Appendix No.1

Summary of professional accomplishments

Ferrocenyl compounds with anticancer activities

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Łódź 2014

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1 Personal data

1.1 Name and surname

Damian Plażuk

1.2. Scientific diploma and degrees

June 2001 – M.S. – degree – dissertation titled "Synthesis of selected 'push pull' derivatives of 3-dicyanomethylene-1-indanone and studying their electronic absorption spectra" which was written at the Department of Organic Chemistry UŁ under the supervision of prof. dr hab. Janusz Zakrzewski

June 2005 – Ph.D. dissertation titled "Novel electrophilic reaction of ferrocene" which was written at the Department of Organic Chemistry UŁ under the supervision of prof. dr hab. Janusz Zakrzewski. One part of the experiments was done during a 7-months Marie-Curie Fellowship in Prof. Gerard Jaouen's laboratory (ENSCP, L'Ecole Nationale Supérieure de Chimie de Paris) in Paris, France. I received an award from Sigma-Aldrich Company and the Polish Chemical Society for the best Ph.D. thesis in organic chemistry in 2005.

1.3 History of employments

February 2005 – September 2005 – assistant – Department of Organic Chemistry, University of Łódź

Since October 2005 – assistant professor (pol. adiunkt) Department of Organic Chemistry, University of Łódź

1.4 Summary of scientific achievements (05-02-2014)

Original research publications

- Totally - 30 publications – (22 publications – 1st author, 8 publications – co-author, 2 publications – corresponding author, - 1 review in Comprehensive Heterocyclic Chemistry III, CHC III)

- publications published after receiving Ph.D. degree – 20 publications (13 publications – 1st author, 7 publications – co-author, 2 publications – corresponding author)

- Sum of IF (IF according to year of publish) for all publications: 71.917 (average 2.397 per publication), 72.693 (IF for 2012 – average 2.423 per publication); 71.380 (5Y IF - average 2.379 per publication)

- Total MNiSW points: 785 points (average 26.17 points per publication) (two publications published in *RSCAdvaces* and *MedChemComm* are not included in the MNiSW's list –publications were set up in 2012)

- Sum of IF (according for year of publish) of the publication constituting scientific achievements (8 publications +1 patent): 26.639 (average 3.330 per one publication), 27.219 (Sum of IF for 2012, average 3.402 per publication); 26.474 (5Y IF; average 3.309 per publication) - patent is not included

- Sum of MNiSW's points of the publications Sum of IF (according for year of publish) of the publication constituting scientific achievements (8 publications+1patent): 245 points (average 30.6 points per publication) – patent is not included

- Sum of IF (according for year of publish) before receiving Ph.D. degree.: 20.696 (average 2.070 per publication), 21.211 (IF for 2012, average 2.121 per publication), 20.670 (5Y IF, average 2.067 per publication)

- Sum of MNiSW's points before receiving Ph.D. degree.: 250 points (average 25.0 points per publication)

- Patent „*Ferrocene derivatives with anticancer activity*" Patent US8426462 B2 (published also as: EP2331555A1, EP2331555B1, EP2331555B8, US20110190391, WO2010000793A1)

- Sum of IF (according to year of publish) after receiving Ph.D. degree.: 51.221 (average 2.561 per publication), 51.482 (IF for 2012, average 2.574 per publication),

50.707 (5Y IF, average 2.535 per publication)

- Sum of MNiSW's points after receiving Ph.D. degree.: 565 points (average 28.25 points per publication)

- Citations number: 263 (Scopus); 247 (Web of Science) + 5 citation of the review in CHC III; citation number without self-citations: 217 (Scopus); 204 (Web of Science) + 5 citation of the review in CHC III;
- Hirsch index h = 8

2 Indication of achievements according to Art. 16 Paragraph 2 of the Act of Laws from 14 March 2003 on Academic Degrees (Journal of Laws no. 65, item 595 as amended).

2.1 Title of scientific achievement

Indication of achievements according to Art. 16 Paragraph 2 of the Act of Laws from 14 March 2003 on Academic Degrees (Journal of Laws no. 65, item 595 as amended). A series of monothematic publications titled "**Ferrocenyl compounds with anticancer activities**".

2.2 List of publications constituting scientific achievements

H1. **Plażuk D**., Zakrzewski J*., Salmain M., Błauż A., Rychlik B. Strzelczyk P., Bujacz A., Bujacz G.

"Ferrocene-biotin conjugates targeting cancer cells: Synthesis, interaction with avidin, cytotoxic properties and the crystal structure of the complex of avidin with a biotin-linker-ferrocene conjugate"

Organometallics **2013**, 32, 20, 5774-5783

IF = 4.145 (current 4.145) (5Y IF=3.653)

MNiSW' points = 40

Citation numbers (without self-citations): 1

My contribution to this work consisted of managing the research project, performing synthesis of all compounds, analyzing the results as well as writing the experimental and discussion parts of the manuscript. My estimated contribution as a percentage is 65%.

H2. Strzelczyk P., Bujacz A*., **Plażuk D**., Zakrzewski J., Bujacz G.

"Structural investigation of the interactions of biotinylruthenocene with avidin"

Chemico-Biological Interactions **2013**, 204, 1, 6-12 (IF za rok 2012)

IF = 2.967 (current 2.967) (5Y IF=2.969)

MNiSW' points = 30

Citation numbers (without self-citations): 0

My contribution to this work consisted of synthesis of biotinylruthenocene and co-editing of the manuscript (discussion of the results). My estimated contribution as a percentage is 30%

H3. **Plażuk D**.*, Rychlik B., Błauż A., Domagała S.

"Synthesis, electrochemistry and anticancer activity of novel ferrocenyl phenols prepared via azide-alkyne 1,3-cycloaddition reaction"

J. Organomet. Chem. 2012, 715, 102-112

IF =2.000 (current 2.000) (5Y IF=1.992)

MNiSW' points = 30

Citation numbers (without self-citations): 3

My contribution to this work consisted of managing the research project, performing synthesis of all compounds, analyzing the results as well as writing the experimental and discussion parts of the manuscript, and editing the response to reviewer comments. My estimated contribution as a percentage is 75%.

H4. **Plażuk D**.*, Wieczorek A., Błauż A., Rychlik B.

„Synthesis and biological activities of ferrocenyl derivatives of paclitaxel"

MedChemComm 2012, 3, 4, 498-501

IF =2.722 (current 2.722) (5Y IF=2.722)

MNiSW' points = no data

Citation numbers (without self-citations): 2

My contribution to this work consisted of managing research project, performing synthesis of paclitaxel derivatives, overseeing the progress of work, analyzing the results as well as writing the manuscript, and editing the response to reviewer comments. My estimated contribution as a percentage is 75%

H5. **Plażuk D**., Zakrzewski J.*, Salmain M.

„Biotin as acylating agent in the Friedel-Crafts reaction. Avidin affinity of biotinyl derivatives of ferrocene, ruthenocene and pyrene and fluorescence properties of 1-biotinylpyrene"

Org. Biomol. Chem. 2011, 9, 2, 408-417

IF =3.696 (current 3.568) (5Y IF=3.490)

MNiSW' points = 35

Citation numbers (without self-citations): 5

My contribution to this work consisted of managing research project, performing synthesis all of compounds, analyzing the results as well as writing the experimental and co-writing of discussion (chemistry) parts of the manuscript. My estimated contribution as a percentage is 70%

H6. **Plażuk D**., Top S., Vessières A., Plamont M.-A., Huché M., Zakrzewski J., Makal A., Woźniak K., Jaouen G*.

