Author's review of her research

(annex 2b)

PhD Magdalena Małecka

Department of Theoretical and Structural Chemistry
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2014

1. Personal data

1.1.Name and surname: Magdalena Małecka

1.2. Education, scientific diploma and degrees

1982 – 1987 – Chemistry studies, University of Lodz, Department of Mathematics, Physics and Chemistry
1987 – M.Sc. degree
1999 – PhD dissertation – ' Structural studies on complexes of copper(II) chloride with phenylpyrazoles'
2012 – initiation of the habilitation procedure
2013 – withdrawal of the habilitation on the habilitant's request; four reviews were obtained, three of them recommended further stages of the procedure, one review suggested to extend the list of scientific achievements and resubmission

1.3. Employment

1987 – 1997 – University of Lodz, Department of Crystallography, specialist chemist, scientific and technical worker
1997 – 1999 – University of Lodz, Department of Crystallography, assistant
1999 – University of Lodz, Department of Crystallography (now Department of Theoretical Chemistry and Crystallography) – researcher/ lecturer

1.4. Scientific achievements - statistics of published articles

The results of my research are summarized and published in the following papers. Also the results were presented on the conferences (according to the Web of Science database, data from 30 October 2014.):

- total number of publications: **- 57**
- **13** structural reports published in Acta Crystallographica E
- before receiving Ph.D. degree: **3** (**2** from Journal Citation Report)
- after receiving Ph.D. degree **54** papers (**41** from Journal Citation Report, **13** – structural reports)
- sum of Impact Factor: **72.884** (**71.814** after receiving Ph.D. degree)
- sum of MNiSW points: **1046**
- citations number: **402;** without self-citations: **330**
- Hirsch index: **12**
- number of oral presentations on conferences and in other academic center for invitation: **9**
- number of poster presentations on international and national conferences: **50**
- number of reviewed articles in international journals:**16**
- *New Journal of Chemistry, CrystEngComm, Structural Chemistry, Crystal Growth and Design i inne..*

2. Scientific achievements submitted for the habilitation procedure

As an achievement resulting from Article 16, section 2 of the Act on Academic Degrees and Titles and about Degrees and Titles in the Field of Fine Arts of March 14, 2003 (Dz.U. No 65/2003, item 595, with subsequent amendments) 12 of scientific publications are designed [H1-H12]:

2.1. Title of scientific achievement

"Structural and electronic aspects of intra- and intermolecular interactions in organic compounds with potential biological activity"

2.2. List of publications comprising the scientific achievements

The contribution in all structural works is estimated as 100% in terms of crystallographic part with the exception of [H11] article, where I declare my contribution to be equal to 70%.

H1. **Magdalena Małecka***, Elżbieta Budzisz
Investigations on benzo[1,2]oxaphosphinane derivatives.
Acta Crystallographica (2001), **C57**, 929-931.

*corresponding author
IF(2013) = 0.535, $IF_5(2013)$ = 0.442
My contribution to this work consisted of managing research project, performing X-ray measurements and the refinement of structures, analyzing the results as well as writing the manuscript (a crystallographic part). I declare my contribution to be equal to 70%.

H2. Elżbieta Budzisz, Ewa Nawrot, **Magdalena Małecka**
Synthesis, antimicrobial and alkylating properties of 3-phosphonic derivatives of chromone
Archive der Pharmazie (2001), **334**, 381-387.

IF(2013) = 1.396, $IF_5(2013)$ = 1.712
My contribution is related to carrying out the X-ray measurement with data integration, solving and the refinement of the structure, and writing the crystallographic part of the manuscript. I declare my contribution to be equal to 30%.

H3. **Magdalena Małecka**, Sławomir J. Grabowski, ElżbietaBudzisz
Crystal and molecular structures of 3-[1-(2-hydroxyethylamino)-ethylidene]-chroman-2,4-dione and 2-methoxy-3-[1-(benzylamino)-ethylidene]-2,3-dihydro-2,4-dioxo-2λ^5-benzo[e][1,2] oxaphosphinane and DFT study of intramolecular H-bonds of related compounds.
Chemical Physics (2004), 297, 235-244.

IF(2013) = 2.028, $IF_5(2013)$ = 1.857
My contribution is related to carrying out the X-ray measurement with data integration, solving and structures' refinement, and co-writing the manuscript (crystallographic part). I declare my contribution to be equal to 40%.

H4. Elżbieta Budzisz, **Magdalena Małecka**, Magdalena Woźniczka, Aleksander Kufelnicki
Crystal structure, protolytic properties and alkylating activity of 3-(1-amino-ethylidene)-2-methoxy-2-oxo-2,3-dihydro-2λ^5-benzo[e][1,2]oxaphosphinin-4-one
Journal of Molecular Structure (2005), **753**, 113-118.

IF(2013) = 1.595, $IF_5(2013)$ = 1.585
My contribution is related to carrying out the X-ray measurement with data integration, solving and structures' refinement, and co-writing the manuscript (crystallographic part). I declare my contribution to be equal to 40%.

H5. Sławomir J. Grabowski, **Magdalena Małecka**
Intramolecular H-Bonds: DFT and QTAIM Studies on 3-(Aminomethylene)pyran-2,4-dione and its Derivatives
Journal of Physical Chemistry A (2006), **110**, 11847-11854.

IF(2013) = 2.779, IF$_5$(2013) = 2.856
My contribution is related to performing theoretical calculations. The concept and results of the were discussed with co-author. I declare my contribution to be equal to 50%.

H6. **Magdalena Małecka***
Intramolecular N-H…O resonance-assisted hydrogen bonds in crystal structures of oxaphosphinanes and chromones—DFT calculations and AIM analysis
Journal of Molecular Structure (2007), **831**, 135–143.

*corresponding author
IF(2013) = 1.595, IF$_5$(2013) = 1.585
My contribution is related to performing theoretical calculations, writing the manuscript. I declare my contribution to be equal to 100%.

H7. **Magdalena Małecka***
DFT studies and AIM analysis of intramolecular N–H…O hydrogen bonds in 3-aminomethylene-2 methoxy-5,6-dimethyl-2- oxo-2,3-dihydro-2λ^5-[1,2]oxaphosphinin-4-one and its derivatives
Structural Chemistry (2010), **21**, 175–184.

*corresponding author
IF(2013) = 1.900, IF$_5$(2013) = 1.622
My contribution is related to performing theoretical calculations, writing the manuscript. I declare my contribution to be equal to 100%.

H8. **Magdalena** Małecka*, LiliannaChęcińska, AgnieszkaRybarczyk-Pirek, Wolfgang Morgenroth, Carsten Paulmann
Electron density studies on hydrogen bonding in two chromone derivatives
Acta Crystallographica (2010), B66, 687-695.

*corresponding author
IF(2013) = 2.175, IF$_5$(2013) = 1.889
My contribution to this work consisted of managing research project, performing X-ray measurements and the refinement of multipole models, analyzing the results as well as writing the manuscript. I declare my contribution to be equal to 70%.

H9. **Magdalena** Małecka*, Lilianna Chęcińska, Carsten Paulmann
Electron density studies on hydrogen bonding in chromone derivatives. Part II: Comparative Study
Structural Chemistry (2012), 23, 801-807

*corresponding author
IF(2013) = 1.900, IF$_5$(2013) = 1.622
My contribution to this work consisted of managing research project, performing X-ray measurements and the refinement of multipole models, analyzing the results as well as writing the manuscript. I declare my contribution to be equal to 90%.

H10. **Magdalena** Małecka*, Stefan Mebs*, Andrzej Jóźwiak
Electronic Properties of Two Adjacent Intramolecular Hydrogen Bonds and their Effects to the Molecular
Chemical Physics (2012) 407, 20-28.

*corresponding author
IF(2013) = 2.028, IF_5(2013) = 1.857
My contribution to this work consisted of managing research project, concerning X-ray measurements, performing theoretical calculations (except ELI-D and δ calculations) discussing all results and writing the manuscript (except the 2.7 chapter). I declare my contribution to be equal to 70%.

H11. **Magdalena Małecka***, Swastik Mondal, Sander van Smaalen, Carsten Paulmann
Charge density distribution of 3-(1-amino-ethylidene)-2-methoxy-2-oxo-2,3-dihydro-2λ^5benzo[e][1,2]oxaphosphinin-4-one
Acta Crystallographica, **B**69, (2013), 621-628

*corresponding author
IF(2013) = 2.175, IF_5(2013) = 1.889
My contribution is related to managing all works: carrying out the high-resolved X-ray measurement, doing calculation and analyzing the results as well as writing manuscript. I declare my contribution to be equal to 70%.

H12. **Magdalena Małecka***, Elżbieta Budzisz
Structural framework of biologically active coumarin derivatives. Crystal structures and Hirshfeld surface analysis
CrystEngComm, (2014), 16, 6654-5553.

*corresponding author
IF(2013) = 3,858, IF_5(2013) = 3,908
My contribution to this work consisted of managing research project, performing X-ray measurements and the refinement of structures, analyzing the results as well as writing the manuscript (except the lipophilicity part). I declare my contribution to be equal to90%.

