

A Strong Link Between Organic Chemistry and Chemical Crystallography Started a Century Ago

Biserka Kojić-Prodić,* Krešimir Molčanov

Ruđer Bošković Institute, Zagreb, Croatia

* Corresponding author's e-mail address: kojic@irb.hr

RECEIVED: June 6, 2019 * REVISED: September 9, 2019 * ACCEPTED: August 25, 2019

THIS PAPER IS DEDICATED TO PROF. KATA MLINARIĆ-MAJERSKI ON THE OCCASION OF HER 70TH BIRTHDAY

Abstract: The article sheds light on some historical crossings of organic chemistry and chemical crystallography. It connects past and present bringing into the focus Prof. Kata Mlinarić-Majerski's research. An impact of structural chemistry on organic synthesis and reactivity is shown. X-ray structure analysis was established as a unique method to determine the composition and architecture of synthetic and natural organic molecules, already in the second decade of the last century; some of historical and scientific milestones are shown. Numerous controversies were solved, when intriguing molecular structures had been determined and the nature of chemical bond was clarified. An absolute structure (chirality) determination using an anomalous dispersion of X-rays was an important step forward, particularly in pharmaceutical industry. Structural data provided by X-ray crystallography, stored by Cambridge Structural Data Centre have been of great impact on many areas of science. They are closely related to intra- and intermolecular forces and structure/function correlations directing us to synthesis of compounds with designed properties. The developments of supramolecular chemistry, crystal engineering, materials science, and most of all of molecular machines have been assisted by chemical crystallography. The essay does not aim to review the complete scientific opus of Prof. K. Mlinarić-Majerski but it is focused on some of the highlights of her research. The interdisciplinary approach in her research is related to the use of X-ray structural analysis to define molecular architecture, conformational chirality, conformational isomerism, and get insight into reaction paths, interactions governing molecular assembling, and to recognise chemical properties of new compounds. In these researches the X-ray crystallographers were involved.

Keywords: research highlights of Prof. K. Mlinarić-Majerski, an impact of chemical crystallography on organic chemistry

BRILLIANT HISTORICAL EXAMPLES

TO understand the contemporary research it is worth to turn back to the past in order to spot the historical milestones and to recognise the impact of tradition on new trends in science. Many important discoveries of the last century widened up our views, and opened up new roads in science. In order to be focused to the relation of organic chemistry and structural chemistry based on X-ray structure analysis, some of the most relevant examples are presented. In early days of X-ray diffraction intriguing molecules attracted X-ray crystallographers, who for the first time resolved their chemical constitution and molecular architecture. One might disagree that we are referring to inorganic compounds instead of organic; it can

be a matter of a preference but in any case diamond and graphite comprise the carbon atoms only. The structure of diamond helped to understand the geometry of adamantane, which is undoubtedly classified as an organic molecule. In addition to simple table salt, the father and son Bragg, the Nobel laureates in 1915, determined the structure of diamond^[1] in 1913, whereas J. D. Bernal^[2] solved the structure of the second allotrope of carbon-graphite in 1924. The entirely different crystal structures of these two allotropes show the impact of different electronic structures on their characteristic chemical and physical properties. Unlimited human mind and hard work based on previous knowledge reached the third allotrope - fullerene (Csp² + Csp³) (R. E. Smalley, R. Curl, H.W. Kroto, 1966 Nobel Prize), which developed to nanomaterials and led to the fourth allotrope - graphene (A. Geim, K. Novoselov, 2010 Nobel Prize) (Figure 1).

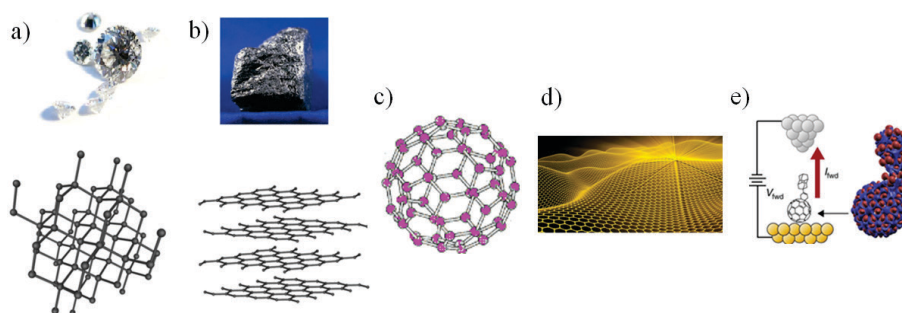


Figure 1. Four allotropes of carbon atom: a) Diamond structure, b) graphite structure, c) fullerene, and d) graphene (two-dimensional structure of Csp^2 atoms). Different crystal structures are related to their different properties, which can be combined in e) complex materials.^[3]