"Organometallic cyclic polyphenols derived from 1,2-(α-keto tri or tetra methylene)ferrocene show strong antiproliferative activity on hormone-independent breast cancer cells"

Dalton Trans. **2010**, 39, 32, 7444-7450

IF =3.647 (current 3.806) (5Y IF=3.889)

MNiSW' points = 35

Citation numbers (without self-citations): 5

My contribution to this work consisted of managing research project, performing synthesis all of compounds, analyzing the results and co-writing of the manuscript (comparison of the activity of synthesized compounds to activity of ferrocifene isomers). My estimated contribution as a percentage is 60%

H7. Gormen M., **Plażuk D**., Pigeon P., Hillard E. A., Plamont M.-A., Top S.*, Vessieres A., Jaouen G.* "Comparative toxicity of [3]ferrocenophane and ferrocene moieties on breast cancer cells"

Tetrahedron Lett. **2009**, 51, 1, 118-120

IF =2.660 (current 2.397) (5Y IF=2.376)

MNiSW' points = 30

Citation numbers (without self-citations): 24

My contribution to this work consisted of planning and performing synthesis of two compounds, analyzing the results as well as co-writing of the manuscript (discussion of the results). My estimated contribution as a percentage is 35%

H8. **Plażuk D**., Vessieres A., Hillard E. A., Buriez O., Labbe E., Pigeon P., Plamont M.- A., Amatore C., Zakrzewski J., Jaouen G.*

"A [3]Ferrocenophane Polyphenol Showing a Remarkable Antiproliferative Activity on Breast and Prostate Cancer Cell Lines"

J. Med. Chem., 2009, 52, 15, 4964-4967

IF =4.802 (current 5.614) (5Y IF=5.383)

MNiSW' points = 45

Citation numbers (without self-citations): 44

My contribution to this work consisted of managing research project (planed and realized during "Columbus" FNP fellowship), performing synthesis of all compounds, analyzing the results as well as co-writing of the manuscript (experimental and discussion of the results). My estimated contribution as a percentage is 70%

H9. G. Jaouen, A. Vessieres-Jaouen, D. Plażuk „*Ferrocene derivatives with anticancer activity"* patent US8426462 B2 (published also as: EP2331555A1, EP2331555B1, EP2331555B8, US20110190391, WO2010000793A1)

IF =no data

MNiSW' points = no data

Citation numbers (without self-citations): 0

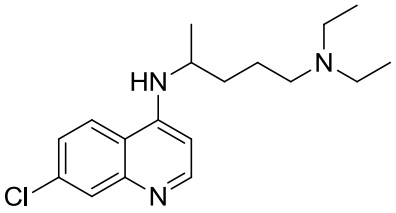
My contribution to this work consisted of managing research project (planed and realized during "Columbus" FNP fellowship), performing synthesis of all compounds as well as co-writing of the patent (an experimental part). My estimated contribution as a percentage is 33%

2.3 Brief description of the scientific goal and the results described in the publications constituting scientific achievements

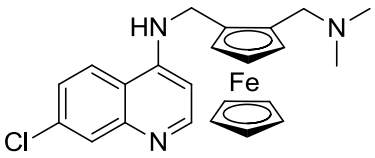
Scientific goal

The search for new, effective, non-toxic and selectively acting compounds possessing anti-cancer properties is still a subject of great interest among scientists. The first and so far

sole organometallic compound, salvarsan (containing a carbon-arsenic bond), was used early in the 20th century to treat syphilis. However, up to today, no single organometallic compound is used as a drug. One of the most promising areas in the search for new organometallic compounds that can be used in chemotherapy are ferrocene derivatives. Currently, according to my knowledge, only one ferrocenyl analog **2** of the antimalarial drug chloroquine **1** is in phase II of clinical trials.[1]

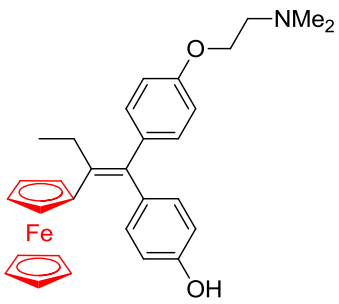


Chloroquine
1



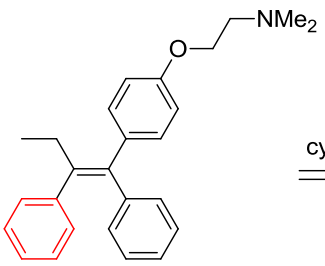
Ferroquine
2

The first mention of the biological properties of ferrocene derivatives, metallocene known since 1951,[2] were already published in the 1970s.[3,4] However, only Prof. Gerard Jaouen's (ENSCP, France) research led to synthesis of the ferrocenyl analog **3** of the well-known anticancer drug tamoxifen **4** (more specifically, its active metabolite – hydroxytamoxifene **5**).



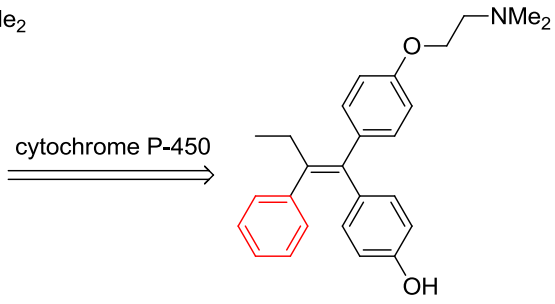
Hydroxiferrocifen

3



Tamoxifen

4



Hydroxytamoxifen
active metabolite

5

The search for anticancer activity of hydroxyferrocifen **3** towards breast cancer cell lines demonstrated that the ferrocenyl analog exhibits much higher activity than tamoxifen. Further investigation showed that compound **3**, in contrast to **4**, is active towards hormone-independent (estrogen-independent) breast cancer cell lines, which constitute ca. 1/3 of all breast cancer

[1] D. Dive, C. Biot, *ChemMedChem*, **2008**, 3, 383-391
[2] T. J. Kealy, P. L. Pauson *Nature* **1951**, 168, 1039
[3] V. J. Fiorina, R. J. Dubois and S. Brynes, *J. Med. Chem.*, **1978**, 21, 393-395
[4] E. I. Edwards, R. Epton and G. Marr, *J. Organomet. Chem.*, **1975**, 85, C23-C25

types[5,6]. Since then continuously growing interest in the search for new organometallic compounds, mainly ferrocene derivatives, as a potentially useful anticancer, antibacterial, and anti-malarial drug candidate has been observed. The main scientific goal of my work is the synthesis of new ferrocenyl compounds exhibiting anticancer activity.

Results

During my Ph.D. study, in 2003, I spent 7 months on a Marie-Curie Fellowship in Prof. Gerard Jaouen's laboratory (L'Ecole Nationale Supérieure de Chimie de Paris, Paris, France). In the course of this fellowship I worked on the synthesis of new organometallic rhenium derivatives (η^5-CpR)Re(CO)$_3$ (R-benzhydryl groups, R=($R^1C_6H_4$)($R^2C_6H_4$)CH-), exhibiting high affinity to estrogen receptors[7]. Encouraged by the interesting results obtained by Prof. Jaouen during his studies on ferrocifene, I decided to synthesize a series of ferrocenyl polyphenols without a double bond between the ferrocenyl and phenolic groups. Despite the lack of conjugate double bonds between the ferrocenyl and hydroxyphenyl group, the prepared compounds showed very interesting anticancer activity.[8,9]. After my return to Poland I continued my investigations into new electrophilic reactions of ferrocene.

After defending my Ph.D. thesis in 2005 I decided to broaden the area of my investigations to cover the synthesis of ferrocenyl compounds exhibiting anticancer activity. In 2006 I received a postdoctoral fellowship in the "Columbus" framework, funded by the Foundation for Polish Science and held in Prof. G. Jaouen's laboratory (ENSCP, Paris, France). During the first step of my investigation I decided to check the influence of the "inflexibility" of the ferrocifenol **6** molecule, due to its stopping the possibility of free rotation around single bonds between ferrocen-C= and C_2H_5-C=, on the anticancer activity of such compounds. This should increase the molecule's interaction with the receptor in comparison to the mother molecule, which must adopt a geometry before interacting with the receptor and, consequently, decrease entropy and make weaker interaction with the receptor. I chose ferrocenophanes as the target molecules. I prepared two series of diphenols, **7** and **8**, and **9** and **10** (**Fig. 1**., only the most active compounds are shown). The desired compounds were prepared in a McMurry

[5] S. Top, J. Tang, A. Vessieres, D. Carrez, D. Provote, G. Jaouen, *Chem. Commun*. **1996**, 955-956
[6] S. Top, B. Dauer, J. Vaissermann, G. Jaouen, *J. Organomet. Chem.*, **1997**, 541, 355-361
[7] D. Plażuk, F. Le Bideau, A. Pérez-Luna, E. Stéphan, A. Vessières, J. Zakrzewski, G. Jaouen, *Appl. Organomet. Chem* **2006**, 20, 3, 168-174
[8] E. A. Hillard, A. Vessières, F. Le Bideau, D. Plażuk, D. Spera, M. Huché, G. Jaouen *ChemMedChem* **2006**, 1, 5, 551-559
[9] D. Plażuk, A. Vessières, F. Le Bideau, G. Jaouen, J. Zakrzewski *Tetrahedron Lett.* **2004**, 45, 28, 5425-5427

reaction starting from corresponding ferrocenyl ketones (**Fig. 2**): [3]ferrocenophan-1-one **11**, [3]ferrocenophan-2-one **12**, 1,2-(*α*-ketotri-(tetra)methylene)ferrocene **13**, **14**, and 4,4'-dihydroxybenzophenone (an example of synthesis of **7** is presented in **Scheme 1.**).