2.3. Description of the scientific aim and the results achieved

Abbreviations used in the text

ChD – chromone derivative
OxP- oxaphosphiniane derivative
IHB – isolated hydrogen bond
RAHB – resonance-assisted hydrogen bond
±CAHB – charge-assisted hydrogen bond
PAHB – polarization-assisted hydrogen bond
NBO – Natural Bond Orbitals
QTAIM – Quantum Theory Atoms in Molecules
BCP – bond critical point
RCP – ring critical point
CCP –cage critical point
SP – Single Point calculation
ρ_{BCP} – electron density at bond critical point
$\nabla^2\rho_{BCP}$ – Laplacian of electron density
ε – bond ellipticity
H_{BCP} – total electron energy density
G_{BCP} – electron kinetic energy density
V_{BCP} – electron potential energy density
SF – Source Function
S(H/D/A) – contribution to the electron density at bond critical point for H/D/A atom

Introduction

The main aim of this series of scientific publications was to examine in detail and compare geometrical parameters with electron density parameters, which characterize the intra- and intermolecular interactions in the crystal structure of biologically active compounds.

I focused my research on the molecules of chromone and oxaphosphinane derivatives, which were synthesized by the cooperator Prof. Elżbieta Budzisz as a continuation of her studies searching for new compounds of anti-cancer activity. The obtained compounds display a wide spectrum of biologically relevant properties including antitumor activity, therefore the studies of the crystal structure were carried out in order to confirm new molecular structures. Moreover, our interest is focused on ambiguous observations of the NMR spectra, which suggests the existence of a tautomeric equilibrium.

A common characteristic feature of the crystal structure of chromone and oxaphosphinane derivatives is not only the existence the intramolecular hydrogen bond which is a part of planar six-membered rings but also intermolecular interactions which play an important role in the crystal lattice arrangement.

The crystal structure was determined on the basis of X-ray diffraction data. In some cases, where it was possible thanks to high quality crystals, I determined the experimental electron density from a high-resolution X-ray diffraction data. Moreover, I performed several theoretical calculations, which allowed me to analyze topological properties of the electron density.

A different approach gave me opportunity to characterize intra- and intermolecular interactions by geometrical and topological/energetic parameters.

Hydrogen Bond

Hydrogen bond is one of the most popular scientific topics, which is extensively examined by experimental as well as theoretical studies. Many scientific articles proved the crucial role of hydrogen bonds in different biological systems, such as the determination of the binding polypeptide chains, determination of the protein tertiary structure and the influence on a way of connecting base pairs in nucleic acids. [1] In structural chemistry the hydrogen bond belongs to the most important interactions which affect the arrangement of molecules in the crystal lattice.[2]

The discovery of hydrogen bond cannot be attributed to one person. It is worth mentioning that the pioneering work about this type of interaction appeared over 100 years ago and was published by German scientist[3],[4]. Later in 1912 Moore and Winmill[5] described the hydrogen atom as a mediator of interaction between two atoms. In 1920 Latimer and Rodebush[6] first proposed the term 'hydrogen bond' (*hydrogen nucleus held between 2 octets constitutes a weak 'bond'*).

The variety of hydrogen bonds allows one to perform several different classifications of this kind of interaction. Firstly, one can distinguish two types of hydrogen bonds:

i. intermolecular hydrogen bond which is formed between two independent molecules,
ii. intramolecular hydrogen bond which occurs when the donor and acceptor atoms are an integral part of the same molecule, and the spatial arrangement forced the formation of a hydrogen bridge.

The observations related to the hydrogen bond distinguish the homonuclear hydrogen bonds (the donor and the acceptor are the same atoms) hydrogen bonds and heteronuclear ones (the donor and the acceptor are different types of atoms).

The binding energy is another criterion for the classification of hydrogen bonds. The hydrogen bonds are classified as follows:

i. very strong and strong hydrogen bonds with covalent character (energy > 24 kcal/mol)
ii. the medium-strength hydrogen bonds with partially covalent character (energy range 12 kcal/mol – 24 kcal/mol),
iii. weak hydrogen bonds with electrostatic character (energy < 12 kcal/mol).

Gilli and co-workers[7] pointed out the additional effects, which strengthen the hydrogen bonds and classified hydrogen bonds as 4 types:

i. isolated hydrogen bonds, (IHB) which belong to weak interactions,
ii. charge-assisted hydrogen bonds, (±CAHB), often classified as strong hydrogen bonds,
iii. resonance-assisted hydrogen bonds, (RAHB), often strong and covalent in nature, where the enhancement of hydrogen bond strength is the result of π-electron delocalization,
iv. polarization-assisted hydrogen bonds, (PAHB) of medium strength.

Resonance-assisted hydrogen bonds

The concept of resonance-assisted hydrogen bonds was proposed by Gilli and co-workers for O-H…O intramolecular hydrogen bonds in β-diketones. Jeffrey i Saenger[8] called that type of bonds the cooperativity bonds with conjugated multiple π- bonds (π- bond cooperative H-bond). Between the donor and acceptor atoms there is a system of single and double bonds, where π-electron delocalization is possible. The π-delocalization results subsequently in the following structural consequences: the shortening of formally single bonds: C-C(d2) and C-O/N(d4), and the elongation of formally double bonds: C=C(d3) and C=O(d1) (Scheme 1). For homonuclear systems one can observed elongation of O-H bond even to the midpoint of O…O distance. with the RAHBs system

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[1] a) T. Steiner*, Angew Chem Int Ed*, 2002, 41, 48-76; G.A. Jeffrey, *An Introduction to Hydrogen Bonding,* Oxford, University Press, New York, 1997; b) S. Scheiner, *Hydrogen Bonding,* Oxford University Press, New York, 1997;c) M. Nomura, S. Kinoshita, H. Satoh, T. Maeda, K. Murakami, M. Tsunoda, H. Miyachi, K. Awano, *Bioorg. Med. Chem. Lett.,* 1999, 9, 533–538; d) W. G. Harter, H. Albrect, K. Brady, B. Caprathe, J. Dunbar, J. Gilmore, S. Hays, C. R. Kostlan, B. Lunneya, N. Walker, *Bioorg. Med. Chem. Lett.,* 2004, 14, 809–812; e) M. C. Van Zandt, E. O. Sibley, E. E. McCann, K. J. Combs, B. Flam, D. R. Sawicki, A. Sabetta, A. Carrington, J. Sredy, E. Howard, A. Mitschler, A. D. Podjarny, *Bioorg. Med. Chem*., 2004, 12, 5661–5675.

[2] G. R. Desiraju, T. Steiner, The weak hydrogen bond in structural chemistry and biology, Oxford University Press, New York, 1999.

[3] A.Werner, *Liebigs Ann*., 1902, 322, 261- 297.

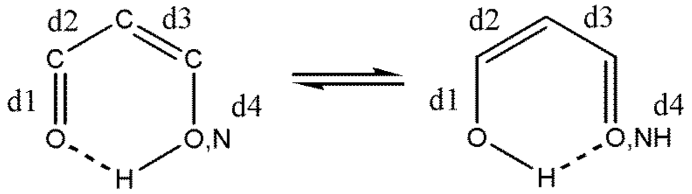
[4] A.Hantzsch, *Chemische Berichte,* 1910, 43, 3049- 71.

[5] T. S. Moore, T. F. Winmill, 1912, *J. Chem. Soc.*, 101, 1635–1676.

[6] W. M. Latimer, W. H. Rodebush, *J. Am. Chem. Soc.* 1920, 42, 1419–1433.

[7] G. Gilli, P. Gilli, *J. Mol. Struct*., 2000, 552, 1-15.

[8] G.A. Jeffrey, W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer-Verlag, Berlin, 1990.



Scheme 1. RAHB model for homo- and heteronuclear systems with two possible tautomeric forms.

Research method

The crystal structures are rich sources of information on molecular interactions. The crystal structure may be investigated based on X-ray or neutron data.

In the late 1970s, the studies of combined X-ray and neutron data for hydrogen bonds were presented.[9] The authors observed a very strong O-H…O hydrogen bond, with the hydrogen positioned on a two-fold symmetry (in the middle of two O atoms). The authors found a significant accumulation of the electron density between hydrogen and both oxygen atoms suggesting the presence of covalency in both H…O interactions. Later, Flensburg[10] studied the experimental charge density in methylammonium hydrogen succinate monohydrate, which confirmed the covalent character of strong O-H…O interaction.

In order to characterize the hydrogen bond the quantum chemical calculations are also used. Theoretical calculations allow us to obtain the molecular structure and binding energy. Moreover, some other approaches can be applied such as QTAIM (Quantum Theory Atom in Molecules)[11] and NBO (Natural Bond Orbital)[12] to analyze charge density distribution for hydrogen-bonded systems. QTAIM theory provides many topological properties of the bond critical point (BCP): electron density (ρ_{BCP}), the Laplacian of the electron density ($\nabla^2\rho_{BCP}$), total electron energy (H_{BCP}) and bond ellipticity (ε). Topological analysis of the electron density was adopted in the study of hydrogen bonds by Koch and Popelier, [13] who formed eight criteria for the existence of hydrogen bonds.

I used most of those methods in my research. In some cases, where the crystal quality permitted, I performed high-resolution X-ray data collection (synchrotron), which allows one to determine experimental distribution of electron density.