Dame K. Lonsdale determined the crystal structures of benzene and hexamethylbenzene,^[4] which revealed the planarity of the benzene ring, and calculated the values of carbon bond angles (120°) and bond lengths (1.39 \AA) (hexachlorobenzene, the only one available in the literature, Figure 2). Her experimental results disclosed the 60-year discussion among chemists and supported Kekule's hypothetical model. In early days of the 20th century, it was difficult to reconcile the new view of ionic compounds (the structure of NaCl)^[1] with classical chemical ideas of that time.

The crystal structure of penicillin, solved by D. C. Hodgkin in 1949, revealed for the first time the presence of a four-membered β -lactam ring, unknown to organic chemists of that time.^[5] Her determination of the vitamin B-12

structure showed the existence of metal-carbon chemical bond and a corrinoid ligand system, not previously encountered in natural compounds. A completely new field of organometallic chemistry emerged from this finding. D. C. Hodgkin was the first scientist who used X-ray diffraction to determine the structures of biologically active molecules, and for her research results won the Nobel Prize in 1964.

From Pasteur's time chirality was a scientifically formulated phenomenon, however, experimental evidence of definition of molecular chirality came from X-ray diffraction. J. M. Bijvoet^[6] in 1949 discovered how X-ray anomalous scattering can be used to determine the absolute configuration of chiral molecules exemplified by the structure of sodium rubidium tartrate. From Bijvoet's finding came the evidence that, by mere chance, Fischer assignment of glyceraldehyde was correct and thus the assignments of sugar stereochemistry. The Bijvoet's method and Barton's principles of conformational analysis accelerated the development of stereochemistry. These findings were followed by Nobel Prizes awarded to R. B. Woodward, D. H. R. Barton, O. Hassel, V. Prelog, and J. W. Cornforth for stereochemistry related research.

The fascinating field of organic synthesis related to the total synthesis of natural compounds has remained a challenge from the early years of 20th century to the present days due to the complexity and significance for the applications. At the beginning, the total synthesis was the only method to reveal the molecular constitution of numerous different classes of natural compounds. However, the X-ray structure analysis developed by time in its efficiency has been widely applicable to establish molecular architectures and chirality of various compounds. For many reasons, among which the most important one is to illustrate the interplay of curiosity and technology driven research, we decided to highlight the story of (-)-reserpine, an alkaloid isolated (1952) from a root of *Rauvolfia serpentina* plant.^[7] The organic chemists were intrigued to identify and characterise that alkaloid due to its pharmaceutical value

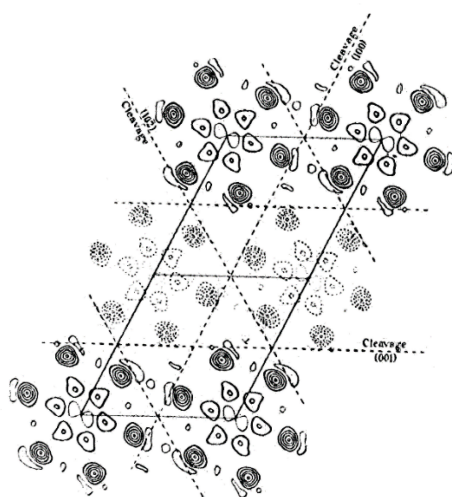


FIG. 6.—Projection on (010) Plane.

Figure 2. Electron density map of hexachlorobenzene (the Fourier map of hexachlorobenzene derivative available in old literature). The structure confirmed the planarity of an aromatic ring with all C–C bonds of equal length.

known long ago in Indian medicine. At that time the total synthesis was the only way to do it. In 1956 R. B. Woodward performed the very complex synthesis through about twenty steps;^[8,9] the compactly arranged 21 skeletal atoms in five rings (A-E, Figure 3) comprising five contiguous chiral centres (in ring E) and one more at C3 (C/D rings junction) made quite a challenge to synthesis. Quite many papers and reviews dealing with analysis of original synthetic route (Scheme S1 in the Supporting Information)^[10] and novel strategies of constructed constitutional subunits of reserpine followed; however, they are out of a scope of this essay.