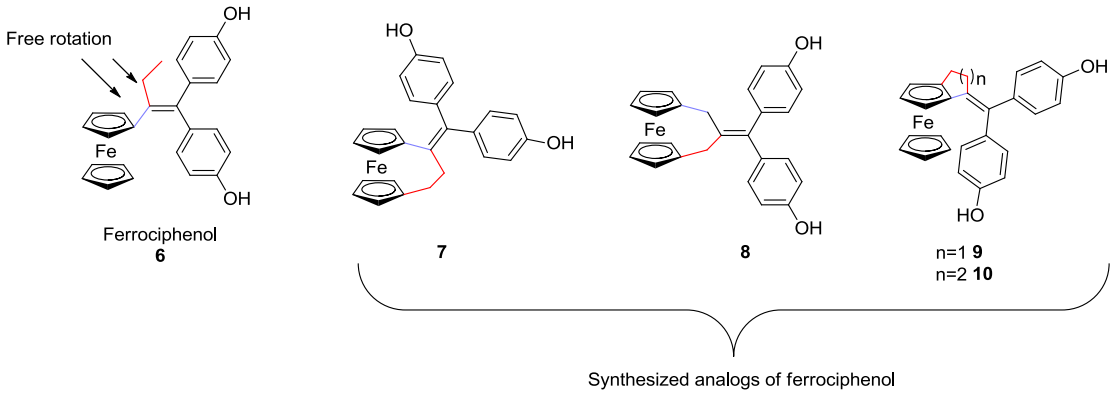


Fig. 1. Ferrociphenol and its synthesized analogs

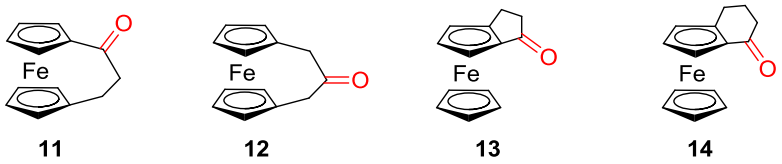
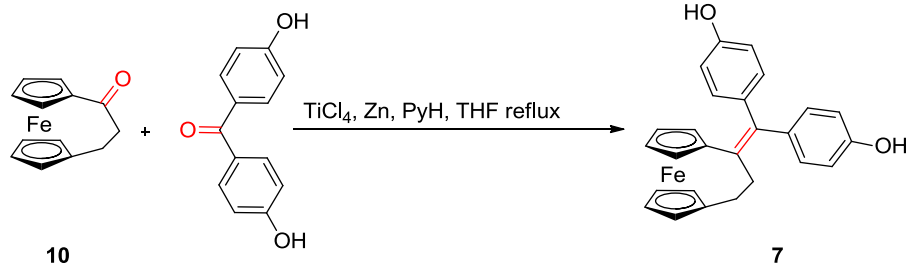


Fig. 2. Ketones used in a McMurry reaction for the synthesis of the compounds described in the papers **H8** i **H6**.



Scheme 1. Synthesis of **7**

Surprisingly, a simple structural modification of **3** led to compound **7**, which exhibited very high antiproliferative activity towards hormone-independent cancer cell lines (for MDA-MB-231 and PC-3 the IC_{50} value was 0.09±0.01 μM and 0.094±0.006 μM, respectively). Compound **8** was 10 times less active towards these cancer cell lines – the IC_{50} value was ca. 30-40% higher than that for ferrocifenol. Both compounds, **7** and **8**, at as low a concentration

as 10 nM exhibited proliferative activity on the hormone-dependent cancer cell lines[10] [**H8**]. Continuing the search for ferrocenophane polyphenols, I synthesized compounds **9** and **10** (**Fig. 1**). It is interesting to note that two different effects were observed for both compounds. An estrogenic effect was observed at a low concentration (10 nM) and a cytotoxic effect was observed at a higher concentration (100 nM) of the compounds. Moreover, it has been shown that compound **10** is more estrogenic than **9**. Synthesized compounds used as the racemic form (the compounds exhibit planar-chirality) demonstrate better interaction with estrogenic receptor β (ERβ), while the level of this receptor in the cancer cell is much lower than that of estrogenic receptor α (ERα). A molecular modeling study and an affinity study to both estrogenic receptors (ERα and ERβ) were carried out in order to explain the differences in the interaction of the synthesized compounds with both of these receptors[11] [**H6**]. Four new derivatives were prepared (**Fig. 3.**) (derivatives of *(R)*- and *(S)*-3-methyl-[3]ferrocenophan-1-one, 2-methyl-[3]ferrocenophan-1-one, and 1,1'-(α-ketopentamethylene)ferrocene) to check the influence of the modification of the alkyl chain in the ferrocenophane moiety on the anticancer activity of the compounds. Introduction of a methyl group in position 2 or 3 led to a decrease in anticancer activity. Moreover, anticancer activity towards breast cancer cell line MDA-MB-231 of *(S)* isomer was 3.5 times lower than that of *(R)*-isomer (IC_{50}=2.7 μM for ***(S)*-15**, and IC_{50}=0.78 μM for ***(R)*-15**). The presence of a methyl group at position 2 also gave a less active compound in comparison to **7** (IC_{50}=0.63 μM)[12] [**H9**].

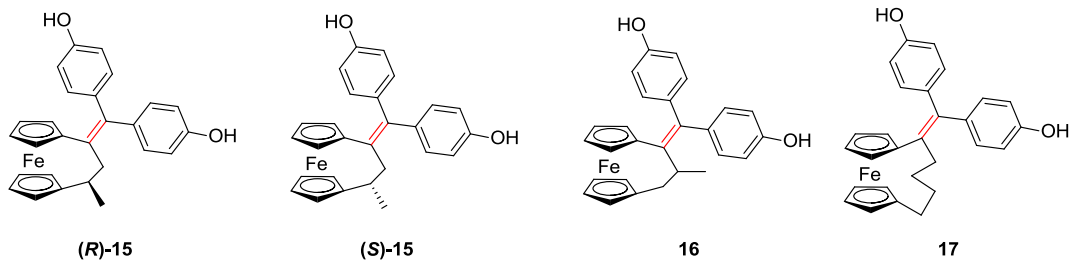


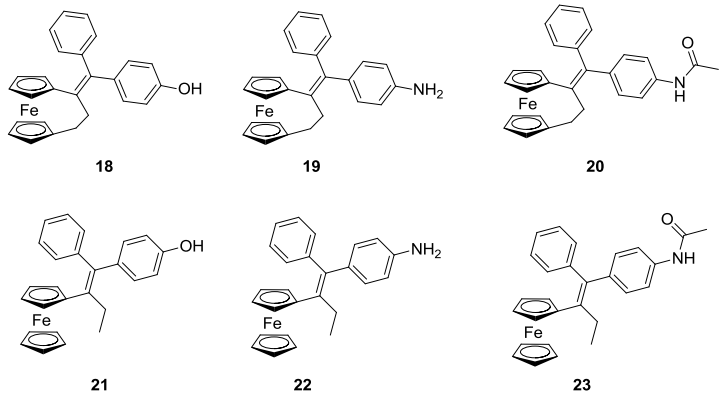
Fig. 3. Structures of selected synthesized and patented compounds[12]

[10] D. Plażuk, A. Vessieres, E. A. Hillard, O. Buriez, E. Labbe, P. Pigeon, M.-A. Plamont, C. Amatore, J. Zakrzewski, G. Jaouen *J. Med. Chem.*, **2009**, 52, 15, 4964-4967 - **[H8]**

[11] D. Plażuk, S. Top, A. Vessières, M.-A. Plamont, M. Huché, J. Zakrzewski, A. Makal, K. Woźniak, G. Jaouen *Dalton Trans.* **2010**, 39, 32, 7444-7450 – **[H6]**

[12] G. Jaouen, A. Vessieres-Jaouen, D. Plazuk, „*Ferrocene derivatives with anticancer activity"* Patent US8426462 B2 (opublikowano również jako: EP2331555A1, EP2331555B1, EP2331555B8, US20110190391, WO2010000793A1) **[H9]**

Continuing work on ferrocenophane, I decided to check the influence of the change of the hydroxy group on the anticancer activity of [3]ferrocenophane and ferrocifenol derivatives. According to the suggested mechanism of anticancer activity, the presence of a substituent, such as an OH group, is crucial for its anticancer activity. Moreover, it is known that an exchange of the OH group to an NH_2 group led to an increase in anticancer activity[13]. Monohydroxy-, monoamino-, and monoacetamide- derivatives of [3]ferrocenophan-1-one **18-20** and, for comparison, derivatives of propionylferrocene **21-23** were prepared in a McMurry reaction. The mixture of *(E)* and *(Z)* isomers were used for the bio-tests.



The IC_{50} values of the synthesized compounds towards the cancer cell line MDA-MB-231 were as follows: 0.47±0.01 μM (**18**); 1.13±0.07 μM (**21**); 0.21±0.03 μM (**19**); 0.86±0.04 μM (**22**); 0.47±0.04 μM (**20**); and 0.65±0.01 μM (**23**). As can be seen, ferrocenophane derivatives (**18-20**) are more cytotoxic that the ferrocene derivatives (**21-23**). It is worth noticing that removing one of the hydroxy groups from **7** led to a large decrease in the cytotoxicity of the monohydroxycompound **18** (IC_{50}=0.47±0.01 μM), in comparison to **7** (IC_{50}=0.09±0.01 μM (**7**))[14] [**H7**].

