

Schiff bases – interesting range of applications in various fields of science

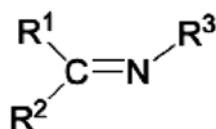
Katarzyna BRODOWSKA*, Elżbieta ŁODYGA-CHRUŚCIŃSKA – Institute of General Food Chemistry, Lodz University of Technology, Lodz, Poland

Please cite as: CHEMIK 2014, **68**, 2, 129–134

Introduction

Schiff bases are condensation products of primary amines and carbonyl compounds and they were discovered by a German chemist, Nobel Prize winner, Hugo Schiff in 1864 [1].

Structurally, Schiff base (also known as imine or azomethine) is an analogue of a ketone or aldehyde in which the carbonyl group (C=O) has been replaced by an imine or azomethine group (Fig. 1) [2]. Schiff base ligands are essential in the field of coordination chemistry, especially in the development of complexes of Schiff bases because these compounds are potentially capable of forming stable complexes with metal ions [3].



R^1 , R^2 , and/or R^3 = alkyl or aryl

Fig. 1. General structure of Schiff bases [4]

A large number of Schiff base complexes are characterized by an excellent catalytic activity in a variety of reactions at high temperature ($>100^\circ\text{C}$) and in the presence of moisture. In recent years, there have been numerous reports of their use in homogeneous and heterogeneous catalysis [5, 6].

Schiff bases and their metal complexes are increasingly being used as catalysts in various biological systems, polymers and dyes. Moreover, it is confirmed that these compounds can act as enzyme preparations [7].

Due to the excellent selectivity, sensitivity and stability of Schiff bases for specific metal ions such as Ag(II), Al(III), Co(II), Cu(II), Gd(III), Hg(II), Ni(II), Pb(II), Y(III) and Zn(II), a large number of different Schiff base ligands have been used as cation carriers in potentiometric sensors. Studies in terms of catalytic properties of Schiff bases exhibit the catalytic activity in the hydrogenation of olefins. One of the more interesting applications of these compounds is the possibility to use them as effective corrosion inhibitors. This phenomenon is the spontaneous formation of a monolayer on the surface to be protected [1].

The interest in metal complexes in which the Schiff bases play a role as the ligands are increasing as evidenced by the number of publications appearing annually (approximately 500) [8]. So much interest in imines can be explained by the fact that they are widely distributed in many biological systems and they are used in organic synthesis and chemical catalysis, medicine, pharmacy and chemical analysis, as well as new technologies [9].

Application in medicine and pharmacy

Imine complexes have a broad range of biological properties: antitumor, antiviral, antifungal, antibacterial [10]. They are also used

in the treatment for diabetes and AIDS. As biological models, they help in understanding the structure of biomolecules and biological processes occurring in living organisms. They participate, inter alia, in photosynthesis and oxygen transport in organisms. They are involved in the treatment of cancer drug resistance, and often tested as antimalarials. It also could be used for the immobilization of enzymes [11, 12].

Biological activity

Schiff bases are characterized by an imine group $-\text{N}=\text{CH}-$, which helps to clarify the mechanism of transamination and racemization reaction in biological system [1].

It exhibits antibacterial and antifungal effect in their biological properties [13, 14]. Metal-imine complexes have been widely investigated due to antitumor and herbicidal use. They can work as models for biologically important species [13].

Antibacterial properties

Mortality increase caused by infectious diseases is directly related to the bacteria that have multiple resistance to antibiotics. The development of new antibacterial drugs enriched by innovatory and more effective mechanisms of action is clearly an urgent medical need [15].

Schiff bases are identified as promising antibacterial agents. For example, N-(Salicylidene)-2-hydroxyaniline (Fig. 2) is active against *Mycobacterium tuberculosis* [4].