To accomplish such a complex synthesis, a high mental capacity and laboratory skills were needed, and finally R. B. Woodward was awarded by Nobel Prize in 1965. The high professionalism of the Harvard University was transferred to our organic chemists by Vinko Škarić, Woodward's postdoctoral fellow. The crystal structure of alkaloid reserpine comprising forty-four light atoms was solved by Isabella and Jerome Karle (in 1968) using symbolic addition and tangent formula,^[11] a new mathematical approach for solving crystal structures of organic molecules. Their result was in agreement with the synthesis-derived data (Figure 3). However, the absolute configuration was not determined although the Bijvoet method for determination of absolute structure was already known.^[6] To resolve the problem of chirality an enantiomerically pure precursor was used to synthesise the natural product with the correct absolute configuration as a single isomer.^[12] The total synthesis of the cardiovascular drug and antipsychotic agent (tranquilizing drug) with unambiguously determined absolute stereochemistry was a strong request imposed by Hoffmann-LaRoche, which led to blockbuster drugs Librium and Valium. To highlight the reserpine story, one more Nobel Prize should be mentioned, which was awarded to H. Hauptman and J. Karle for direct methods for structure determination (also used for elucidation of reserpine molecular structure) in 1985.^[11] As reserpine circulates in

body organs (brain, liver, spleen, kidney, and crosses placental barrier) it is important to learn how reserpine affects cell signalling. Therefore, the protein complexes with reserpine have been intensively studied over the last decade and interactions *in vivo* of this drug is still an unfinished story.

At the present time the total synthesis of natural compounds is a very important branch of synthetic organic chemistry due to their use as potential drugs in human medicine, veterinary and agrochemistry. There are plenty of recently published papers related to this very topic and it is quite a challenge to select the most impressive ones; the total synthesis of the antibiotic (+)-pleuromutilin in 18-steps is finally disclosed^[13] and the most recently published 11-step total synthesis of teleocidins B-1-B-4,^[14] which were motivated by a search for new antibiotics.

X-ray structure analysis has provided enormous amount of structural data and closely related information on intra- and intermolecular forces responsible for crystal packing. The Cambridge Crystallographic Data Centre has stored atomic coordinates of solved crystal structures of organic compounds and metal complexes with organic ligands by X-ray and neutron diffraction since 1965. The founders of CCDC J. D. Bernal and Olga Kennard had "a passionate belief that the collective use of data would lead to discovery of new knowledge, which transcends the results of individual experiments".^[15] Their credo turned to the reality faster than anyone could imagine; in the year 2019, CSD includes over one million deposited crystal structures. With the rapid developments in computing this collection was encoded in electronic form and became known as the Cambridge Structural Database (CSD),^[15] which provides checking of deposited data and user friendly software to search, retrieve and analyse data. CSD has been of tremendous importance in organic synthesis, particularly in synthesis of molecular machines, supramolecular chemistry, crystal engineering, materials science, and theoretical chemistry related to studies of molecules. To justify the statement, a brief overview of available data is provided to those interested in this efficient tool. Atomic coordinates (error-free data) of selected crystal structure; molecular geometry library - bond distances and angles, torsion angles defining molecular conformation; metal coordination - coordination number, shape and its symmetry, ligand coordination modes; crystal structure architecture and topology; analysis of crystal packing, motifs, synthons; symmetry and chirality. The analysis based on these structural data points to intra- and intermolecular forces responsible for crystal packing and to properties of studied molecule: hydrogen bonding, C-H... π interactions, aromatic ring...H₂O, aromatic ring...halogen, anion... π , lone pair... π , cation... π , σ -hole interactions including halogen, chalcogen and pnictogen contacts. There is an open

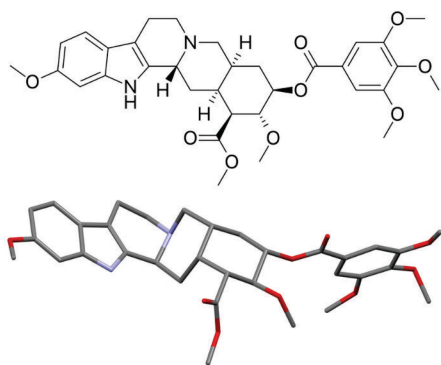


Figure 3. Reserpine structure was determined by I. and J. Karle by X-ray structure analysis.^[11]

area for collaboration of experimentalists and theoreticians. Moreover, the structural data stored in CSD together with dedicated software are in permanent use in many branches of chemistry, life sciences, particularly supramolecular chemistry, and materials science.^[15]