Continuing my research on the synthesis of new ferrocenyl phenols exhibiting anticancer activity, I decided to synthesize ferrocifenol analogs containing a 1*H*-1,2,3-triazole group (which is isosteric to the ethylene bond), as a linker between the phenyl and ferrocenyl moieties (**Fig.4**).

[13] P. Pigeon, S. Top, O. Zekri, E. A. Hillard, A. Vessieres, M.-A. Plamont, O. Buriez, E. Labbe, M. Huche, S. Boutamine, C. Amatore, G. Jaouen *J. Organomet. Chem.* **2009**, 694, 895-901
[14] M. Gormen, D. Plażuk, P. Pigeon, E. A. Hillard, M.-A. Plamont, S. Top, A. Vessieres, G. Jaouen *Tetrahedron Lett*. **2009**, 51, 1, 118-120 - **[H7]**

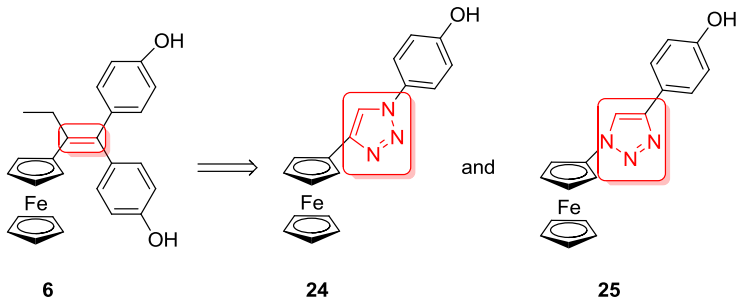
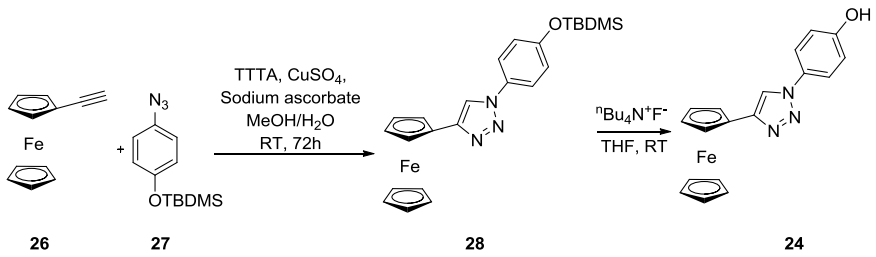


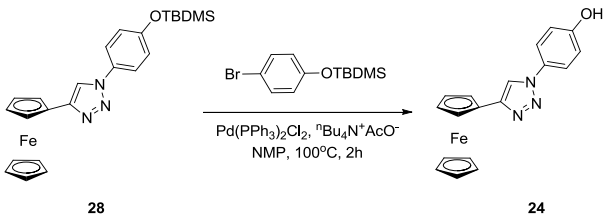
Fig. 4. Ferrocenyl 1*H*-1,2,3-Triazole

A series of compounds type **24**, 4-aryl-1-ferrocenyl-1*H*-1,2,3-triazole, were prepared in two steps. First, in the 1,3-cycloaddition reaction, catalyzed by Cu(I) salts, of ethynylferrocene with corresponding benzyl and phenyl azides, the desired 1*H*-1,2,3-triazoles were formed. In the next step the protective groups were removed. A similar series of compounds type **25**, 1-aryl-4-ferrocenyl-1*H*-1,2,3-triazole, were prepared starting from azidoferrocene and corresponding ethynylarenes. An example synthesis of 4-ferrocenyl-1-(4-hydroxyphenyl)-1*H*-1,2,3-triazole is shown in **Scheme 2**.



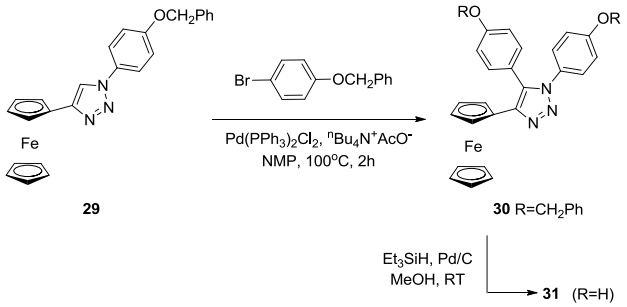
Scheme 2. Synthesis of 4-ferrocenyl-1-(4-hydroxyphenyl)-1*H*-1,2,3-triazole

A key step in this synthesis was to select a protecting group of the hydroxyl group. The first choice, a methyl group (as phenyl methyl ethers), was difficult to remove under typical deprotecting conditions using boron tribromide – the desired phenols were formed in low yield. Because of this troublesome step I decided to use the *tert*-butyldimethylsilyl (TBDMS) group as a protecting group. This group is easily cleaved in reaction with *tetra*-butylammonium fluoride (TBAF). However, in the synthesis of compounds containing two 4-hydroxyphenyl groups at position 1 and 5 of 1*H*-1,2,3-triazole it was necessary to use another protecting group. I found that during C-H arylation of 4-ferrocenyl-1*H*-1,2,3-triazolu **28** with TBDMS as a protecting group, only deprotected phenol **24** was isolated as a sole product (**Scheme 3**).



Scheme 3.

To remove this troublesome step I chose the benzyl moiety as a protecting group. The benzyl group can easily be cleaved in reaction with triethylsilane and Pd/C in methanol solution (**Scheme 4**).



Scheme 4. Synthesis of 4-ferrocenyl-1,5-bis(4-hydroxyphenyl)-1*H*-1,2,3-triazole

Anticancer activity (determined in cooperation with Dr. Błażej Rychlik, Faculty of Biology and Environmental Protection, UŁ) of the synthesized phenols was carried out on two breast cancer cell lines, hormone-dependent MCF-7 and hormone-independent HCC38. All of the synthesized phenols are non-active towards these hormone-dependent cancer cell lines (the most active compounds exhibit IC_{50}=84.0 μM – MCF-7). Compounds type **34** are the most active towards cancer cell lines HCC38 (1-Ary-4-Fc-1*H*-1,2,3-Triazol; Fc-ferrocene; Ary-arene): Ary=4-HOC_6H_4 (IC_{50}=15.3 μM); Ary=3,5-$(HO)_2C_6H_3$ (IC_{50}=22.9 μM). The presence of a benzyl group instead of a phenyl group completely removed the cytotoxic activity of the resulting compounds. It is interesting to note that introducing the second 4-hydroxyphenyl group at position 5 of 1*H*-1,2,3-triazole decreased the cytotoxic activity two-fold (IC_{50}=30.6 μM). Only one of the compounds of type **25** (4-Ary-1-Fc-1*H*-1,2,3-Triazole) exhibited moderate activity (Ary=4-HOC_6H_4 (IC_{50}=48.9 μM)), while the other compounds

were non-active. An electrochemical study of the synthesized phenols did not correlate with their anticancer activity[15] [**H3**].

In the next part of my research on the synthesis of ferrocenyl anticancer active compounds, it seemed interesting to use biotin as a vector that would be able to recognize cancer cells. The use of biotin as a vector should allow to efficiently kill only cancer cells without, or with small, negative effects on healthy cells. It is well-known that cancer cells exhibit overexpression of transporter SMVT (sodium-dependent multivitamin transporter), which is responsible for vitamin (folic acid and biotin) transport to the cells[16,17,18]. Biotin is a growth factor for the cells (including the fast growth of cancer cells), thus it seemed to be a good choice for this study. Among known and widely used biotin conjugates with other molecules, the most popular method of conjugation of biotin is based on the formation of amide and ester bonds. Because such types of bonds can be relatively easily hydrolyzed in the cell, I decided to explore the presence of the carboxylic group in the biotin moiety in Friedel-Crafts acylation. The formed ketones should be resistant to hydrolysis (this would require to break the C-C bond) in the cells. It has been found that under mild conditions (an equimolar amount of trifluoroacetic anhydride and trifluoromethanesulfonic anhydride), biotin can be used as an acylating agent for the acylation of arenes, e.g. metalocenes (ferrocene and ruthenocene) and other reactive arenes (pyrene). Synthesized biotinylketones **32** exhibit a similar to biotin affinity to avidin (IC_{50}=33±2 nM for biotinylferrocene; IC_{50}=24±7 nM for biotin)[19,20] [**H5** and **H2**]. Compound containing one or two linker moieties, -NH(CH_2)CO-, between biotin and ferrocene were also prepared in the Friedel-Crafts acylation of ferrocene with the corresponding acids (biotin-linker-COOH) **33**, **34**. The anticancer activity of the prepared compounds clearly showed a correlation of the cytotoxic activity with the level of expression of the SMVT (correlated with the level of gene *Slc5a6*) (in cooperation with Dr. Błażej Rychlik, Faculty of Biology and Environmental Protection, UŁ).

