński, J. Jurczak;

"High-pressure transesterification of sterically hindered esters",

**Tetrahedron Letters,** 2012, 53, 5287-5289, IF=2.347.

**[P9]** K. Kaniewska, J. Romański, M. Karbarz;

"Oxidation of ferrocenemethanol grafted to a hydrogel network through cysteine for triggering volume phase transition",

**RSC Advances,** 2013, 3, 23816-23823, IF=3.289.

**[P10]** J. Romański, P. Nowak, A. Maksymiuk, C. Chapuis, J. Jurczak;

"Diastereoselective 1,3-dipolar cycloadditions of both electronically modified phenyl-nitrile oxides and stilbenes",

**RSC Advances,** 2013, 3, 23105-23118, IF=3.289.

**[P11]** J. Romański, P. Piątek;

"Selective Ammonium Nitrate Recognition by a Heteroditopic Macrotricyclic Ion-Pair Receptor",

Journal of Organic Chemistry, 2013, 78, 4341-4347, IF=4.785.

**[P12]** M. Mackiewicz, J. Romański, M. Karbarz;

"New ampholytic microgels based on N-isopropylacrylamide and alpha-amino acid: changes in swelling behavior as a function of temperature, pH and divalent cation concentration",

**RSC Advances**, 2014, 4, 48905-48911, IF=3.289.

**[P13]** M. Mackiewicz, K. Kaniewska, J. Romański, E. Augustin, Z. Stojek, M. Karbarz;

"Stable and degradable microgels linked with cystine for storing and environmentally triggered release of drugs",

**Journal of Materials Chemistry,** 2015, 3, 7262-7270, IF=4.872.