Structural studies of oxaphosphinane and chromone derivatives

Research into intramolecular and intermolecular hydrogen bonds originated in structural studies of a series of oxaphosphinane (OxP) and chromone (ChD) derivatives (Scheme 2). The compounds were investigated by X-ray diffraction data and the results are presented in papers: [H1-H4, H8-H12] and structural reports [P42-P44].

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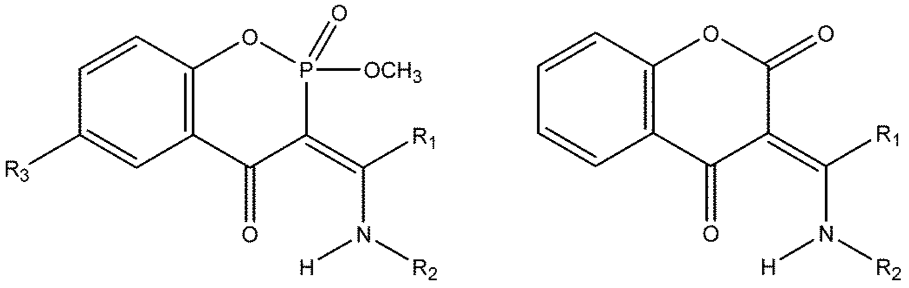
[9] E. D. Stevens, S. C. Lehmann, P. Coppens, *J. Am. Chem. Soc.*, 1997, 99, 2829–2831.

[10] C. Flensburg, S. Larsen, R. F. Stewart, *J. Phys. Chem. 1995,* 99,10130–10141.

[11] R.F.W. Bader, *Atoms in Molecules: A Quantum Theory*, Oxford University Press, Oxford, UK, 1990

[12] F. Weinhold, C.R. Landis, *Valency and Bonding. A Natural Bond Orbital Donor–Acceptor Perspective*, Cambridge University Press: Cambridge, 2005.

[13] U. Koch, P. Popelier*, J. Phys. Chem*., 1995, 99, 9747-9754.



	R1	R2	R3
OxP1 [H2]	Ph	CH_2Ph	CH_3
OxP2 [H2]	Ph	CH_2Ph	H
OxP3 [P42]	Ph	CH_2CH_2OH	H
OxP4 [H1]	CH_3	CH_2CH_2OH	H
OxP5 [H1]	CH_3	CH_2CH_2OH	CH_3
OxP6 [H3]	CH_3	CH_2Ph	H
OxP7 [H4, H11]	CH_3	H	H
ChD1 [H9, P43]	CH_3	CH_2Ph	-
ChD2 [H3]	CH_3	CH_2CH_2OH	-
ChD3 [H8]	CH_3	H	-
ChD4 [H8]	Ph	CH_3	-
ChD5 [H12]	Ph	$CH_2Ph(OCH_3)_3$	-
ChD6 [H12]	H	$CH_2Ph(OCH_3)_3$	-
ChD7 [H12]	H	$CH_2CH_2CH_2(C_3H_3N_2)$	-

Scheme 2. Scheme of the investigated compounds: oxaphosphinane derivatives (OxP) and chromone drivatives (ChD).

The oxaphosphinane derivatives (OxP) consist of a benzene ring fused with an oxaphosphinane ring and different aminoethylidene substituents at position 3. The oxaphosphinane ring is not planar and often adopts the half-chair or half-boat conformation. The exception is one crystal structure of OxP2 [H2], where the puckering parameters are equal to almost 0, which suggests a planar ring. This results in the lowest value of the dihedral angle between oxaphosphinane and the benzene ring. Consequently, that almost planar fragment exhibits structural similarity to nalidixic acid, a well-known an active therapeutic that is used as a control reference in determining biological activity. The planar oxaphosphinane ring seems to be a structural feature responsible for biological activity resulting in wrong DNA replication. The phosphorus atom adopts distorted tetrahedral geometry with three P-O bonds and elongated apical P-C bond (from the oxaphosphinane ring).

The chromone derivatives (ChD) consist of two fused rings: benzene ring and pyran ring, which are always coplanar, as well as various substituents at position 3.

As it was mentioned above, at position 3 different aminoethylidene fragments are substituted, which creates a possibility of forming the intramolecular N-H…O hydrogen bond (the oxygen atom at position 4 is the donor). Intramolecular hydrogen bonds are mostly part of planar six-membered rings within the O=C-C=C-N-H motif, described by the graph-set notation as S(6).[14] The donor atom is separated from the acceptor atom by alternating single and double bonds. It was observed that the formally double bonds (d3 and d1) appear to be longer whereas the formally single bonds (d2 and d4) appear to be shorter than the reference values.[15] This observation leads to the conclusion that π-electron delocalization

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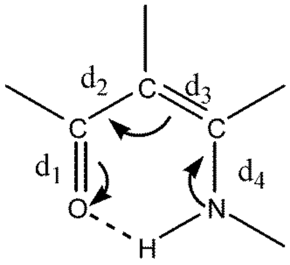
[14] M. C. Etter, *Acc. Chem. Res.*, 1990, 23, 120–125.

[15] F. H. Allen, D. G. Watson, L. Brammer, A. G.Orpen, R. Taylor, *International Tables for X-ray Crystallography*, 2009, Vol. C, ch. 9.5, pp. 790–811. Amsterdam: Kluwer Academic Publishers. Acta B

exists within six-membered rings and the hydrogen bond can be classified as a resonance-assisted hydrogen bond (RAHB) [H1-H4, H8-H12].



Scheme 3. Scheme of π-electron delocalization within the closed six-membered ring.

Different substituents at position 3 together with spatial arrangement resulted in the formation other N-H…O intramolecular hydrogen bonds which close the five-membered ring (compounds 1 and 2, H1). Additionally, the O-atom from ethoxy substituents plays a role of donor for several conventional intermolecular hydrogen bonds (compounds 1 and 2, H1). In the case of crystal structure of compound 3 [H12] the imidazole group forms the N-H…N hydrogen bond (Fig. 1).

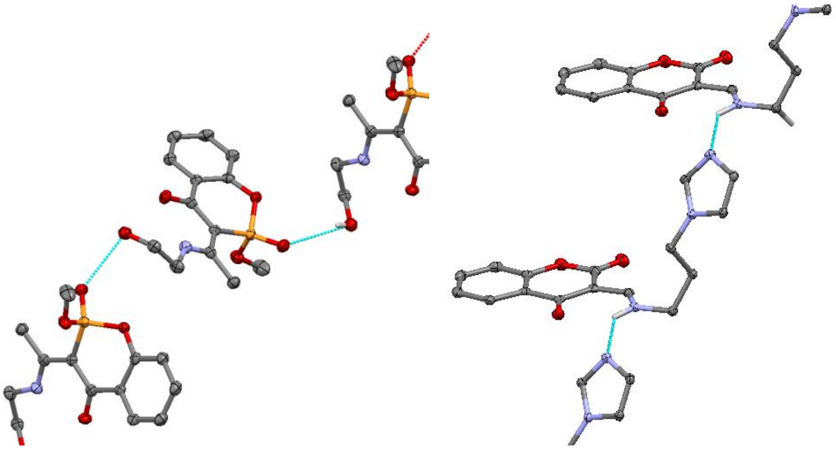


Figure 1. Examples of intermolecular hydrogen bonds in the crystal structures of oxaphosphinane and chromone derivatives. On the left O-H...O hydrogen bond (O-atom from ethoxy group as donor), on the right N-H...O hydrogen bond (N atom from amine group as donor).

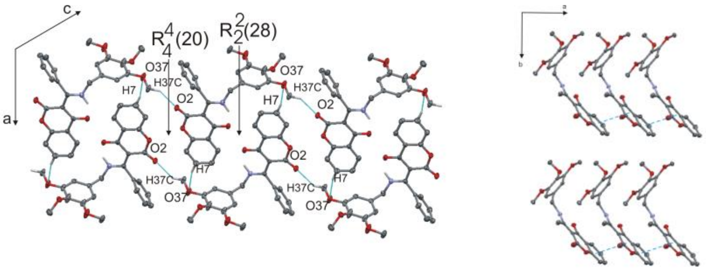
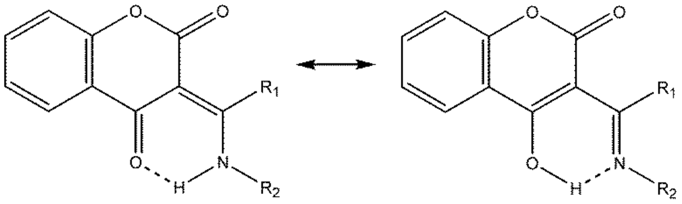


Figure 2. Examples of structural motifs in the crystal lattice of chromone derivatives On the left the formation of 2D sheet of molecules is shown with the structural motif of $R^4_4(2)$ and $R^2_2(28)$ formed by C-H…O interaction. On the right there are two ribbons generated through π…π stacking interaction.