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[15] D. Plażuk, B. Rychlik, A. Błauż, S. Domagała *J. Organomet. Chem.* **2012**, 715, 102-112 - **[H3]**

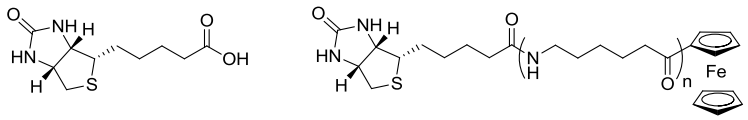
[16] Yang, W.; Cheng, Y.; Xu, T.; Wang, X.; Wen, L.-P., *Eur. J. Med. Chem*. **2009**, 44 (2) 862–868

[17] Bildstein, L.; Dubernet, C.; Couvreur, P., *Adv. Drug Delivery Rev*. **2011**, 63 (1–2) 3– 23

[18] Russell-Jones, G.; McTavish, K.; McEwan, J.; Rice, J.; Nowotnik, D., *J. Inorg. Biochem*. **2004**, 98 (10) 1625– 1633

[19] Plażuk D., Zakrzewski J., Salmain M. *Org. Biomol. Chem.* **2011**, 9, 2, 408-417 - **[H5]**

[20] Strzelczyk P., Bujacz A., Plażuk D., Zakrzewski J., Bujacz G *Chemico-Biological Interactions* **2013**, 204, 1, 6-12 – **[H2]**



biotyna

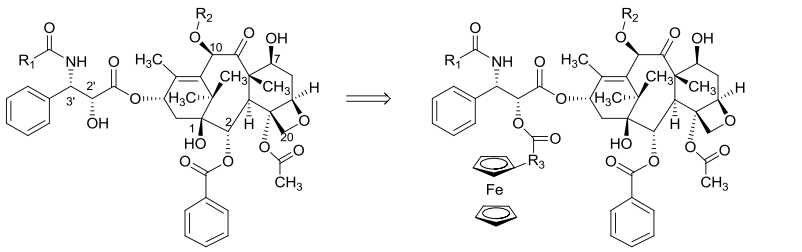
n=0 **32**
n=1 **33**
n=2 **34**

The prepared compounds were selectively active (IC_{50}=13.0±3.6 μM for **32**, IC_{50}=26.2±1.4 μM for **33**, IC_{50}=78.5±1.9 μM for **34**) towards cancer cell lines exhibiting overexpression of the SMVT (SW620 cancer cell line), whereas they were not active towards cancer cell lines with a low level of SMVT (COLO-205 and HCT116)[21] [**H1**]. The X-ray structure of the complexes of avidin–biotin-(linker)$_2$-ferrocene and avidin-bitinylruthenocene were determined (despite the many attempts we were unable to obtain crystals of complex **32**-awidn that would be suitable for X-ray analysis)[21,20] [**H1** and **H2**].

I was also interested in determining the influence of the presence of a ferrocenyl group on the cytotoxic activity of known inhibitors of depolymerization of the microtubule, e.g. paclitaxel **35** and docetaxel **36**, towards two different types of cancer cell lines that were resistant to selected chemotherapeutics (in cooperation with Dr. Błażej Rychlik, Faculty of Biology and Environmental Protection, UŁ). A panel of four cancer cell lines, SW620 with different levels of transport proteins ABC, were selected for this study: cancer cell lines resistant to doxorubicin (SW620); etoposide (SW620E); methotrexate (SW620M); and vincristine (SW620V). The level of expression of the ABCB1 protein in the selected cell lines was as follows: SW620V>>SW620D>SW620E>>SW620M=SW620. The ferrocenyl group was introduced to the taxane moiety by selective 2'-*O*-acylation of paclitaxel and docetaxel by selected ferrocenecarboxylic acids using DIC (N,N'-diisopropylcarbodiimide) as a coupling agent. It is worth noticing that synthesized ferrocenyl conjugates with taxanes exhibit the same or much higher cytotoxicity in comparison to the pattern compounds (the range of IC_{50} is 0.388 up to 3.07 μM). Moreover, these compounds were active towards cancer cell lines that were resistant to drugs (the most active compounds: IC_{50}=16.5 μM (SW620D), docetaxel IC_{50}=35.16 μM, paclitaxel – non-active; IC_{50}=1.56 μM (SW620E), docetaxel IC_{50}=21.27 μM, paclitaxel – non-active; IC50=0.701 μM (SW620M), docetaxel IC_{50}=0.259 μM, paclitaxel IC_{50}=6.38 μM)[22] [**H4**]. The synthesized compounds were more efficient towards the cancer cell lines with a low level of the ABCB1 protein (SW620 and SW620M). Most of the docetaxel conjugates were

[21] Plażuk D., Zakrzewski J., Salmain M., Błauż A., Rychlik B. Strzelczyk P., Bujacz A., Bujacz G. *Organometallics* **2013**, 32, 20, 5774-5783 - **[H1]**
[22] Plażuk D., Wieczorek A., Błauż A., Rychlik B *MedChemComm* **2012**, 3, 4, 498-501 - **[H4]**

less active than the mother compound. However, one of the docetaxel-ferrocene conjugates was 13.6 times more active than docetaxel against cancer cell lines with a moderate level of the ABCB1 protein (SW620E).



Paclitaxel: 35 R_1=Ph, R_2=Ac
Docetaxel: 36 R_1=^{t}BuO, R_2=H

Ferrocene coniugates with paclitaxel and docetaxel

3. Other scientific publications and achievements

3.1. Other publications

Below is a list of other publications, which are not part of the achievements outlined in Section 2.2

List of publications published before receiving Ph.D. degree

P1. **Plażuk D.**, Zakrzewski J.

"Friedel-Crafts reaction of dimethyl 2-oxopropylphosphonate and diethyl 2,2-diethoxyethylphosphonate with electron-rich arenes"

Phosphorus, Sulfur and Silicon and the Related Elements **2005**, 180, 2, 2709-2715

IF =0.564 (current 0.601) (5Y IF=0.661)

MNiSW' points = 15

Citation numbers (without self-citations): 1

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as co-writing of the manuscript (an experimental part and discussion of results). My estimated contribution as a percentage is 70%

P2. **Plażuk D.**, Zakrzewski J.*, Rybarczyk-Pirek A., Domagała S.

"Ferrocenecarbothioamide and N-ethoxycarbonylferrocenecarbothioamide: Synthesis, structure and application in synthesis of 2,4-diferrocenylthiazole"

J. Organomet. Chem. **2005**, 690, 19, 4302-4308

IF =2.025 (current 2.000) (5Y IF=1.992)

MNiSW' points = 30

Citation numbers (without self-citations): 8

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as co-writing of the manuscript (an experimental part and discussion of results). My estimated contribution as a percentage is 70%

P3. **Plażuk D**., Warkentin J*., Werstiuk N. H.

"Reactions of allyloxy(methoxy)carbene in solution. Carbene rearrangement and Claisen rearrangement of the carbene dimer"

Tetrahedron **2005**, 61, 24, 5788-5796

IF =2.610 (current 2.803) (5Y IF=2.899)

MNiSW' points = 30

Citation numbers (without self-citations): 6

My contribution to this work consisted of performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as co-writing of the manuscript (an experimental part and discussion of results). My estimated contribution as a percentage is 60%

P4. Rybarczyk-Pirek A. J., **Plazuk D.,** Zakrzewski J.

„5-Ferrocenyl-5-methyltetrahydrofuran-2-one, the product of the Friedel-Crafts reaction of ferrocene with γ-methylenebutyrolactone"

Acta Crystallographica Section E: Structure Reports Online **2005**, 61 (4), m644-m646

IF =0.581 (current – no data) (5Y IF=0.278)

MNiSW' points = no data

Citation numbers (without self-citations): 0

My contribution to this work consisted of performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript. My estimated contribution as a percentage is 60%

P5. **Plażuk D.,** Vessières A., Le Bideau F., Jaouen G., Zakrzewski J.

"Synthesis of benzyl- and benzhydrylferrocenes via Friedel-Crafts alkylation of ferrocene. Access to ferrocenyl bisphenols with high affinities for estrogen receptors"

Tetrahedron Lett. **2004**, 45, 28, 5425-5427

IF =2.484 (current 2.397) (5Y IF=2.899)

MNiSW' points = 30

Citation numbers (without self-citations): 6

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part, and co-writing a discussion part of the manuscript. My estimated contribution as a percentage is 70%

P6. Plażuk D., Rybarczyk-Pirek A., Zakrzewski J.