Supramolecular chemistry – chemistry beyond the molecule – chemistry of intermolecular (noncovalent) bonds was significantly shaped by J.-M. Lehn and his contribution was recognized by Noble Prize in 1987. Generally, this field provides the essential building elements, which can be used in enormously large number of combinations, using interaction forces of various energy scales, to generate molecules of different size and properties in animate and inanimate world. Among the most complex ones are molecular machines of living bodies (such as photosystem I and II, ribozyme) and those of synthetic origins such as molecular shuttles, carbon nanotubes, nanoparticles of various composition and size for different applications). Essentially such gigantic molecules are built of ‘small’ molecules assembled through variety of intermolecular interactions named in the previous paragraph.^[16,17]

In our scientific community supramolecular chemistry related research was initiated by M. Žinić about thirty years ago, and it is remained a vivid topic of many synthetic chemists these days. A part of K. Mlinarić-Majerski’s scientific interest was directed to supramolecular chemistry, which brought her into intensive collaboration with X-ray crystallographers and theoretical chemists. Last two decades a group of inorganic chemists in Zagreb intensified the research of metal organic frameworks using organic ligands.

The strong networking of many disciplines and branches of science is an imperative to reach high competence in the research and to maintain the open road between science and technology. The most impressive multidisciplinary results of technological value deal with graphene and its numerous modifications and the unpredictable applications.^[18]

Adamantane – Fascinating Chemistry - a Life-Long Inspiration to K. Mlinarić-Majerski

It would be out of scope of this essay to go into more detailed description about organic chemistry at Rudjer Bošković Institute, however, some basic information on the activities, that influenced a scientific life of K. Mlinarić-Majerski, enable us to pick up a real dimension of her scientific achievements. It cannot be neglected to observe that high scientific level of organic chemistry, particularly synthesis in Zagreb, had been laid down on a firm ground established by V. Prelog, and later on strong support of pharmaceutical factory Pliva. Generations of skilled and well-educated organic chemists spent formative years in

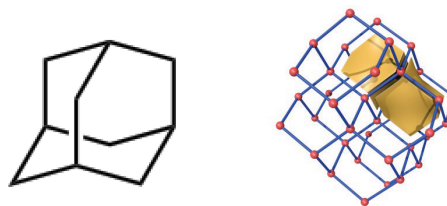


Figure 4. Adamantane chemical diagram and its crystal structure.

our laboratories and developed their careers in Pliva. In the laboratories of Rudjer Bošković Institute many interesting fields related to synthetic organic chemistry were established: carbohydrate synthesis developed by D. Kegević, nucleoside synthesis introduced by V. Škarić, stereospecific syntheses introduced and developed by V. Šunjić, and finally, the fundamental principles of physical organic chemistry were initiated by D. Sunko and S. Borčić, and further developed by Z. Majerski, K. Mlinarić-Majerski and M. Maksić. In those years scientific collaboration between Ruđer Bošković Institute and the University of Zagreb was common practice. In such highly motivated and competent environment Prof. Mlinarić-Majerski carried out her successful scientific carrier inspired by a unique molecule adamantane of a cage-like architecture (Figure 4).

Adamantane is a natural compound (isolated from petrol in 1932) and attracted many organic chemists to synthesize it in laboratories, although its synthesis was not straightforward due to its complex structure. V. Prelog was among them and started synthesis with Meerwein’s ester (1,3,5,7-tetracarboxymetoxibicyclo [3.3.1]nonano-2,6-dione) as a precursor but with a very low yield;^[19] the more efficient route was worked out by P. von R. Schleyer with a yield of 30–40 %, however, several possible routes of intermediates and their conversions to adamantane were not stated in the original paper.^[20] Z. Majerski spent his postdoctoral study (1968–1970) with Prof. von Schleyer, where he developed his scientific interest on strained hydrocarbons. The non-standard stereochemistry of carbon atoms in such molecules had intrigued Zdenko Majerski and Kata Mlinarić-Majerski to synthesize and study reactivity of propellanes,^[21,22] however later on, they continued with chemistry of adamantane.^[23–25] The results were presented in a book chapter by K. Mlinarić-Majerski.^[26] Definitely, adamantane molecule has been a focal point of her research interest. Numerous adamantane derivatives were produced analysing their reactivity, molecular structure, stereochemistry, their chemical properties, and possible applications. Adamantane found its way to pharmaceutical applications (anti-Parkinson’s drug and anti-viral agent), and K. Mlinarić-Majerski was challenged to apply her four patents. Adamantane-based biomimetics were prepared by her also.