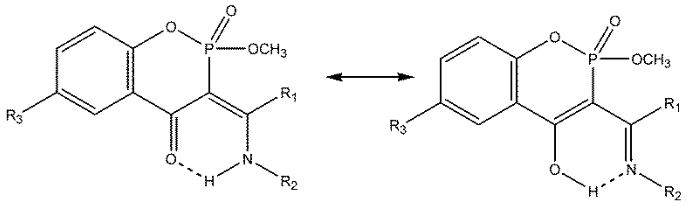
What is more, in the crystal structure in which there is no strong donor, the role of non-conventional hydrogen bonds such as C-H…O, C-H…π i π…π increases. Therefore, I observed a several structural motifs and molecular arrangement for all the investigated crystal structures (Fig. 2).

Intramolecular and intermolecular hydrogen bonds in the crystal structure of oxaphosphinane and chromone derivatives

In some 1H NMR spectra of the investigated compounds taken in DMSO, there is evidence of two tautomeric forms [H1, H3, H4] (Scheme 4). The crystal structures of tautomers 1 and 2 form the intramolecular hydrogen bond closing the six-membered ring with N-H…O (tautomer 1 – the ketoenamine form) and O-H…N (tautomer2 – the enolimine form).



1 **compound ChD** **2**



1 **compound OxP** **2**

Scheme 4. Two possible tautomeric forms for chromone (ChD) and oxaphosphinane derivatives (OxP). Structure 1- form the ketoenamine form , structure 2 – the enolimine form.

Additionally, the CSD search confirmed that the tautomer with intramolecular O-H…N is often observed for Schiff bases. [16]

The tautomerism of the studied molecules can be illustrated by the difference Fourier map for intramolecular hydrogen-bonded fragments (Fig. 3). The highest peak of maximum electron density on the difference map near the N12 atom is not clearly separated from the O8 atom (oxaphosphinane derivative OxP7, [H4]) as it is for other derivatives. Therefore, it can be suggested that there is a slight participation of the enolimine form in the solid state.

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[16] a) A. Filarowski, A. Koll, T. Głowiak, *J. Chem. Soc. Perkin Trans.*, 2. 2002, 835-842. b) M.Z. Zgierski, *J. Chem. Phys*, 2001, 115, 8351-8358. c) P.M. Dominiak, E. Grech, G. Barr, S. Teat, P. Mallinson, K.Woźniak, *Chem. Eur. J.* 2003, 9(4), 963-970. d) I. Król-Starzomska, A. Filarowski, M. Rospenk, A. Koll, *J. Phys. Chem. A*, 108, 2004, 2131-2138. e) S. Bilge, Z. Kiliç, Z. Hayvali, T. Hökelek, S. Safran, *J. Chem. Sc.* 2009, 121, 989-1001, f) M. Sebastian, V. Arun, P.P. Robinson, P. Leeju, D. Varghese, G. Varsha, K.K. Mohammed Yusuff, *J. Coord. Chem.*, 2010, 63(2), 307-314, g) K. Pyta, P. Przybylski, K. Klich, W. Schilf, B. Kamieński, E. Grech, B. Kołodziej, A. Szady-Chełmieniecka, B. Brzezinski, *Struct. Chem.*, 2014, in press

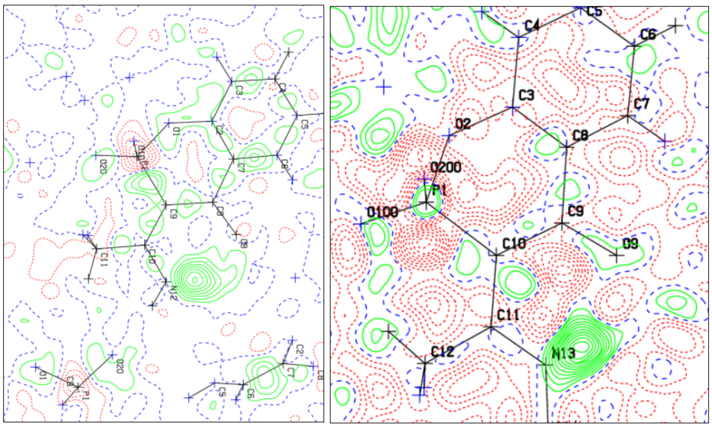
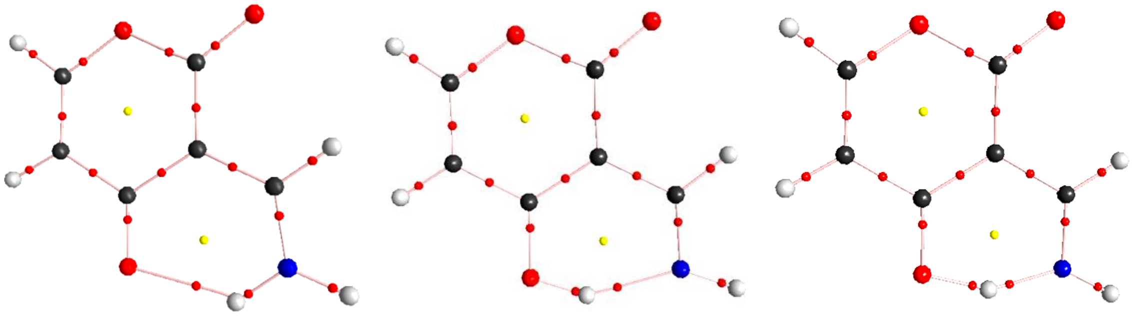


Figure 3. Difference Fourier map in the mean plane of H-bonded ring (on the left OxP7, on the right OxP6). Green lines (positive contours) near N12 and N13 atom illustrated the hydrogen atom position. Contours are drawn at 0.05eA^{-3} intervals.

Hence, the structural studies were complemented by theoretical computations on model systems similar to ChD and OxP molecules for the tautomeric form as well as transition state (Fig. 4).



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form AT
E=-512.1957647

Figure 4. Examples of molecular graphs for the possible tautomeric forms: A1- the ketoanamine form, A2 – the enolimine form, AT – the form for transition state. Below graphs the energies of the model system (in hartrees) are given.

On the basis of the total energy systems it was stated that the systems containing theN-H…O and O-H…N hydrogen bonds are the most stable. Geometrical parameters show that the O-H…N hydrogen bond (hydroxyl group as the donor) are stronger than the N-H…O hydrogen bonds (amino group as the donor). This is in line with Hammond Postulate,[17] according to which the stronger hydrogen bond is observed for the less stable tautomeric form, since the less stable tautomeric form is closer to the transition state and more participates in TS structure. The geometry analysis for bonds within the six-membered ring showed that the greatest equalization of bond distances is observed for model species in transition state. The results were published in article [H3].

Structural studies of oxaphosphinane and chromone derivatives [H1, H2, H3, H4, P42, P43] showed that the N-H…O intramolecular hydrogen bond may be classified as resonance-assisted hydrogen bond (RAHB). It is known, for RAHB systems, that there is a correlation between the delocalization in the π-system and the strength of the hydrogen bond.[18] In view of this I preceded the next stage of my research,

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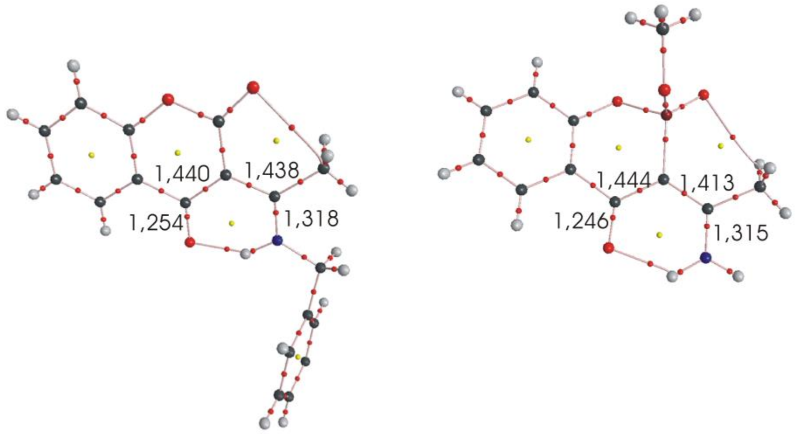
[17] G.S. Hammond, *J. Am. Chem. Soc.*, 1955, 7, 334-338.

[18] G. Gilli, F. Bellucci, V. Ferretti, V. Bertolasi, *J. Am. Chem. Soc.*, 1989, 111,1023-1028.

to aimed to confirming geometrical parameters for RAHB systems with topological energetic parameters using QTAIM theory.

The QTAIM theory is based on the analysis of electron density of the considered system. molecule. The electron density ($\rho(\boldsymbol{r})$) may be considered in the special points named critical points (CP). There are four critical points: the attractor (NA), bond critical point (BCP), ring critical point (RCP), and cage critical point (CCP). The analysis of the electron density at BCP (ρ_{BCP}) and other topological parameters like the Laplacian of the electron density ($\nabla^2\rho_{\mathrm{BCP}}$) provides information on the nature of interactions. For shared interactions (covalent, polarized bonds) the Laplacian of the electron density is negative, whereas for closed-shell interactions (van der Waals, ionic, and hydrogen bonds interactions) the Laplacian is positive. However for very strong hydrogen bonds the Laplacians are negative, which is the evidence of covalent nature of hydrogen interactions.