„β-Ferrocenyl-α,β-unsaturated phosphonates and sulfones"

J. Organomet. Chem. **2004**, 689, 7, 1165-1171

IF =1.905 (current 2.000) (5Y IF=1.992)

MNiSW' points = 30

Citation numbers (without self-citations): 4

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript. My estimated contribution as a percentage is 70%

P7. **Plażuk D.,** Zakrzewski J.

"Acylation of Ferrocene and a 1,1′-Diphosphaferrocene with Acyl Trifluoroacetates in the Presence of Trifluoromethanesulfonic (Triflic) Acid or Some Metal Triflates"

Synthetic Commun.**2004**, 34, 1, 99-107

IF =0.965 (current 1.060) (5Y IF=1.082)

MNiSW' points = 20

Citation numbers (without self-citations): 7

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript. My estimated contribution as a percentage is 70%

P8. **Plażuk D**., Janowska I., Kłys A., Hameed A., Zakrzewski J.

„A convenient synthesis of conjugated ω-arylpolyenals via Wittig reaction with (1,3-dioxan-2-yl-methyl)triphenylphosphonium bromide/sodium hydride"

Synthetic Commun.**2003**, 33, 3, 381-385

IF =0.853 (current 1.060) (5Y IF=1.082)

MNiSW' points = 20

Citation numbers (without self-citations): 4

My contribution to this work consisted of performing synthesis of ferrocenyl, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript. My estimated contribution as a percentage is 40%

P9. **Plażuk D**., Zakrzewski J.

„Friedel-Crafts type reaction of ferrocene with β-ketoesters"

J. Org. Chem. **2002**, 67, 24, 8672-8674

IF =4.564 (5Y IF=4.135) (IF for 2012)

MNiSW' points = 35

Citation numbers (without self-citations): 7

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript. My estimated contribution as a percentage is 60%

P10. Plażuk D., Kłys A., Zakrzewski J., Rybarczyk-Pirek A., Olszak T.A.

„Direct acetoacetylation of ferrocene and a 1,1′-diphosphaferrocene"

Organometallics **2001**, 20, 22, 4448-4450 (podano aktualny IF)

IF =4.145 (5Y IF=3.653) – current IF

MNiSW' points = 40

Citation numbers (without self-citations): 7

My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental, and co-writing a discussion parts of the manuscript. My estimated contribution as a percentage is 70%

List of other publications published after receiving Ph.D. degree

PP1. Wieczorek A., **Plażuk D**., Zakrzewski J*., Makal A., Woźniak K.

"Synthesis and unusual ring transformation of 1-acyl-3-(ferrocenylmethylidene)-piperazine-2,5-diones"

J. Organomet. Chem. **2013**, 745-746, 373-378

IF = 2.000 (current 2.000) (5Y IF=1.992)

MNiSW' points = 30

Citation numbers (without self-citations): 0

My contribution to this work consisted of managing research project, overseeing the progress of the synthesis done by mgr Anna Wieczorek, analyzing the results as well as writing discussion part of the manuscript. My estimated contribution as a percentage is 40%

PP2. Wrona-Piotrowicz A., **Plażuk D**., Domagała S., Zakrzewski J.

„Synthesis of ferrocenyl- and pyrenyl-thioimidates of terminal acetylenes. "Click" reaction with 3 '-azido-3 '-deoxythymidine affording redox-active and fluorescent thymidine conjugates”

Arkivoc **2012**, 6, 412-420

IF =1.057 (current 1.057) (5Y IF=1.206)

MNiSW’ points = 20

Citation numbers (without self-citations): 1

My contribution to this work consisted of managing of part of the research project, performing 1,3-cycloaddition reactions, co-writing an experimental part and discussion of results parts of the manuscript . My estimated contribution as a percentage is 40%

PP3. Plażuk D., Zakrzewski J., Nakatani K., Makal A., Woźniak K., Domagała S.

„Electronic and molecular structures and bulk second-order nonlinear optical properties of ferrocenyl ynones”

RSC Advances **2012**, 2, 8, 3512-3524

IF =2.562 (current 2.562) (5Y IF=2.567)

MNiSW’ points = no data

Citation numbers (without self-citations): 2

My contribution to this work consisted of managing research project, performing DTF calculations, analyzing the results as well as writing an experimental part of the manuscript and co-writing discussion of results part of the manuscript. My estimated contribution as a percentage is 40%

PP4. Makal A. M., **Plażuk D**., Zakrzewski J., Misterkiewicz B., Woźniak K.

„Experimental charge density analysis of symmetrically substituted ferrocene derivatives”

Inorg. Chem. **2010**, 49, 9, 4046-4059

IF =4.326 (current 4.593) (5Y IF=4.551)

MNiSW’ points = 40

Citation numbers (without self-citations): 8

My contribution to this work consisted of synthesis of one compounds as well as co-writing of the part of the manuscript (discussion of results). My estimated contribution as a percentage is 15%

PP5. **Plażuk D.,** Zakrzewski J., Nakatani K.
„New ferrocenylpyridinium salts with bulk second-order nonlinear optical properties"
Polish Journal of Chemistry **2009**, 83, 12, 2105-2111
IF =0.523 (current – no data) (5Y IF=0.523)
MNiSW' points = 15
Citation numbers (without self-citations): 0
My contribution to this work consisted of managing research project, performing synthesis of all compound as well as co-writing of the part of the manuscript (an experimental part and discussion of results). My estimated contribution as a percentage is 65%

PP6. **Plażuk, D**., Zakrzewski J.
„Friedel-Crafts acylation of ferrocene with alkynoic acids"
J. Organomet. Chem. **2009**, 694, 12, 1802-1806
IF =2.347 (current 2.000) (5Y IF=1,992)
MNiSW' points = 30
Citation numbers (without self-citations): 6
My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirm the structure of the products, analyzing the results as well as writing an experimental part of the manuscript and co-writing the discussion of results. My estimated contribution as a percentage is 50%

PP7. **Plażuk D**., Zakrzewski J., Rybarczyk-Pirek A.
„Resolution and absolute configuration of dimethyl hydroxy-(ferrocenylmethyl)phosphonate"
Tetrahedron Asymmetry **2006**, 17, 13, 1975-1978
IF =2.468 (current 2.115) (5Y IF=2.143)
MNiSW' points = 30
Citation numbers (without self-citations): 3
My contribution to this work consisted of managing research project, performing synthesis of all compounds, confirmation of the configuration of the products as well as writing an

experimental part of the manuscriptand co-writing discussion of results. My estimated contribution as a percentage is 70%

PP8. Palusiak M., **Plażuk D**., Zakrzewski J.
"2-[3-Dicyanomethylene-2-(3-methoxybenzylidene)indan-1-ylidene]malononitrile"
Acta Crystallographica Section E: Structure Reports Online **2006**, 62, 7, o3052-o3053
IF =0.567 (current – no data) (5Y IF=0.567)
MNiSW' points = no data
Citation numbers (without self-citations): 1
My contribution to this work consisted of performing synthesis of compound, preparation of the crystal suitable for X-ray analysis, co-writing an experimental part of the manuscript (synthesis of titled compound). My estimated contribution as a percentage is 50%

PP9. Plażuk D., Zakrzewski J., Rybarczyk-Pirek A.
"Diastereoselective addition of dimethyl phosphite to 3,3′,4,4′-tetramethyl-1,1′-diphosphaferrocene-2-carboxaldehyde"
J. Organomet. Chem. **2006**, 691, 13, 3098-3102
IF =2.332 (aktualnie 2.000) (5Y IF=1.992)
MNiSW' points = 30
Citation numbers (without self-citations): 4
My contribution to this work consisted of managing research project, performing synthesis of all compounds as well as writing an experimental part of the manuscript and co-writing discussion of results. My estimated contribution as a percentage is 70%

PP10. Hillard E. A., Vessières A., Le Bideau F., Plażuk D., Spera D., Huché M., Jaouen G.
"A series of unconjugated ferrocenyl phenols: Prospects as anticancer agents"
ChemMedChem **2006**, 1, 5, 551-559
IF =2.835 (5Y IF=3.075) – current IF
MNiSW' points = 35
Citation numbers (without self-citations): 48
My contribution to this work consisted of managing research project, performing synthesis of all compounds, writing an experimental part of the manuscript and co-writing discussion of results. My estimated contribution as a percentage is 40%

PP11. Plażuk D., Le Bideau F., Pérez-Luna A., Stéphan E., Vessières A., Zakrzewski J., Jaouen G.

„Synthesis of cyclopentadienyltricarbonylrhenium substituted benzhydryl species and oestrogen receptor binding properties"

Applied Organometallic Chemistry **2006**, 20, 3, 168-174

IF =1.233 (current 2.011) (5Y IF=1,922)

MNiSW' points = 30

Citation numbers (without self-citations): 4

My contribution to this work consisted of managing research project, performing synthesis of all compounds, analyzing the results as well as writing the part of the manuscript (an experimental part and discussion of results). My estimated contribution as a percentage is 50%

PP12. **Plażuk D**., Zakrzewski J.