Her scientific contribution to supramolecular chemistry is based on macrocyclic crown-ethers,^[27] thioethers, and cryptands with polycyclic cage scaffolds. The extensive experimental work on synthesis of adamantane thiomacrocyclic lactones and testing their complexation properties on heavy and transition metals was an extensive PhD work of Ines Vujasinović, supervised by Prof. K. Mlinarić-Majerski. To understand the experimental findings, a lot of structural analysis was required and an intensive collaboration with chemical crystallographers followed. The conformations and internal ring symmetry, comparative analysis of ring conformations in the free and the metal-complexed states,

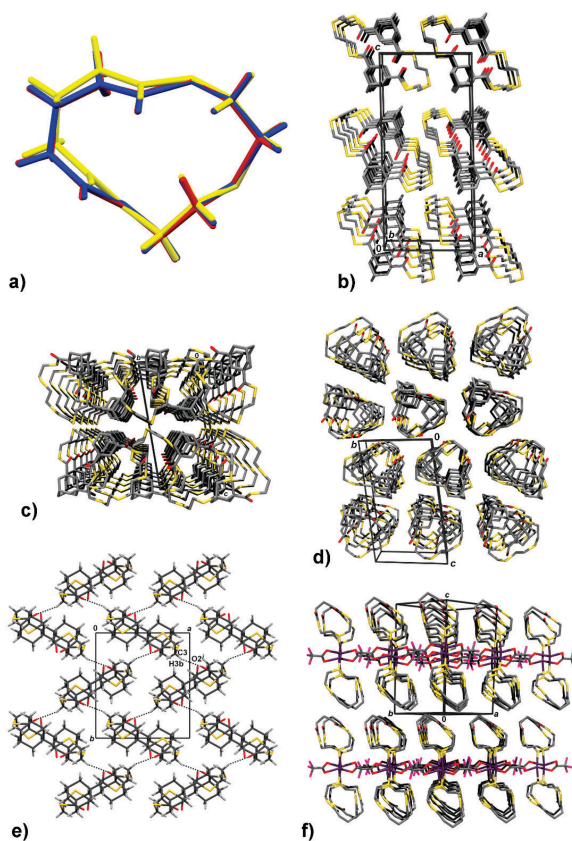


Figure 5. The conformation and assembling of thiamacrocycles in crystals. a) An overlap diagram of the 12-membered thiamacrocyclic ring in a free (red) and two Ag-complexes with 1:1 (yellow) and 1:2 metal to macrocycle ratios (blue). b, c, d) Tubular assemblies (represented by different ring dimensions) are connected by C-H...O bonds including adamantane methylene group and macrocyclic C=O groups. The C-H...S interaction connects tubules into layers, only in structure shown in b). e) A single example of the herringbone pattern in this series is generated by C-H...O hydrogen bonding. f) Crystal packing of the Ag⁺-complex involving two macrocycle rings resembling to calix shapes.^[28]

and analysis of metal coordination of extracted species, were performed. The supramolecular assembling of thiamacrocycles by only weak interactions C-H...O and C-H...S was examined.^[28] In most cases of assembling tubules are formed, whereas a single case of a layered structure with a herringbone pattern was observed (Figure 5e). It was a great fun and excitement to all of us to see that weak interactions create such complex assemblies (Figure 5 b, c and d).

Anion recognition through hydrogen bonds by adamantane-dipyrromethane receptors studies include synthesis, determination of association constants by ¹H NMR, and structural characterization (Figure 6).^[29] The binding energies of the receptor-anion complexes using quantum-chemical methods were calculated to learn more on their stability.

Anion recognition via hydrogen-bonded 1,3-bis-(3-aryluoreido)adamantane receptors was studied in solution and solid state by UV-vis and fluorescence spectrometry. X-ray structure analysis was used to establish the structure of a receptor molecule and four receptor-anion complexes (Figure 7).^[30] The structure of the receptor revealed that incorporation of the adamantane moiety reshaped the receptor into a tweezer-like conformation for the optimal hydrogen bonding network and high selectivity for dihydrogenphosphate anion.