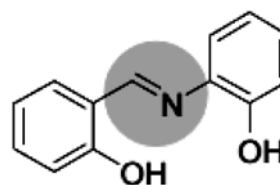


Fig. 2. N-(Salicylidene)-2-hydroxyaniline as the example of bioactive Schiff base [4]

Schiff bases containing 2,4-dichloro-5-fluorophenyl moieties also take part in effective inhibition of bacterial growth [16]. On the other hand, the compounds obtained from furylglyoxal and p-toluidene show antibacterial activity against: *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Proteus vulgaris*. Isatin derived Schiff bases present anti-HIV and antibacterial activity. Other Schiff bases derivatives, which possess antibacterial activity are: benzimidazole, thiazole, pyridine, glucosamine, pyrazolone, hydrazide, thiazolidiones, indole, thiosemicarbazone, p-fluorobenzaldehyde [7].

Antifungal properties

Fungal infections usually are not only limited to the contamination of surface tissues. Recently, there was a considerable increase in the incidence of systemic fungal infections, which are potentially life-threatening [17]. Exploration and development of more effective antifungal agents is necessity, and the individual Schiff bases are considered to be promising antifungal medicines [18].

Corresponding author:

Katarzyna BRODOWSKA – M.Sc., e-mail: kasia.brodowska88@gmail.com

Some of them, such as imine derivatives of quinazolinones possess antifungal properties against *Candida albicans*, *Trichophyton rubrum*, *T. mentagrophytes*, *Aspergillus niger* and *Microsporum gypseum*. Schiff bases and their metal complexes formed between furan or furyl glyoxal with various amines exhibit antifungal activity against *Helminthosporium gramineum* – causing leaf stripe in barley, *Syncephalostrium racemosus* – contributing to fruit rot in tomato and *Colletotrichum capsici* – causing anthracnose in chillies [7].

Biocidal properties

Schiff bases obtained by the synthesis of *o*-aminobenzoic acid and β -keto esters have found biocidal use against *S. epidermidis*, *E. coli*, *B. cinerea* and *A. niger* [2].

By contrast, Schiff bases of isatin derivatives are used in the destruction of protozoa and parasites [19].

Antiviral properties

The use of vaccines may lead to the eradication of pathogens known viruses, such as smallpox, poliomyelitis (polio), whether rubella. Although there are many therapeutic ways to work against viral infections, currently available antiviral agents are not fully effective, which is likely to cause a high rate of mutation of viruses and the possibility of side effects. Salicylaldehyde Schiff bases derived from *l*-amino-3-hydroxyguanidine tosylate are good material for the design of new antiviral agents [4].

Isatin Schiff base ligands are marked by antiviral activity, and this fact is very useful in the treatment of HIV [19]. In addition, it was also found that these compounds have anticonvulsant activity and may be included in the anti-epileptic drugs [20].

Gossypol derivatives also present high antiviral activity. Increasingly, gossypol, often used in medical therapy is replaced by its derivatives, because of their much lower toxicity [21]. Schiff bases have obtained acceptable results for *Cucumber mosaic virus*, whose effectiveness was estimated at 74.7% [7].

Antimalarial properties

Malaria is a disease which when is neglected causes serious health problems. Human malaria is largely caused by four species of the genus *Plasmodium* (*P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*). The search for new drugs, vaccines and insecticides for the prevention or treatment of this disease is a priority. Schiff bases are interesting compounds, which could be part of antimalarial drugs. For example, the compound with such effect is Ancistrocladidine (Fig. 3), which is a secondary metabolite produced by plants of the family Ancistrocladaceae and Dioncophyllaceae, and presenting an imine group in a molecular chain [4].

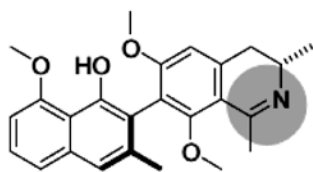


Fig. 3. Ancistrocladaceae – antimalarial activity of bioactive Schiff base [4]

Cryptolepine, valid indolcholine alkaloid, isolated from African plant *Cryptolepis sanguinolenta*, also used in the treatment of malaria, is the product of multi-stage reaction, in which Schiff base is involved [22].