Based on geometrical parameters within the six-membered ring, I found that the π-delocalization effect is strongest for structure ChD1, the distance between the donor atom (N) and the acceptor atom (O) being the shortest. For all derivatives 'Single Point' (SP) calculations were performed in order to analyze topological parameters of the electron density. Potential energy densities at the H…O critical point ($V(r_{BCP})$)[19] were used to estimate the H-bond energy. I confirmed that for the ChD1 structure exists the strongest intramolecular hydrogen bond together with the strongest π-electron delocalization effect. Additionally, the obtained results such as the total electron energy density (H_{BCP}) and the Laplacian value $\nabla^2\rho(r_{\mathrm{BCP}})$ in H…O BCP indicate that the strength of interaction may be classified as medium for all molecules (except OxP7 structure) according to Rozas and co-workers.[20] Moreover, the partially covalent nature[21] was established for all the investigated structures with one exception, OxP7 structure, where the weakest mainly electrostatic hydrogen bond was observed (Fig. 5).



EHB=-17.32 kcal/mol
$\nabla^2\rho_{\mathrm{H\ldots O}}$ = 0.1605 a.u.
$H_{\mathrm{BCP(H\ldots O)}}$ = -0.0075 a.u..

EHB=-9.84 kcal/mol
$\nabla^2\rho_{\mathrm{H\ldots O}}$ = 0.1285 a.u.
$H_{\mathrm{BCP(H\ldots O)}}$ = 0.0004 a.u.

Figure 5. Molecular graphs with geometrical parameters within the six-membered ring [Å]. Below graphs the energies and topological parameters for H….O bond are given.

The analysis of geometrical and topological parameters showed the dependence between electron density at H…O/N-H BCP ($\rho_{(H\ldots O/N\text{-}H)}$) and the H…O/N-H distance. Additionally, the greatest π-delocalization is reflected in higher electron density values at the ring critical point. I found that there is a good correlation between electron density at RCP ($\rho_{\mathrm{(RCP)}}$) and electron density at the H…O bond critical point ($\rho_{(H\ldots O)}$). The above-mentioned above results are published in [H6].

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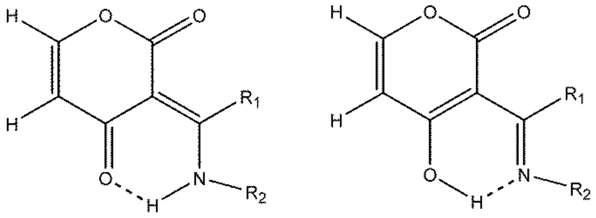
[19] E. Espinosa, E. Molins, C. Lecomte, *Chem. Phys. Lett.*, 1998, 285, 170-173.
[20] I. Rozas, I. Alkorta, J. Elguero, *J. Am. Chem. Soc.,* 2000, 122, 11154-11161.
[21] D. Cremer, E. Kraka, *Angew. Chem.* Int. Ed. Engl., 1984, 23, 627-628.

In Gilli's[22] work the authors pointed out that really strong RAHB can occur when the proton has comparable affinity for the donor D and the acceptor A atom. It could therefore be expected that substitution of the electron-donating or electron-withdrawing atoms into the ring involves two possible tautomeric forms to be isoenergetic and also greater π-delocalization would be elicited in the RAHB system. As a result, this will occur in the geometrical, energetic and topological parameters of the HB electron density.

In view of the above, in the following project I studied the influence of different substituents on delocalization effect in the pseudo-ring created due to the intramolecular hydrogen bond formation (model system of 3-(aminomethylene)pyran-2,4-dione, Scheme 5). The goal of this study was the analysis of geometrical and topological parameters for two possible tautomeric forms as well as for transition state obtained from DFT calculations and QTAIM theory.



R_1, R_2 = H, F, Li, -BeH

Scheme 5 . Possible tautomers of 3-(aminomethylene)pyran-2,4-dione*: form A – tautomer with N-H…O hydrogen bond, form B – possible tautomer with O-H…N hydrogen bond.*

The F atom at the R2 position, as an electron-withdrawing substituent, should cause a decrease of proton affinity of the nitrogen atom and enhance the strength of the hydrogen bond. Such behavior is in line with the rule proposed by Gilli[21] and mentioned earlier in this review. However, the results obtained by us demonstrated that there are no significant differences in bond distances within the six-membered ring even for the systems with the strongest hydrogen bonds. Nevertheless we could not exclude the influence of other interactions which appeared due to heteronuclear species.

The obtained results showed the relationships between the energetical parameters (H, G, V) and the H…O/N distance. Additionally, we observed the relationship between the electron density of the ring critical point and the electron density of the H…O/N contact. The electron density of the ring critical point ($\rho_{(RCP)}$) increases with the increase of the electron density of interactions ($\rho_{(H\ldots O/N\ldots H)}$), but decreases in the case of increasing the electron density of covalent bond ($\rho_{(H\text{-}O/N\text{-}H)}$). Between these two regions, the transition state region exists, which means that there is no sharp border between the hydrogen bond and covalent bond.

As it was mentioned above apart from the intramolecular hydrogen bond other intramolecular interactions were observed such as $Be^{+\delta}\ldots{}^{-\delta}O$, $Li^{+\delta}\ldots{}^{-\delta}O$, $Li^{+\delta}\ldots{}^{-\delta}F$ i $Li^{+\delta}\ldots{}^{-\delta}H$, where $Be^{+\delta}\ldots{}^{-\delta}O$ is the strongest interaction with the electron density value in the range of 0.0728-0.0910 a. u. (for comparison the energy for a trans-linear dimer of water is estimated as 5 kcal/mol and its $\rho_{(H\ldots O}$ = 0.024 a.u.[23]). Such an interaction may be classified as hydride bonding, system X-H…Y, where the atoms X and Y are electropositive atoms whereas the hydrogen atom is negatively charged (Figure 6), unlike the typical hydrogen bonding. The results of these studies are presented in [H5].

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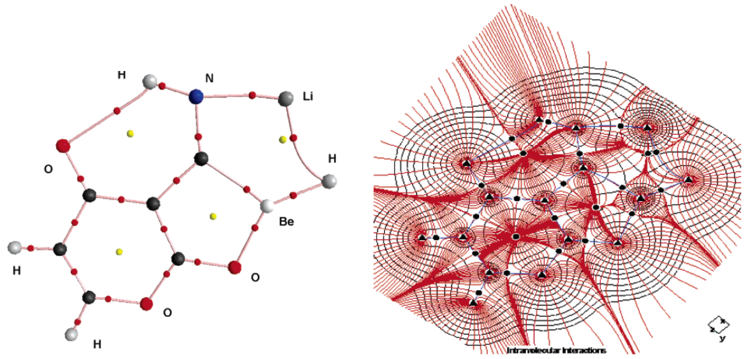
[22] V. Bertolasi, P. Gilli, V. Ferretti, G. J. Gilli, *J. Am. Chem. Soc.*, 1991, 113, 4917-4925.

[23] M. Domagała, S. J. Grabowski, *J. Phys.Chem. A,* 2005, 109, 5683-5688.



a) b)

Figure 6. a) Molecular graph of the derivative with R1=BeH and R2=Li. Some of the atoms are designated; the remaining are carbon atoms. b) Contour map of the electron density (black lines) of the species with the gradient paths (red lines). Triangles correspond to the attractors; circles correspond , to the bond and ring critical points.

In the next step of my theoretical research I chose the model system similar to oxaphosphinane derivatives. I investigated the influence of different substituents on the π- delocalization effect within the pseudo-six membered ring and the strength of the intramolecular hydrogen bond. I analyzed geometrical and QTAIM topological parameters, in particular the bond ellipticity (ε). The results showed higher ellipticity values for d2 bond (formally single bond) and lower ones (in most cases) for d3 (formally double bond). The mean ellipticity value for d2 was 0.168 and for d3 0.217. For comparison pure single, double bonds ellipticity values equal to 0.014 and 0.298 in butane and ethane were given, respectively.[24] Moreover, in some cases, we observed that the lengthening of the d3 bond is compatible with a decrease of the ellipticity value, and the shortening of d2 distance remains in agreement with the increase of ellipticity. This suggests that in some model systems π-electron delocalization exists, however the interpretation of ellipticity is not obvious.

In this project I also investigated the substituent effect on the strength of hydrogen bond. The presented results indicate that the strongest hydrogen bond is observed for the OxP_FNBeH model system in combination with the electron-withdrawing and electron-donating substituents. Topological parameters and the estimated energy pointed out that hydrogen bonds of model systems are rather weak. In contrast to chromone model systems presented in article [H5] this is associated with the lack of planarity and non-aromatic character of the main part of the molecule. The results for oxaphosphine model systems were thoroughly discussed in paper [H7].

Experimental charge density studies on hydrogen bonds

Information about the electron density distribution can be obtained in two ways: from theoretical calculations and on the basis of high-resolution X-ray diffraction data

High-resolution experimental charge density studies are beyond standard crystallography and need special experimental conditions: high-order data (0. 45Å), high-quality monocrystal, low temperature, a very intense beam in order to collect data at high resolution for a long time, and very careful data reduction due to statistical errors. The above-mentioned conditions are available in Hasylab/DESY in Hamburg. We collected data sets for compounds:ChD1, ChD3, ChD4, OxP7 within 3 projects (projects were realized in cooperation with Dr. Lilianna Chęcińska). Experimental charge density distribution studies were presented in articles [H8, H9, H11] and are summarized below.