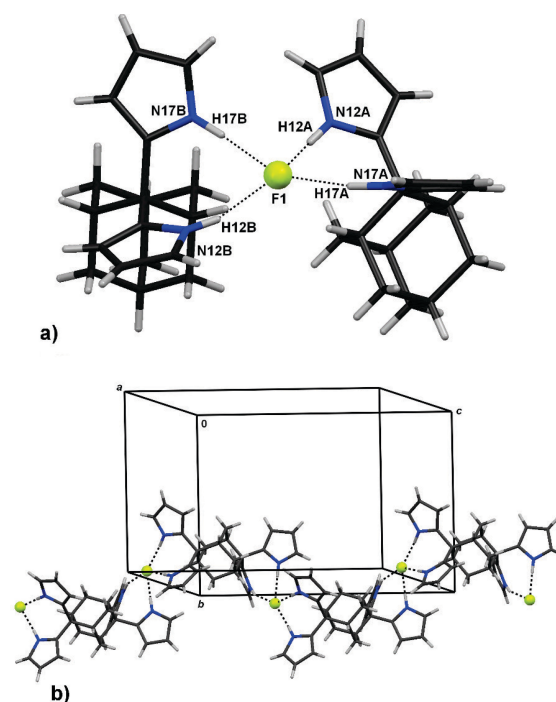
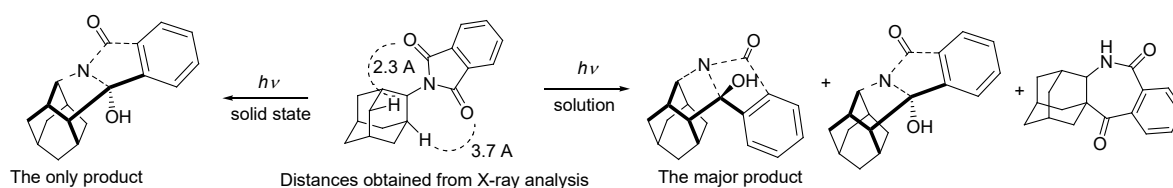


Figure 6. a) Anion recognition ($X = F^-$) is through hydrogen bonding with the substituted adamantane receptor. The anion is in the flattened tetrahedral environment. b) Fluoride anions connect receptor molecules into a chain along [001] direction.^[29]



Scheme 1. Different selectivity of the photochemical reaction of adamantylphthalimide derivative in the solid state and in the solution.^[31]

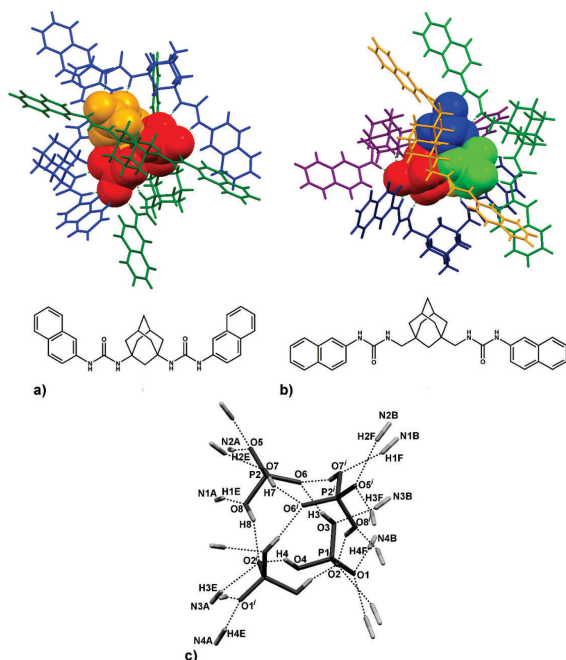


Figure 7. Anion recognition: a) Tetrahedral assemblies of $(1 \cdot \text{H}_2\text{PO}_4)_4$ (left) and $(3 \cdot \text{H}_2\text{PO}_4)_4$ units (right). The receptors **1** and **3** (wire models) are hydrogen bonded to H_2PO_4 anions, shown as van der Waals spheres. Symmetry (in)equivalence is colour-coded. b) Chemical diagram of the receptors **1** and **3**. c) An extensive hydrogen bonding network between the receptor and anion $(1 \cdot \text{H}_2\text{PO}_4)_4$ contributes significantly to the high selectivity for anion recognition.^[30]

Very instructive example of the use of X-ray structure analysis in the study of the structure-reactivity relationship in the solid state on the series of new adamantylphthalimides is given in Scheme 1.^[31] The intramolecular photo-chemical hydrogen atom abstraction in the solid state was detected. It was concluded that the reaction typical of carbonyl compounds in the solid state can be extended to phthalimides, and it is regio- and stereoselective reaction.