„One-step synthesis of aryl-capped vinylferrocenes from ferrocene and aryl-substituted oxiranes"

J. Organomet. Chem. **2006**, 691, 3, 287-290

IF =2.332 (current 2.000) (5Y IF=1.992)

MNiSW' points = 30

Citation numbers (without self-citations): 3

My contribution to this work consisted of managing research project, performing synthesis of all compounds, analysis of the results as well as writing an experimental part of the manuscript and co-writing discussion of results. My estimated contribution as a percentage is 70%

Reviews

PP13. Warkentin, J., **Plazuk, D.**

„Thirranes and Thirrenes" in Comprehensive Heterocyclic Chemistry 3, **2008**, 1, 05, 299-389

My contribution to this work consisted of collecting and managing of the publications about synthesis and reactivity of thiiranes and thirrenes, and writing a corresponding part of the manuscript. My estimated contribution as a percentage is 45%

3.2 Participation in conferences

The results were presented at international conferences and conferences abroad and at Polish conferences as posters and oral communications. Below is a list of the most important conferences:

List of attendance in international and conferences abroad

After receiving the Ph.D. degree

1) **Damian Plażuk**, Anna Wieczorek, Andrzej Błauż, Aleksandra Żal, Błażej Rychlik
"*Synthesis, Anticancer Activities and Tubulin Interactions of Ferrocenyl Analogues of Paclitaxel*"
18th European Symposium on Organic Chemistry, 7-12 Lipca 2013, Marsylia, Francja, - **poster**

2) Anna Wieczorek, **Damian Plażuk,** Janusz Zakrzewski, Anna Makal, Krzysztof Woźniak
"*Synthesis and unusual ring transformation of 1-acyl-3-(ferrocenylmethylene)-piperazine-2,5-diones*"
18th European Symposium on Organic Chemistry, 7-12 Lipca 2013, Marsylia, Francja – **poster**

3) **Damian Plażuk**, Anna Wieczorek, Andrzej Błauż, Aleksandra Żal, Błażej Rychlik
"Organometallic inhibitors of polymerization of tubulin. Synthesis of a ferrocenyl analogs of paclitaxel"
Role of MDR proteins in pharmacokinetics and toxicology 03-07.09.2013, Ryn, Polska – **poster**

4) Anna Wieczorek, **Damian Plażuk**, Andrzej Błauż, Aleksandra Żal, Błażej Rychlik
"Anticancer activities and tubulin interactions of ferrocenyl analogs of paclitaxel"
Role of MDR proteins in pharmacokinetics and toxicology 03-07.09.2013, Ryn, Polska – **poster**

5) **Damian Plażuk**; Michael Salmain; Błażej Rychlik; Andrzej Błauż; Janusz Zakrzewski
"*Biotin as Acylating Agents in The Friedel-Crafts Reaction. Reactivity, Avidin Affinity and Anticancer Activity of Ferrocenyl Compounds* "
XXV International Conference on Organometallic Chemistry, 2-7 września, 2012, Lizbona, Portugalia – **poster**

6) **Damian Plażuk**; Michael Salmain; Błażej Rychlik; Andrzej Błauż; Janusz Zakrzewski
"*Biotin and its derivatives as acylating agents in the Friedel-Crafts reaction. Avidin Affinity, anticancer activity of ferrocenyl compounds and fluorescence properties of pyrene derivatives"*
25th International Symposium on the Organic Chemistry of Sulfur, 24-29 czerwca, 2012, Częstochowa, Polska – **oral communication**

7) **Damian Plażuk** Michael Salmain; Błażej Rychlik; Andrzej Błauż; Janusz Zakrzewski
"*Biotin and its derivatives as acylating agents in the Friedel-Crafts reaction. Avidin Affinity, anticancer activity of ferrocenyl compounds and fluorescence properties of pyrene derivatives"*
Łódź-Giessen Chemistry Workshop 10-14 października, 2012, Łódź – **oral communication**

8) **Damian Plażuk**, Michael Salmain; Błażej Rychlik; Andrzej Błauż; Janusz Zakrzewski
"*Biotin and its derivatives as acylating agents in the Friedel-Crafts reaction. Avidin Affinity, anticancer activity of ferrocenyl compounds and fluorescence properties of pyrene derivatives"*
6th International Symposium on Bioorganometallic Chemistry, 8-12 Lipca 2012, Toronto, Kanada – **oral communication**

9) **Damian Plażuk**, Anna Wieczorek, Błażej Rychlik, Andrzej Błauż
„Synthesis and antitumor activities of ferrocenyl derivatives of Paclitaxel"
ACS National Meeting 25-29 Marzec 2012, San Diego, USA – **poster**

10) Robert Forster, Colm Mallon, Bincy Jose, Lynda Cosgrave, Lorraine Blackmore, Zoe Stack, **Damian Plażuk**, Marc Devocelle, Niamh Moran, Sarah O'Neill, Emily Reddy, and Tia E. Keyes
"Peptide functionalised metal complexes for Raman and fluorescence cellular imaging"
Photonics Ireland Conference 2011 Wrzesień, Dublin, Irlandia 2011 – **oral communication**

11) Janusz Zakrzewski, **Damian Plażuk**, Michèle Salmain, Keitaro Nakatani
„Friedel-Crafts acylation in the synthesis of novel SHG-active molecular materials and bioprobes"
Les Journées d'Automne 2010 du GFP2P, 17-18 novembre, 2010, Cachan, Francja ; **poster**

12) Julia B. Heilmann, **Damian Plażuk**, Anne Vessieres, Gerard Jaouen
"Structural Modifications of Ferrocifens: Synthesis and Biochemical Results on Novel Brest-cancer Drug Candidate"
2nd German French Congress in Organic and Biomolecular Chemistry, Calvi (Corsica, France) 30 czerwiec 5- lipiec 2007 – **poster**

Before receiving the Ph.D. degree

13) **Damian Plażuk**, Janusz Zakrzewski
"Novel electrophilic C-C bond formin reactions of rerrocene and 1,1'-diphosphaferrocene"
XIVth FECHEM Conference on Organometallic Chemistry, 2-7 IX 2001, Gdańsk – **oral communication**

14) **Damian Plażuk,** Janusz Zakrzewski
"Novel Friedel-Crafts-Type reactions of ferrocene"
VIIth Regional Seminar of Ph.D.-Students on Organometallic and Coordination Chemistry, 3-7 III 2002, Bad Kösen, Niemcy – **oral communication**

15) **Damian Plażuk**, Janusz Zakrzewski
"Novel electrophilic reactions of ferrocene"
VIIIth Regional Seminar of Ph.D.-Students on Organometallic and Coordination Chemistry, 29 IX - 3 X 2003, Hrubá Skála, Czechy – **oral communication**

List of attendance in Polish conferences
After receiving the Ph.D. degree

16) Arkadiusz Kłys, **Damian Plażuk**
„Ferrocenylowe pochodne kochicyny-synteza oraz właściwości przeciwnowotworowe"
56 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Siedlce 16-20 września 2013 – **poster**

17) Rafał Flamholc, Janusz Zakrzewski, **Damian Plażuk**, Remi Metivier, Keitaro Nakatami
„Synteza nowych fluorescencyjnych pochodnych pirenu"

56 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Siedlce 16-20 września 2013 – **poster**

18) Anna Wieczorek, **Damian Plażuk**, Janusz Zakrzewski, Anna Makal, Krzysztof Woźniak
„Synteza i przegrupowanie 1-acylo-3-(ferrocenylometyleno)-piperazyno-2,5-dionów”
56 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Siedlce 16-20 września 2013 - **poster**

19) **Damian Plażuk**, Anna Wieczorek, Andrzej Błauż, Aleksandra Żal, Błażej Rychlik
„Synteza, właściwości przeciwnowotworowe oraz oddziaływanie z tubuliną ferrocenylowych analogów paklitaxelu”
56 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Siedlce 16-20 września 2013 – **poster**

20) **Damian Plażuk**, Anna Wieczorek, Błażej Rychlik, Andrzej Błauż
„*Synteza oraz aktywność przeciwnowotworowa ferrocenylowych analogów Taxolu”*
XIV Ogólnopolskie Sympozjum sekcji Chemii Heteroorganicznej PTChem, Łódź 18 listopada 2011 – **poster**

21) **Damian Plażuk**, Błażej Rychlik, Andrzej Błauż
„*Zastosowanie reakcji cykloaddycji azydowo-alkinowej Huisgena w syntezie nowych ferrocenylowych polifenoli oraz badanie ich właściwości przeciwnowotworowych*”
XIV Ogólnopolskie Sympozjum sekcji Chemii Heteroorganicznej PTChem, Łódź 18 listopada 2011 - **poster**