As concerns the RAHB system, I compared the electron density on bonds C=C and C-C within pseudo-rings with the electron density for aromatic bonds C_{ar}-C_{ar}. The electron density is higher and is close to the electron density for aromatic bonds. There is one exception for the OxP7 structure, where the difference between values is of about 0.1 e/Å3 (Fig. 7). Additionally, I examined the ellipticity for those

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[24] P. Popelier , *Atoms in Molecules An Introduction*.,2000, Harlow, England: Pearson Education Limited,

bonds, and found that the ellipticity value is higher for the formally single bond and lower for the formally double bond. It indicates a π-character of bonds within the pseudo-ring for ChD1, ChD3, ChD4 derivatives.

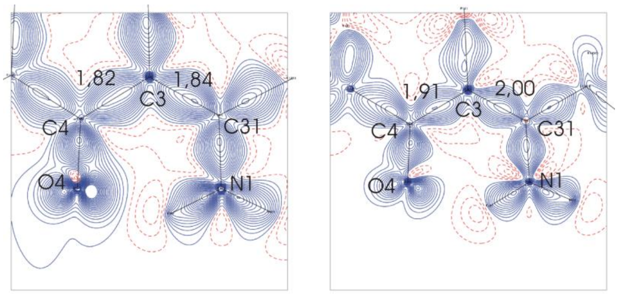

Figure 7. Deformation density map for ChD1 (on the left) and OxP7 structure (on the right) with electron density values (in e/Å^3) on bonds C4-C3 I C3=C31 (formally single and double, respectively). The values of the electron density at C_{ar}-C_{ar} BCP are: 1.90 e/Å^{3}and 2.09 e/Å^{3}for ChD1 and OxP7, respectively.

It became obvious that the π-bonds character is not evident for structure OxP7, therefore the intramolecular hydrogen bond should be characterized by other topological parameters. Hence, the nature of hydrogen bond was revealed by the source function (SF) introduced by Bader and Gatti. [25] The SF values $S(\mathbf{r},\Omega)$ are often reported in terms of their percentage contribution to the electron density at point ***r:***

$$S\%(r,\Omega) = \left[\frac{\mathrm{S}(\mathrm{r},\Omega)}{\rho(r)}\right] 100\%$$

Evaluation of the SF contributions to the density at the hydrogen bond BCP for various kinds of interaction gave the typical value of atomic contribution S% of donor (D), acceptor(A) and hydrogen (H) for different types of bonds.[26] The small positive contribution of hydrogen atoms (H) is observed in the case of ChD1, ChD3, ChD4 structures and confirmed the existence of resonance-assisted hydrogen bonds (RAHB), whereas it is negative for OxP7 and so this hydrogen bond is classified rather as isolated (IHB)(Fig. 8). Therefore the intramolecular hydrogen bond is a resonance assisted one.

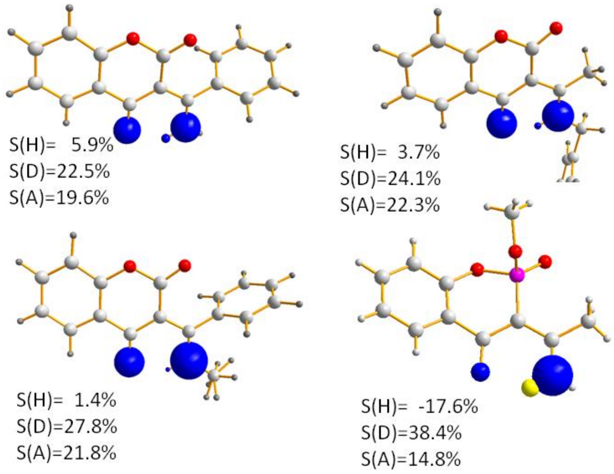

Figure 8. Percentage atomic source contributions in BCP electron density of the N-H…O. Contributions are displayed as spheres whose sizes are proportional to the percentage contribution from each atom involved in the hydrogen bond. Blue color represents a positive contribution and yellow represents negative contribution of the source function

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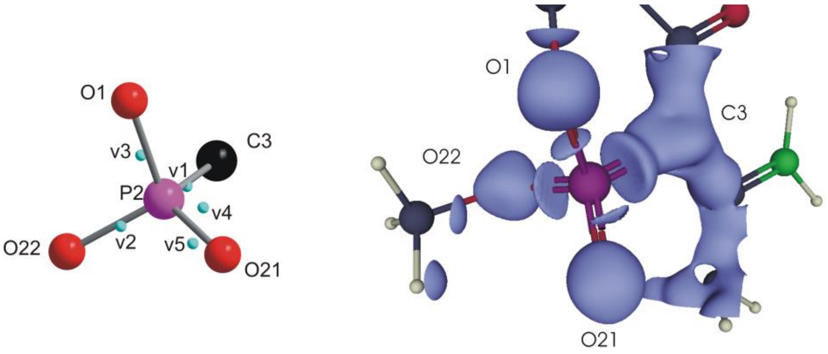
[25] R. F. W. Bader, C. Gatti, *Chem. Phys. Lett*., 1998, 287, 233-238.

[26] a) C. Gatti, L. Bertini, *Acta Cryst*., 2004, A60, 438-449; b) C. Gatti, F. Cargnoni, L. Bertini, *J. Comput. Chem*., 2003, 24, 422-436; c) C. Gatti , D. Lasi, *Faraday Discuss*., 2007, 135, 55-78; d) C. Gatti, *Struct. Bond*., 2012, 147, 193-285.

The presence of C=O and P=O groups and various substituents at position 3 gave the possibility of forming several intermolecular hydrogen bonds: conventional N-H…O and non-conventional C-H…O. Based on multipole model a more qualitative approach was used to study intermolecular hydrogen in detail following the Abramov's work[27] on the energetic organization of atomic interactions. It shows that intermolecular hydrogen bonds belong to weak interactions with electrostatic character ($H_{\mathrm{BCP}}>0$, $\nabla^2\rho(r_{\mathrm{BCP}})$).

In the oxaphosphiniane molecule the P atom adopts tetrahedral geometry with P-C_{ring}, P-O_{ring}, P=O_{Me} and P=O P-O bonds. Nowadays, the concept of the P bonds model[28] says that the P atom can build: one σ bond and three π-back-bonds, one σ bond and two π-back-bonds and three bent Ω bonds (banana bonds). The topological analysis revealed that one P=O bond has significant ionic character, with a positive value of the Laplacian at the BCP. Additionally, the spatial arrangement of valence shell charge concentration (VSCC) together with the ellipticity value indicates that there is the absence of σ bond between P2 and O21 atoms and there is a possibility of the formation of banana or bent bonds (Fig. 9).



a) b)

Figure 9. a) Graphical representation of the VSCCs around the P atom with numbering scheme. The values of ∇^2 are: v1 = -14.04, v2 = -8.30, v3 = -3.32, v4 = -1.12, v5 = -0.41 e/Å^5; (b) isosurface of negative Laplacian in VSCC of the P atom at -0.5 e/Å^5 isolevel

For all three chromone derivatives I compared topological parameters: the electron density (ρ_{BCP}) and its Laplacian ($\nabla^2\rho(r_{\mathrm{BCP}})$) within a common fragment of the molecule. The analyzed data shows a strong similarity of three chromone derivatives, confirming the transferability of their electronic properties. The transferability of submolecular or atomic electronic properties provides a tool to use fragments as building blocks for additive electronic structure of macromolecules, proteins and peptides. This is essential for creating still new atomic properties databases, whose development began in the last decade.[29]

Real-space bonding indicators for intramolecular hydrogen bonds

Because the application of the source function was very useful for classification of intramolecular hydrogen bonds, we explored further the descriptors for π-delocalization in the six-membered chelate ring and for the intramolecular hydrogen bond. Another research project focused on the analysis of the crystal structure with two adjacent intramolecular hydrogen bonds. The possible tautomeric forms are

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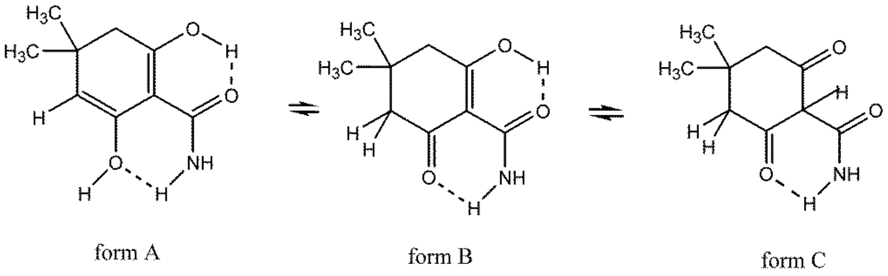
[27] Yu. A. Abramov, Yu. A., *Acta Cryst*., 1997, A53, 264–272.