Among many thought-provoking results is the recent study of very stable host – guest complexes formed by cucurbit[n]urils ($n = 7, 8$) and cationic diamondoids

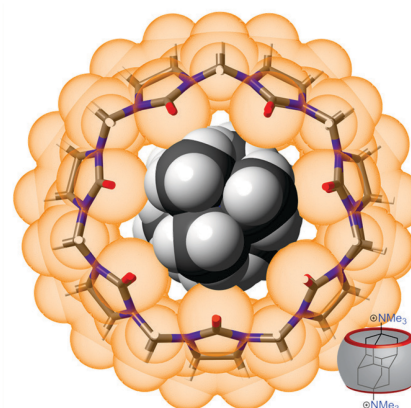


Figure 8. The stable host-guest complexes are shaped by $\text{N}^+ - \text{H} \cdots \text{O}$ interactions.^[32]

involving $\text{N}^+ - \text{H} \cdots \text{O}$ hydrogen bonding (Figure 8).^[32,33] The extensive research was conducted by M. Šekutor, who was a PhD student under K. Mlinarić-Majerski's mentorship. The results obtained, opened up a very successful career to M. Šekutor. Synthesis of novel types of diamondoids - *molecular lego*, and investigations of their properties are of great potential in nanotechnology, materials science, drug delivery, and medicine.^[34]

Prof. K. Mlinarić-Majerski created a productive research team and among her collaborators, there are a few 'science stars' shining on the new roads of organic synthesis. Thanks to long lasting fruitful collaboration among Prof. K. Mlinarić-Majerski, Dr. Marina Šekutor and Dr. Nikola Basarić, and many joint papers, a prosperous future of the research group is assured.

Supplementary Information. Supporting information to the paper is attached to the electronic version of the article at: <http://doi.org/10.5562/cca3534>.

PDF files with attached documents are best viewed with Adobe Acrobat Reader which is free and can be downloaded from Adobe's web site.

REFERENCES

- [1] W. H. Bragg, W. L. & Bragg, *Proc. R. Soc. London A* **1913**, *89*, 277–291. <https://doi.org/10.1098/rspa.1913.0084>

