

Editorial

Ferrocene and Its Derivatives: Celebrating the 70th Anniversary of Its Discovery

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Ferrocene is already 70 years old! A respectable age, as claimed by the authors of this Special Issue. It is well known how it all began. The birthday of ferrocene can most likely be considered 15 December 1951, when a two-page paper by T. Kealy and P. L. Pauson, titled “A New Type of Organo-Iron Compound”, was published in *Nature*.

However, the traditional but erroneous structure, $C_5H_5-Fe-C_5H_5$, proposed by the authors, where the iron atom was connected to two carbon atoms by simple sigma bonds, cost them the Nobel Prize.

Soon after, in March of the following year, the visionary leader R. Woodward depicted ferrocene, as is now customary, in the form of a sandwich, received by *JACS* on 24 March 1952.

Two months later, in June, R. Woodward and co-authors wrote: “... We now wish to record experiments which demonstrate typically aromatic properties of this unique iron compound, for which we propose the name *ferrocene*.”, received by *JACS* on 2 June 1952.

The discovery of ferrocene was the beginning of a new era in chemistry. The concept of valence, to put it mildly, was turned upside down. The iron atom in ferrocene is equally bonded to ten (!) carbon atoms at once. Such compounds were called ‘sandwich compounds’ because of the metal atom being positioned, or sandwiched, between two plane-parallel cyclopentadienyl rings. By now, compounds of this structure have been synthesized with almost all the transition metals of the Periodic Table.

Ferrocene and similar complexes are unique carriers of a completely new type of bond between the transition metal and carbon. In 1973, G. Wilkinson and E.O. Fischer were awarded the Nobel Prize in Chemistry with the following wording: “*For investigation of chemistry of organometallic compounds (for their pioneering work performed independently on the chemistry of the organometallic, so called sandwich compounds)*”.

Since the early 1950s, both the theoretical aspects of ferrocene chemistry and practical applications have been explored over the course of many years, continuing to the present. The authors in this Special Issue, who honored the journal *Inorganics* and prepared their excellent manuscripts for this Special Issue dedicated to the 70th anniversary of ferrocene, have reflected on the main milestones and outlined the current trends in the development of ferrocene chemistry.

Altogether, this Special Issue comprises five original research articles and three review articles.

The original research articles and reviews within this thematic issue introduction are represented, in no particular order, by the name of the corresponding author or authors.

Ivan Kodrin, Mojca Čakić Semenčić and co-authors [1] evaluated the antimicrobial and antioxidant effects of ferrocene dipeptides previously synthesized by them: so-called peptidomimetics. Hydrophobic L- and D-amino acids, such as valine, leucine and phenylalanine, varied in the studied compounds. To increase the resistance of dipeptides to proteolytic cleavage, a ferrocene modification of dipeptides through an amide bond was implemented.



Citation: Snegur, L.V. Ferrocene and Its Derivatives: Celebrating the 70th Anniversary of Its Discovery.

Inorganics **2023**, *11*, 75. <https://doi.org/10.3390/inorganics11020075>

Received: 26 January 2023

Revised: 30 January 2023

Accepted: 1 February 2023

Published: 3 February 2023



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The best activities were demonstrated by ferrocene dipeptides based on D-amino acids against very harmful bacteria, namely *P. aeruginosa* (a Gram-negative bacterium), *B. subtilis* (a Gram-positive bacterium), and *S. aureus* (a Gram-positive bacterium). It is noteworthy that it was Fc-based D-amino acids that turned out to be more active than their chiral L-analogs.

Radovan Herchel and colleagues synthesized and carefully studied, using physical methods including X-ray crystallography, a new ligand representing 1,1'-disubstituted ferrocene with sterically hindered substituents via the dehydrochlorination reaction of 1,1'-dicarbonyldichloride ferrocene and 4-amino-3,5-di(pyridyl)-4*H*-1,2,4-triazole [2]. The polymer complex of this ligand with an iron(II) salt was studied by ^{57}Fe Mössbauer spectroscopy and magnetometry. In addition, DFT calculations were performed for the ligand and its polymer complex. This research aimed at the design and creation of multifunctional materials.

Yuliya S. Rozhkova, Yuri V. Shklyaev and co-workers reported an efficient and easy approach to the synthesis of novel racemic planar-chiral ferrocene-fused *aza*-heterocycles, 3,4-dihydroferroceno[c]pyridines and 1*H*-ferroceno[c]pyrroles. After optimizing the reaction conditions (solvent-free reaction, methane sulphonic acid, 60 °C and 1:1.2:8 Fc-alcohol/nitrile/acid), a wide range of nitriles (18 compounds with aryls and alkyls) and thiocyanates were prepared using the Ritter reaction, yielding ferrocene-based planar chiral products. The proposed reaction mechanism was discussed. These compounds, according to the authors, may be of interest as bioactive agents [3].

Rita Skoda-Földes and colleagues described the synthesis and characterization, including cyclic voltammetry, of five new ferrocene-benzofuran hybrids with various linkers and evaluated their cytotoxicity [4]. Ferrocene-triazole-benzofurans were prepared with equal success (yields 82–84%) either using a copper catalyst or by Cu-catalyzed process on a polymer-modified silica support.

Ian R. Butler and his team presented a fascinating story about the synthesis of ferrocene-based ligands as pre-catalysts for the so-called Alpha process (over the period of 1996 to 2006). [5]. Extensive synthetic searches and catalytic trials have been carried out, the latter under industrial operating conditions. Product selectivity was always >99%. Despite significant success, the project was not completed and was not commercialized, probably due to financial or other reasons. It is gratifying that the authors provided previously undisclosed catalysis and structural data material within this Special Issue. This is certainly an “Original story”.

In addition to the above collection of original papers, this Special Issue contains three review articles covering applications in the catalysis of planar-chiral heterocyclic ferrocenes, recent advances in the bio-organometallic chemistry of ferrocenes, and progress in mechanistic research, from ferrocene migrations and molecular rearrangements to recent biosciences.

Irina Utepova and colleagues, continuing the ‘ligand story’, presented a comprehensive review that exhaustively analyzed a wide range of data on the selectivity and catalytic activity of planar chiral heterocyclic ferrocenes in metal-catalyzed processes [6]. Of particular note is the perfect and easy-to-perceive graphic form of information presentation. The review covers the first two decades of the 21st century: the period covering the rise of this trend in catalysis.

Michael J. McGlinchey brings readers back to the old discussion about the stabilization of the ferrocene-carbocation center [7]. Several classical reactions are discussed, involving ferrocenyl migrations or rearrangements, as well as unexpected cyclizations. The author introduces readers to more recent applications of these processes in high-performance liquid chromatography and analytical detection techniques, and currently in the realm of bioactive organometallic complexes. This fascinating review can certainly be used as a lecture material for students specializing in organometallic chemistry.

In conclusion, the current trends in the bio-organometallic chemistry of ferrocenes are briefly presented [8]. In addition, Prof. McGlinchey is one of those who, since the mid-1980s, brought the term “bio-organometallic chemistry” into popular use.

Thus, this Special Issue presents the main trends of modern ferrocene chemistry, including synthesis, catalysis, bio-organometallic chemistry, mechanistic and computational aspects.

I wish to thank all the authors for their excellent contributions. I also thank all my editorial and publishing colleagues who have enabled this Special Issue to come into being. I hope for further cooperation both with the authors of this Special Issue and with *Inorganics*, as well as with the MDPI publishing house.

For more information, the readers are advised to visit the site: https://www.mdpi.com/journal/inorganics/special_issues/ferrocene_derivatives.

Conflicts of Interest: The author declares no conflict of interest.

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