Anticancer properties

Some Schiff bases have a high antitumor activity. Imine derivatives of *N*-hydroxy-*N*'-aminoguanidine block ribonucleotide reductase in tumor cells, so that they are used in the treatment of leukemia [23].

Schiff bases of PDH [N-(1-phenyl-2-hydroxy-2-phenyl ethylidene)-2',4'-dinitrophenyl hydrazine], PHP [N-(1-phenyl-2-hydroxy-2-phenyl ethylidene)-2'-hydroxy phenyl imine] and HHP [N-(2-hydroxy benzylidene)-2'-hydroxy phenyl imine] reduce the average tumor weight (reduction in tumor growth increases with increasing dose) and decrease the growth of cancer cells in mice EAC cells. In addition, they have ability to rebuild depleted haematological parameters, such as hemoglobin, red blood cells (RBC) and white blood cells (WBC) towards the right content. They also show protective effect on hematopoietic system [24].

Application in modern technologies

Photo- and thermochromic properties of Schiff bases as well as their biological activity make them applicable in modern technology. Among others, they are used in optical computers, to measure and control the intensity of the radiation, in imaging systems, as well as in the molecular memory storage, as organic materials in reversible optical memories and photodetectors in biological systems [25, 26].

Due to photochromic properties, Schiff compounds could behave as photostabilizers, dyes for solar collectors, solar filters. They are also exerted in optical sound recording technology [25].

Among others, worthy of interest in the properties associated with Schiff rules include: properties of liquid crystal [27], chelating ability [28], thermal stability [29], optical nonlinearity [30] and the ability to create the structure of a new type of molecular conductors using electrical properties to proton transfer [31]. Because of its thermal stability Schiff bases can be used as stationary phase in gas chromatography [29]. The optical nonlinearity of these compounds allows us to use them as electronic materials, opto-electronic (in optical switches) and photonic components [30].

Imine derivatives can be exerted to obtain conductive polymers. Schiff bases as an electrical conductor possess a variety range of uses: as catalysts in photoelectrochemical processes, electrode materials and micro-electronic equipment, organic batteries or electrochromic display device (graphical output devices) [7].

Due to the presence of the imine group, the electron cloud of the aromatic ring and electronegative nitrogen, oxygen and sulfur atoms in the Schiff bases molecules, these compounds effectively prevent corrosion of mild steel, copper, aluminium and zinc in acidic medium [32].

Application in synthesis and chemical analysis

Schiff bases are a group of organic intermediates, which are very often used in the synthesis and chemical analysis. They are exerted in the production of pharmaceutical and agrochemical industry. In the reaction with hydrogen cyanide Schiff bases may form α -amino acid precursors (Strecker synthesis). Moreover, chiral Schiff bases are used as initial substrates for the asymmetric synthesis of α -amino acids, and as catalysts in asymmetric synthesis. Furthermore, the imines obtained by the condensation reaction of arylamines and carbonyl compounds have determined a group of intermediates used in the preparation of important compounds (arenediazonium nitrates, *N*-arylarene carboxamides, the appropriate amines and cyanamides, β -lactams) [13].

Otherwise, Schiff bases are precursors of reaction of polycyclic derivatives of quinoline and isoquinoline receiving by oxidative ring closure under the influence of ultraviolet light. They are also used for the preparation of acyclic and macrocyclic compounds, such as: cryptats, coronates and podates [25].

These compounds lead to the formation of Ruhemann's purple (reaction between an amino acid and ninhydrin), which allows to detect and assist in the identification of fingerprints [33].

Summary

Schiff bases have been widely explored for industrial applications. However, the biological activity of this class of compounds still requires further investigation. Both Schiff bases and their metal complexes are interesting research subject that constantly provides us with new information about newly created compounds.