- [2] J. D. Bernal, *Proc. R. Soc., London, A*, **1924**, 106, 749–773. <https://doi.org/10.1098/rspa.1924.0101>
- [3] J. C. Randel, F. C. Niestemski, A. R. Botello-Méndez, W. Mar, G. Ndabashimiye, S. Melinte, J. E. P. Dahl, R. M. K. Carlson, E. D. Butova, A. A. Fokin, P. R. Schreiner, J.-C. Charlier, H. C. Manoharan, *Nature Commun.* **2014**, 5, 4877–4882. <https://doi.org/10.1038/ncomms5877>
- [4] K. Lonsdale, *Nature* **1928**, 122, 810–810; *Proc. R. Soc. Lond. A*, **1929**, 123, 494–515. <https://doi.org/10.1038/122810c0>
- [5] D. Crowfoot Hodgkin, C. W. Bunn, B. W. Rogers-Low, A. Turner-Jones, *The X-ray Crystallographic Investigation of the Structure of Penicillin*, Oxford University Press, Oxford, **1949**. <https://doi.org/10.1038/123515a0>
- [6] J. M. Bijvoet, *Proc. K. Ned. Akad. Wet.* **1949**, 52, 313–314. <https://doi.org/10.1177/0040571X4905235013>
- [7] J. M. Müller, E. Schlittler, H. J. Bein, *Experientia* **1952**, 8, 338–338. <https://doi.org/10.1007/BF02174406>
- [8] R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, R. W. Kierstead, *J. Am. Chem. Soc.* **1956**, 78, 2023–2025. <https://doi.org/10.1021/ja01590a079>
- [9] R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, R. W. Kierstead, *Tetrahedron*, **1958**, 2, 1–57. [https://doi.org/10.1016/0040-4020\(58\)88022-9](https://doi.org/10.1016/0040-4020(58)88022-9)
- [10] F.-E. Chen, J. Huang, *Chem. Rev.* **2005**, 105, 4671–4706. <https://doi.org/10.1021/cr050521a>
- [11] I. L. Karle, J. Karle, *Acta Cryst.* **1968**, B24, 81–91. <https://doi.org/10.1107/S0567740868001731>
- [12] G. Stork, *Pure Appl. Chem.*, **1989**, 61, 439–442. <https://doi.org/10.1351/pac198961030439>
- [13] E. P. Farney, S. S. Feng, F. Schäfers, S. E. Reisman, *J. Am. Chem. Soc.* **2018**, 140, 1267–1270. <https://doi.org/10.1021/jacs.7b13260>
- [14] H. Nakamura, K. Yasui, Y. Kanda, P. S. Baran, *J. Am. Chem. Soc.* **2019**, 141, 1494–1497. <https://doi.org/10.1021/jacs.8b13697>
- [15] R. Taylor, P. A. Wood, *Chem. Rev.* **2019**, 119, 9427–9477. <https://doi.org/10.1021/acs.chemrev.9b00155>
- [16] J. W. Steed, J. L. Atwood, *Supramolecular Chemistry*, 2nd ed. Wiley, New York, **2009**. <https://doi.org/10.1002/9780470740880>
- [17] G. R. Desiraju, J. J. Vittal, A. Ramanan, *Crystal Engineering, A Textbook*, World Scientific Publishing, Singapore, **2011**. <https://doi.org/10.1142/8060>
- [18] M. Aliofkhazraei, *Advances in Nanostructured Composites: Vol. 1 Carbon Nanotube and Graphene Composites*, CRC Press, Taylor & Francis Group, Boca Raton, **2019**. <https://doi.org/10.1201/9781315118406>
- [19] V. Prelog, R. Seiwerth, *Chem. Ber.* **1941**, 74, 1644–1648. <https://doi.org/10.1002/cber.19410741004>
- [20] P. von R. Schlayer, *J. Am. Chem. Soc.* **1957**, 79, 3292–3292. <https://doi.org/10.1021/ja01569a086>
- [21] K. Mlinarić-Majerski, Z. Majerski, *J. Am. Chem. Soc.* **1980**, 102, 1418–1419. <https://doi.org/10.1021/ja00524a033>
- [22] K. Mlinarić-Majerski, Z. Majerski, *J. Am. Chem. Soc.* **1983**, 105, 7389–7395. <https://doi.org/10.1021/ja00363a029>
- [23] K. Mlinarić-Majerski, M. Vinković, J. L. Fry, *J. Org. Chem.* **1994**, 59, 664–667. <https://doi.org/10.1021/jo00082a029>
- [24] K. Mlinarić-Majerski, D. Šafar Cvitaš, J. Veljković, *J. Org. Chem.* **1994**, 59, 2374–2380. <https://doi.org/10.1021/jo00088a018>
- [25] K. Mlinarić-Majerski, M. Kaselj, *J. Org. Chem.* **1994**, 59, 4362–4363. <https://doi.org/10.1021/jo00095a004>
- [26] K. Mlinarić-Majerski, *Distorted Saturated Hydrocarbons: Molecules with Inverted Carbon Atoms, Strained Hydrocarbons*, H. Dodziuk, Ed. Wiley-VCH Verlag GmbH & Co KGaA, Weinheim, **2009**.
- [27] K. Mlinarić-Majerski, D. Pavlović, M. Luić, B. Kojić-Prodić, *Chem. Ber.* **1994**, 127, 1327–1329. <https://doi.org/10.1002/cber.19941270724>
- [28] I. Vujašinić, J. Veljković, K. Molčanov, B. Kojić-Prodić, K. Mlinarić-Majerski, *J. Org. Chem.* **2008**, 73, 9221–9227.
- [29] M. Alešković, N. Basarić, K. Mlinarić-Majerski, K. Molčanov, B. Kojić-Prodić, K. M. Kesharwani, B. Ganguly, *Tetrahedron* **2010**, 66, 1689–1698. <https://doi.org/10.1016/j.tet.2010.01.018>
- [30] V. Blažek, K. Molčanov, K. Mlinarić-Majerski, B. Kojić-Prodić, N. Basarić, *Tetrahedron* **2013**, 2, 517–526. <https://doi.org/10.1016/j.tet.2012.11.030>
- [31] N. Basarić, M. Horvat, O. Franković, K. Mlinarić-Majerski, J. Neudörfl, A. G. Griesbeck, *Tetrahedron* **2009**, 65, 1438–1443. <https://doi.org/10.1016/j.tet.2008.12.010>
- [32] L. Cao, M. Šekutor, P. Y. Zavalij, K. Mlinarić-Majerski, R. Glaser, L. Isaacs, *Angew. Chem. Int. Ed.* **2014**, 53, 988–993. <https://doi.org/10.1002/anie.201309635>
- [33] D. Sigwalt, M. Šekutor, L. Cao, P. Zavalij, Y. Peter, J. Hostaš, H. Ajani, P. Hobza, K. Mlinarić-Majerski, R. Glaser, L. Isaacs, *J. Am. Chem. Soc.* **2017**, 139, 3249–3258. <https://doi.org/10.1021/jacs.7b00056>
- [34] S. Stauss, K. Terashima, *Diamondoids: Synthesis, properties and Applications*, Taylor & Francis Group, Singapore, **2017**. <https://doi.org/10.1201/9781315364667>