[28] D. G. Gilheany, *Chem. Rev*., 1994, 94, 1339–1374; b) E. Denehy, J. M. White, S. J. Williams, *Inorg. Chem*., 2007, 46, 8871–8886.

[29] a) Bank ELMAM: B. Zarychta, V. Pichon-Pesme, B. Guillot, C. Lecomte, C. Jelsch, *Acta Cryst*., 2007, A 63, 108–125; b) S. Domagała, B. Fournier, D. Liebschner, B. Guillot, C. Jelsch, *Acta Cryst*., 2012, A 68, 337–351; c) baza Invariom: B. Dittrich, T. Koritsanszky, P. Luger, *Angew. Chem. Int. Ed. Engl*., 2004, 43, 2718–2721; d) B. Dittrich, C. Hübschle, P. Luger M. A. Spackman, *Acta Cryst*., 2006, D 62, 1325–1335; e)bank UBDB: T. Koritsanszky, A. Volkov, P. Coppens, *Acta Cryst*., 2002,. A 58, 464–472, f) A. Volkov, X. Li, T, Koritsanszky, P. Coppens, *J. Phys. Chem*., 2004, A 108, 4283–4300; g) P. Dominiak, A. Volkov, X. Li, M. Messerschmidt, P. Coppens, *J. Chem. Theory Comput.* 2007, 3, 232-247; h) K. Jarzembska, P. Dominiak, Acta Cryst., 2012, A68, 139-147.

studied (Scheme 6) and their theoretical populations in the gas-phase determined that form B is stable which was confirmed by the X-ray analysis.



Scheme 6. Scheme of compound 2- hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-ene carboxy amide (form B) with its tautomeric forms.

On the basis of crystal structure six smaller models (without the methyl groups, which are equivalent to H atoms) with two adjacent intramolecular hydrogen bonds were optimized. For all three models theoretical structure factors were generated from the wave function files using TONTO.[30] Refinement against the theoretical structure factors led to the theoretical multipole models and thus the source function (SF) was determined. Finally, the QTAIM analysis and ELI-D (Electron Localizability) and delocalization index (δ) were performed. [31]

The values of the donor, acceptor and hydrogen atomic contribution with negative S(H) confirm the lack of π-electron delocalization within the N-H…O hydrogen-bonded ring and thus suggest that these hydrogen bonds are isolated (IHB) rather than resonance-assisted (RAHB). However, the O-H…O hydrogen bonds were classified as resonance-assisted (RAHB). It is worth mentioning that our studies addressing N-H…O in terms of source function enriched the SF prototypical values[32] since it is more applied to O-H…O. [33]

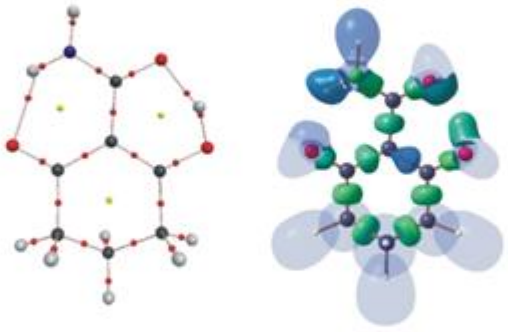


Figure 10. Theoretical AIM-topology (left) and ELI-D distribution in model 11. In the latter one, the basins are double coded for clarity with respect to their sizes: small basins are green and solid whereas large basins are increasingly blue and transparent. One finds the d3a bond (C5-C10) to be significantly larger which reflects its double-bond character. The electronic effects of two intramolecular hydrogen bonds are clearly visible.

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[30] D. Jayatilaka, D. J. Grimwood, TONTO: A Fortran Based Object-Oriented System for Quantum Chemistry and Crystallography, User Manual, The University of Western Australia, Perth, Australia, 2003.

[31] a) M. Kohout, *Int. J. Quant. Chem.*, 2004, 97, 651-658, b) R.F.W. Bader, M.E. Stephens, *J. Am. Chem. Soc.*, 1975, 97, 7391-7399.

[32] M. Schmidtmann, L.J. Farrugia, D.S. Middlemiss, M.J. Gutmann, G.J. McIntyre, C.C. Wilson, *J. Phys. Chem.*, 2009, A113, 13985-13997.

[33] a) J. Overgaard, B. Schiott, F.K. Larsen, B.B. Iversen, *Chem. Eur. J.*, 2001,17, 3756- 3767; b) D.E. Hibbs, J. Overgaard, R.O. Piltz, *Org. Biomol. Chem.*, 2003, 1, 1191-1198; c) J. Sorensen, H.F. Clausen, R.D. Poulsen, J. Overgaard, B. Schiott, *J. Phys. Chem., 2007,* A111, 345-351; d) C. Gatti, *Struct. Bond.*, 2012, 147, 193–286.

The calculated ELI distribution shows that the electron pairs of unbound valence basins of the O-atoms are asymmetrically distributed since a significantly smaller amount of electrons is located in the basin involved in the intramolecular hydrogen bond. For those models asymmetry is always larger for O-H…O contacts. The delocalization index also indicates that the resonance effects are more pronounced within the ring closed by O-H…O interaction (Fig. 10).

Real space bonding descriptors correlate well with each other and become a useful tool to characterize the delocalization effect. The results of this project are published in article [H10].

Structural framework in the crystal structure of chromone

Weak intermolecular interactions play an essential role in crystal packing.[2] The aim of next project was to investigate and describe different crystal packing arrangement for three biologically active compounds (Fig. 11). We focused on how different interactions and crystal packing are related to lipophilicity, a parameter which is indicative of biological activity.

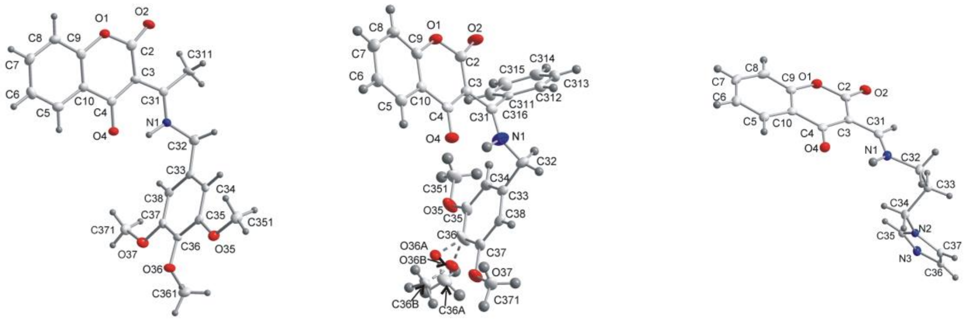

Figure 11. Crystal structure of chromone derivatives ChD5, ChD6 i ChD7 (compound I, II and III).

In the crystal structure of compound ChD5 there are two C-H…O hydrogen bonds from chains C(13) and C(9). Alternatively two chains are linked to the $R^4_4(36)$ ring extended to form the infinite two-dimensional layer on plane (100). Such layers are connected by another C-H…O interaction forming the chain C(9) along the [100] direction. This substructure is reinforced by π…π interactions which build 2-D ribbons extending along the [100] direction (Fig. 12).

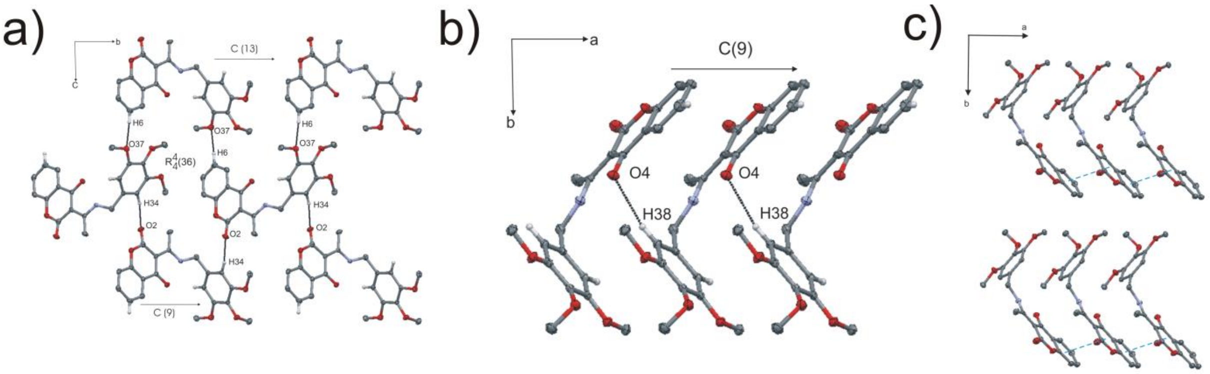

Figure 12. a) Formation of the 2D supramolecular network in I (ChD5) generated through C–H…O hydrogen bonds. b) Formation of the 2D sheet in I (Chd5) generated through the C–H…O4 hydrogen bond. c) Formation of two ribbons generated through π⍰π stacking interactions propagating along the [100] direction.

In the case of crystal packing of compound ChD6 the molecular framework can be described as two different substructures. One substructure is formed by two C-H…O interactions generating one sheet of molecules with two rings $R^2_2(28)$ and $R^4_4(20)$. These sheets of molecules are linked by π…π stacking interactions (Fig. 13).