Literature

- Ashraf M. A., Mahmood K., Wajid A.: *Synthesis, Characterization and Biological Activity of Schiff Bases*. IPCBEE, 2011, **10**, 1–7.
- Kalaivani S., Priya N. P., Arunachalam S.: *Schiff bases: facile synthesis, spectral characterization and biocidal studies*. IJABPT, 2012, **3**, 219–223.
- Souza P., Garcia-Vazquez J. A., Masaguer J. R.: *Transition Met. Chem.*, 1985, **10**, 410.
- Silva da C., Silva da D., Modolo L., Alves R.: *Schiff bases: A short review of their antimicrobial activities*. J. Ad. Res., 2011, **2**, 1–8.
- Naeimi H., Safari J., Heidarneshad A.: *Dyes Pigments*, 2007, **73**, 251.
- Lippard S. J., Berg J. M.: *Principles of bioinorganic chemistry*. University Science Books, California, 1994.
- Kumar S., Dhar D. N., Saxena P. N.: *Applications of metal complexes of Schiff bases – a review*. J. Sci. Ind. Res., 2009, **68**, 181–187.
- Krygowski T. M., Woźniak K., Anulewicz R., Pawlak D., Kołodziejki W., Grech E., Szady A.: *Through-Resonance Assisted Ionic Hydrogen Bonding in 5-Nitro-N-salicylidene-ethylamine*. J. Phys. Chem., 1997, **101**, 9399–9404.
- Upadhyay K. K., Kumar A., Upadhyay S., Mishra P. C.: *Synthesis, characterization, structural optimization using density functional theory and superoxide ion scavenging activity of some Schiff bases*. J. Mol. Struct., 2008, **873**, 5–16.
- Radecka-Paryzek W., Pospieszna-Markiewicz I., Kubicki M.: *Self-assembled two-dimensional salicylaldimine lanthanum(III) nitrate coordination polymer*. Inorg. Chim. Acta, 2007, **360**, 488–496.
- Boghaei D. M., Askarizadeh E., Bezaatpour A.: *Molecular and Biomolecular Spectroscopy*. Spectrochim. Acta Part A, 2008, **69**, 624–628.
- Prashanthi Y., Kiranmai K., Subhashini N. J. P., Shivaraj: *Synthesis, potentiometric and antimicrobial studies on metal complexes of isoxazole Schiff bases*. Spectrochim. Acta Part A, 2008, **70**, 30–35.
- Ashraf M., Wajid A., Mahmood K., Maah M., Yusoff I.: *Spectral Investigation of the Activities of Amino Substituted Bases*. Orient. J. Chem., 2011, **27**, 2, 363–372.
- Golcu A., Tumer M., Demirelli H., Wheatley R.: *Cd(II) and Cu(II) complexes of polydentate Schiff base ligands: synthesis, characterization, properties and biological activity*. Inorg. Chim. Acta, 2005, **358**, 1785–1797.
- Rice L. B.: *Unmet medical needs in antibacterial therapy*. Biochem Pharmacol., 2006, **71**, 7, 991–995.
- Yang X., Wang Q., Huang Y., Fu P., Zhang J., Zeng R.: *Synthesis, DNA interaction and antimicrobial activities of copper (II) complexes with Schiff base ligands derived from kaempferol and polyamines*. Inorg. Chem. Com., 2012, **25**, 55–59.
- Sundriyal S., Sharma R. K., Jain R.: *Current advances in antifungal targets and drug development*. Curr. Med. Chem., 2006, **13**, 11, 1321–1335.
- Rehman W., Baloch M. K., Muhammad B., Badshah A., Khan K. M.: *Characteristic spectral studies and in vitro antifungal activity of some Schiff bases and their organotin (IV) complexes*. Chin. Sci. Bull., 2004, **49**, 2, 119–122.
- Pandeya S. N., Sriram D., Nath G., De Clercq E.: *Synthesis, antibacterial, antifungal and anti-HIV activity of Schiff and Mannich bases of isatin with N-[6-chlorobenzothiazol-2-yl]thiosemicarbazide*. Indian J. Pharm. Sci., 1999, **61**, 358–361.