22) **Damian Plażuk**, Anna Wrona-Piotrowicz, Sławomir Domagała, Janusz Zakrzewski
„*Ferrocenylowe i pirenylowe tioimidany zawierające terminalne grupy acetylenowe: synteza i reakcje kliknięcia z AZT”*
XIV Ogólnopolskie Sympozjum sekcji Chemii Heteroorganicznej PTChem, Łódź 18 listopada 2011 - **poster**

23) **Damian Plażuk**, Janusz Zakrzewski, Błażej Rychlik, Michele Salmain
„*Biotyna i jej analogi jako odczynniki acylujące w reakcji Friedela-Craftsa ferrocenu, rutenocenu oraz pirenu. Powinowactwo koniugatów do awidyny, właściwości cytotoksyczne*

pochodnych ferrocenowych, oraz fluorescencja pochodnych pirenowych"
54 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Lublin, 18-22 września 2011 – **poster**

24) Sylwia Belica, Bartłomiej Pałecz, **Damian Plażuk,** Janusz Zakrzewski
„Termodynamika oddziaływań awidyny z biotyną oraz jej pochodnymi"
54 Zjazd Naukowy Polskiego Towarzystwa Chemicznego i Stowarzyszenia Inżynierów i Techników Przemysłu Chemicznego, Lublin, 18-22 września 2011 - **poster**

25) **Damian Plażuk**, Janusz Zakrzewski, Michèle Salmain
„*Bezpośrednie Biotynylowanie Ferrocenu, Rutenocenu i Pirenu w Reakcji Friedela-Craftsa*"
Postępy w Chemii Związków Heteroorganicznych. XIII Ogólnopolskie Sympozium Sekcji Chemii Heteroorganicznej PTChem, Łódź, 19 listopada 2010 r., **poster**

26) **Damian Plażuk**, Janusz Zakrzewski
„*Acylowanie Friedla-Craftsa ferrocenu nienasyconymi kwasami karboksylowymi*"
VIII Ogólnopolskie Sympozjum Chemii Organicznej, Łódź, 10-12 kwietnia 2008 **- poster**

27) **Damian Plażuk**, Janusz Zakrzewski, Anna Makal, Krzysztof Woźniak
„*Nieoczekiwane epoksydowanie 2-(dicyjanometylideno)-1,1'-trimetylenoferrocenu tlenem atmosferycznym*"
Postępy w Chemii Związków Heteroorganicznych. XI Ogólnopolskie Sympozium Sekcji Chemii Heteroorganicznej PTCh, Łódź, 27 listopada 2008 r., **poster**

Before receiving the Ph.D. degree

28) **Damian Plażuk**, Janusz Zakrzewski, Agnieszka Rybarczyk-Pirek
"α-Hydroksyfosfoniany ferrocenylowe i 1,1'-difosfaferrocenylowe"
XLVIII Zjazd PTChem i SIiTPChem, Poznań, 18-22.09.2005, **poster**

29) **Damian Plażuk**, Janusz Zakrzewski, Agnieszka Rybarczyk-Pirek
„*Fosfoniany ferrocenylowe i 1,1'-difosfaferrocenylowe*"
Postępy w Chemii Związków Heteroorganicznych. VIII Ogólnopolskie Sympozium Sekcji Chemii Heteroorganicznej PTChem, Łódź, 24 listopada 2005 r., **poster**

30) Anna Wrona, **Damian Plażuk**, Janusz Zakrzewski, Agnieszka Rybarczyk-Pirek, Marcin Palusiak, Sławomir Domagała
„*Ferrocenylowe tioamidy i tiazole*"
XLVIII Zjazd PTChem i SIiTPChem, Poznań, 18-22.09.2005 – **poster**

31) **Damian Plażuk**, Janusz Zakrzewski
"Friedel-Crafts alkenylation of ferrocene with arylepoxide"
IX th Regional Seminar of PhD-students on Organometallic and Organophosphorous Chemistry; Szklarska Poręba, Poland, April 10-14, 2005 – **oral communication**

32) **Damian Plażuk**, Janusz Zakrzewski
VIth Polish Symposium of Organic Chemistry, 18-20 IV 2002, Łódź

3.3. Awards for scientific activity

- 2010 – 2013 – scholarship from the Polish Ministry of Science and Higher Education for outstanding young scientists
- 2011 - Team Award of the Rector of the first degree for a series of publications
- 2006 - Team Award of the Rector of the first degree for a series of publications
- 2006 - distinction for the best PhD thesis in organic chemistry - PTCh and Sigma-Aldrich company award

3.4. Internships in foreign or domestic research and academic centers

- **2009-2010** - Ireland, National Centre for Sensor Research, Dublin City University, Dublin, 12 months - post-doc - prof. Tia Keyes

- **2006-2007** - France, Laboratoire de Chimie Organométallique, Ecole Nationale Superieure de Chimie de Paris (ENSCP), Paryż, 12 month –post-doc in the framework of "Columbus" fellowship (founded by Foundation for Polish Science - FNP) – prof. Gerard Jaouen

- **2004 -** Canada, McMaster University, Hamilton, Ontario, 4 month - Fellowships in prof. J. Warkentin's laboratory

- **2003** - France, Laboratoire de Chimie Organométallique, Ecole Nationale Superieure de Chimie de Paris (ENSCP), Paris, 7 months - Marie-Curie Fellowship, prof. Gerard Jaouen

3.5. Participation in scientific grants

Participation in scientific grants as a project leader

- **2013-2016** „*Organometallic inhibitors of tubulin polymerisation. Synthesis, anticancer activities and tubulin affinities*" **OPUS (775.700 PLN)** – National Science Centre, project no 2012/05/B/ST5/00300, Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **Project leader**

- **2011-2013** „*Synthesis and investigation of a New ferrocenyl compounds of potential anticancer activities*" **Habilitation grant (137.800 PLN)** – National Science Centre, project no N N204 185640, Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **Project leader**

- **2010-2011** „*Synthesis and activity of new organometallic compounds with potential application in cancer chemiotherapy*" – **Grant Iuventus Plus (200.000 PLN, Edition 2010)** – MNiSW, project no IP2010 032270 - Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **Project leader**

- **2007-2008** Supporting grant, Foundation for Polish Science (40.000 PLN), Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **Project leader**

Participation in scientific grants as a investigator/main investigator

- **2011-2014** – Project 2011/01/B/ST5/03933 –„*Synthesis and investigation of reactivity and anticancer activity of selected 2,5-diketopiperazines containing ferrocenyl group*" National Science Centre, Department of Organic Chemistry, Faculty of

Chemistry, University of Łódź, The nature of participation: **Main investigator**

- **2009-2012** - Project 1546/B/H03/2009/36 "Application of the „click" chemistry and Mitsunobu reaction for synthesis of bioconjugates" – Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **investigator**

- **2006-2009** Project PBZ-KBN-118/T09/12 " *Elaboration of methods of preparation of molecular and macromolecular organometallic compounds as new materials or precursors with special properties, in particular, electronic, optoelectronic, magnetic, ceramic and biomaterials"* Department of Organic Chemistry, Faculty of Chemistry, University of Łódź, The nature of participation: **investigator**

3.6. Other teaching, scientific and organization activities

I reviewed scientific papers in international journals as follows:

Molecules
Journal of Organometallic Chemistry

I reviewed scientific project applications for:

The National Centre for Research and Development
Foundation for Polish Science

Teaching activity

Since 2005 I am a lecturer on all years of study. I am participating in the following activities for all years students of Faculty of Chemistry and 1st year students of Faculty of Biology and Environmental Protection UŁ:
organic chemistry laboratory,
inorganic chemistry laboratory
seminars

Scientific assistance to students

I have been a promoter or supervisor of master's theses and undergraduate work. I was a promoter / supervisor of 9 works.

Scientific assistance for Ph.D. students

I am a co-promoter of the Ph.D. thesis titled “Synthesis and biological activities of ferrocenyl analogs of polymerization inhibitors of tubulin” of M.Sc. Anna Wieczorek.

Achievements and initiatives to improve the teaching process:

I am co-author of the syllabus of the organic chemistry laboratory for 1st-year MSc students.

I am co-author of the manual for the organic chemistry laboratory for 2nd- and 3rd-year B.Sc. students

The activities of popular science

I am a lecturer at the Academy of Interesting Chemistry, at Department of Chemistry, University of Lodz. I gave a lecture of popular science for high school students in 2011.

Participation in committees

I am a member of the Faculty Committee on Research

Assistance in the organization of scientific conferences

The Sixth International Conference on Heteroatom Chemistry; Łódź 22-27.06.2001

Membership in scientific organizations

I am a member of:

Polish Chemical Society

American Chemical Society

Club of Foreign Fellows FNP