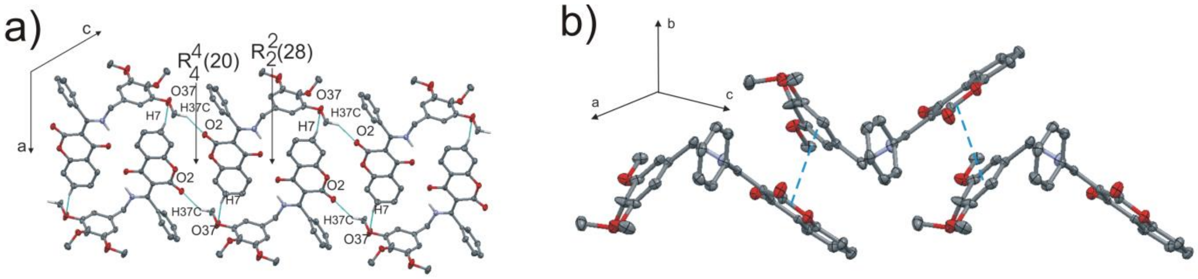

Figure 13. a) Formation of the 2D sheet in II (ChD6) generated through C-H…O hydrogen bonds. b) The π⍰π stacking interaction between the pyrane and trimethoxybenzene rings in the crystal lattice of II (ChD6).

The crystal packing of compound III (ChD7) seems to be stabilized by a combination of intermolecular N-H…O, C-H…O and C-H…π hydrogen bonds and π…π interactions. The N atom acts as a donor to the N atom forming the N-H…N hydrogen bond propagating the C(8) chain. The other chain C(11) is formed by C-H…O interaction. The combination of these interactions creates the ring $R^2_2(9)$. Moreover another $R^2_2(16)$ motif is formed by C-H…O interaction. In another substructure the C-H…O hydrogen bond generates 1D zig-zag chain along the [001] direction (Fig. 14).

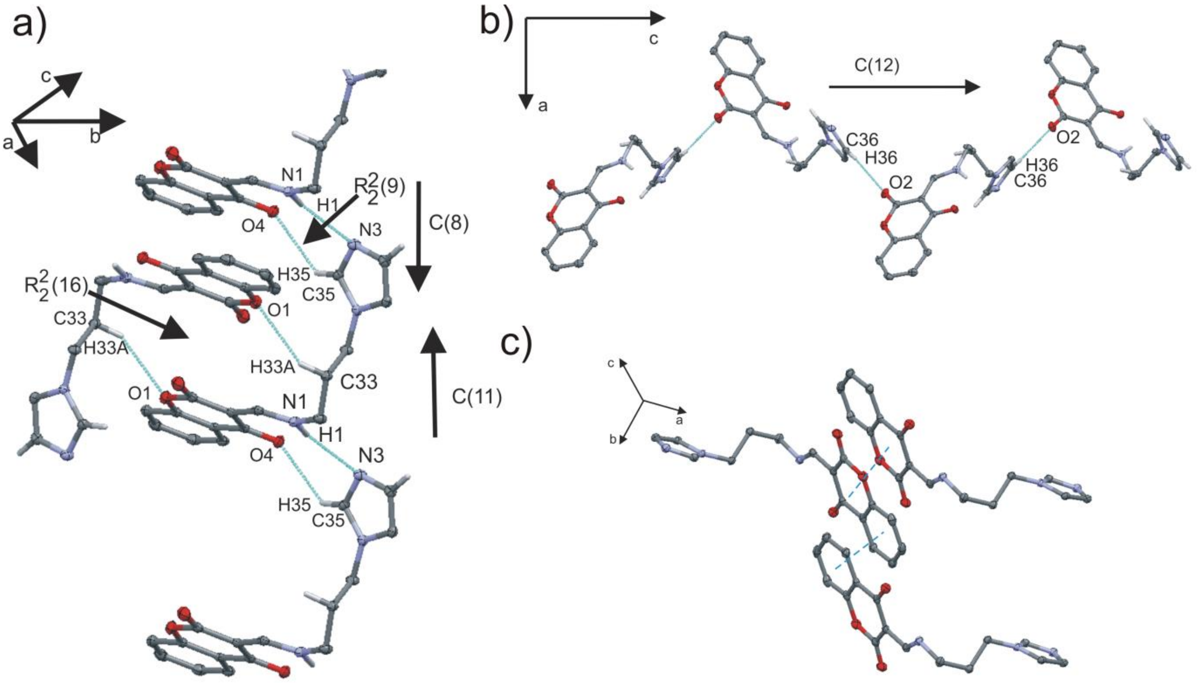

Figure 14. Substructures in the crystal lattice of III (ChD6) a) two chains C(8) i C(11), formed by N-H…O and C-H…O hydrogen bonds and two rings $R^2_2(9)$ and $R^2_2(16)$ as the combination of these interactions b) chain C(12) formed by C-H…O interaction c) π…π stacking interaction in ChD7.

The chromone structures presented here originate from the group of derivatives whose biological activity was proven.[34] Looking for the relation between unique structural features and biological activity, I examined the lipophilicity described as log *P* in terms of different interactions. On the basis of Hirshfeld surface analysis[35] I compared the log P value with the contribution of different interactions in the Hirshfeld surface. I found that the contribution of C…H interactions correlates well with the log *P* value.

A detailed description of the arrangement of chromone molecules in the crystal structures with their representation on the Hirshfeld surface is presented in work [H12].

Summary

In the presented review of the author's research the structural and electronic studies are summarized in terms of intermolecular and intramolecular interactions in oxaphosphinane and chromone derivatives. During the studies I performed X-ray measurements, including high resolution data collection, analysis of the crystal structure, quantum-chemical calculations for several model systems. The main conclusions are as follows:

- the changes of geometrical parameters within the six-membered chelate ring were observed indicating the hydrogen bond as resonance-assisted hydrogen bond.
- on the basis of topological parameters and the estimated energy, the hydrogen bonds were classified as medium with partially covalent character,
- X-ray diffraction studies and quantum-chemical calculations showed the structure with N-H…O hydrogen bonds as more stable than the systems with O-H…N interaction,
- for the studied model species a relationship was found between the H…O/N-H distance and electron density at the corresponding BCP,
- the effect of delocalization in the chelate ring is reflected by higher electron density at the ring critical point,
- energetic parameters such as H, G, V correspond well with the H…N/O distance as well as electron density at H….O/N BCP and the ring critical point; this conerncs different substituents,
- for the above-mentioned systems no changes in geometrical parameters were observed, not even for the strongest hydrogen bonds,
- the ellipticity analysis is a good indicator for π- electron delocalization within the six-membered ring, especially for the results obtained from experimental charge density analysis,
- experimental charge density analysis showed that the bonds within the six-membered ring have higher electron density values,
- the results obtained from experimental charge density analysis allowed for application of the Source Function (SF) and confirmed that in three cases the intramolecular hydrogen bond is resonance-assisted,
- P=O bond reveals partially ionic character and can be described as a bent bond,
- the analyzed experimental charge density data for chromone derivatives confirmed their transferability of the electronic properties of submolecular fragments, which is essential for creating new atomic properties databases,
- for model species with two intramolecular adjacent hydrogen bonds, the N-H…O hydrogen bonds were classified as isolated, whereas the O-H…O hydrogen bonds as resonance-assisted,
- the above-mentioned conclusion was drawn on the basis of the Source Function analysis for prototypical hydrogen bonds,

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[34] a) E. Budzisz, E. Brzezińska, U. Krajewska and M. Różalski, *Eur. J. Med. Chem*., 2003, 38, 597-603; b) K. V. Sashidara, S. Avula, K. Sharna, G. R. Palanti and S. R. Bathula, *Eur. J. Med. Chem*., 2013, 60, 120–127; (c) S. Y. Park, M. Ebihara, Y. Kubota, K. Fuabiki and M. Matsui, *Dyes Pigm.,* 2009, 82, 258–267.

[35] a) M. A. Spackman and P. G. Byrom, *Chem. Phys. Lett*., 1997, 267, 215-220; b) M. A. Spackman and D. Jayatilaka, *CrystEngComm*, 2009, 11, 19-32; c) M. A. Spackman, J. J. McKinnon, D. Jayatilaka, *CrystEngComm,* 2008, 10, 377-388; d)F. L. Hirshfeld, *Theor. Chim. Acta*, 1977, 44, 129-138.

- ELI-D distribution and delocalization index together with topological parameters and the source function support each other and become good descriptors for π-electron delocalization within chelate ring,
- the analysis of the biological activities showed that some derivatives have alkylating properties and are interesting antibacterial agents
- the lipophilicity index- log P correlates well with the C…H contact contribution in the Hirshfeld surface.

My main goal of the studies was to characterize deeper the hydrogen bonds. For this purpose I carried out theoretical calculations and experimental studies which were beyond standard methods- that is the experimental electron density studies. The application of the ellipticity, the Source function, the ELI-D descriptors and delocalization index increased the range of parameters, which could be used to characterize the resonance-assisted hydrogen bond. The obtained results can be useful in terms of cognitive and application aspects, e.g. the prototypic values of the N-H…O hydrogen bond.

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