- Sridhar S. K., Pandeya S. N., Stables J. P., Ramesh A.: *Anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin derivatives*. Eur. J. Pharm. Sci., 2002, **16**, 129–132.
- Przybylski P., Maluszyńska M., Brzeziński B.: *Spectroscopic and semiempirical studies of new Schiff base of gossypol with allylamine in solution*. J. Mol. Struct., 2005, **750**, 152–157.
- Dutta B., Some S., Ray J. K.: *Thermal cyclization of 3-arylamino-3-(2-nitrophenyl)-propenal Schiff base hydrochlorides followed by triethyl phosphite mediated deoxygenation: a facile synthesis of quindolines*. Tetrahedron Lett., 2006, **47**, 377–379.
- Jesmin M., Ali M. M., Khanam J. A.: *Antitumour activities of some Schiff bases derived from benzoin, salicylaldehyde, amino phenol and 2,4 dinitrophenyl hydrazine*. Thai J. Pharm. Sci., 2010, **34**, 20–31.
- Ozasan M., Karagoz I. D., Kilic I. H., Guldur M. E.: *Ehrlich ascites carcinoma*. Afr. J. Biotechnol., 2011, **10**, 13, 2375–2378.
- Tanaka K., Shimoura R., Caira M. R.: *Synthesis, crystal structures and photochromic properties of novel chiral Schiff base macrocycles*. Tetrahedron Lett., 2010, **51**, 2, 449–452.
- Pistolis G., Gegiou D., Hadjoudis E.: *Effect of cyclodextrin complexation on thermochromic Schiff bases*. J. Photochem. Photobiol. A: Chem., 1996, **93**, 2–3, 179–184.
- Mocanu A. S., Ilis M., Dumitrascu F., Ilie M., Circu V.: *Synthesis, mesomorphism and luminescence properties of palladium(II) and platinum(II) complexes with dimeric Schiff base liquid crystals*. Inorg. Chim. Acta., 2010, **363**, 4, 729–736.
- Issa Y. M., Sherif O. E., Abbas S. M.: *Chelation behaviour of Ce(III), Th(IV), and UO₂(VI) with 5,7-Dihydroxy-6-formyl-2-methylbenzopyran-4-one Schiff bases*. Monatshefte für Chemie, 1998, **129**, 985–998.
- Atta A. M., Shaker N. O., Maysour N. E.: *Influence of the molecular structure on the chemical resistivity and thermal stability of cured Schiff base epoxy resins*. Prog. Org. Coat., 2006, **56**, 100–110.
- Jia J. H., Tao X. M., Li Y. J., Sheng W. J.: *Synthesis and third-order optical nonlinearities of ferrocenyl Schiff base*. Chem. Phys. Lett., 2011, **514**, 1–3, 114–118.
- Amany M. A., Ibrahim: *Electrical and thermal behaviour of some Schiff bases and their charge transfer complexes with acidic acceptors*. Thermochim. Acta., 1992, **197**, 1, 211–217.
- Emregül K. C., Düzgün E., Atakol O.: *The application of some polydentate Schiff base compounds containing aminic nitrogens as corrosion inhibitors for mild steel in acidic media*. Corr. Sci., 2006, **48**, 3243–3260.
- Mastalerz P.: *Podręcznik chemii organicznej*. Wyd. Chem., Wrocław 1996.

Translation into English by the Author

* Katarzyna BRODOWSKA – M.Sc., graduated from the Faculty of Biotechnology and Food Sciences, Lodz University of Technology (specialization: Food Technology and Human Nutrition). Currently she is a student of the first year of 3rd degree studies at the Institute of General Food Chemistry who executes the “Bioavailability of selected chelate compounds with flavonoid analogues” research project.
e-mail: kasia.brodowska88@gmail.com

Elżbieta ŁODYGA-CHRUŚCIŃSKA – (Ph.D.) Assoc. Professor, graduated from the Faculty of Chemistry, Lodz University of Technology. Currently she is team leader of Bioinorganic Chemistry and Environmental Analysis. She is the author of numerous national and foreign research papers.
e-mail: elalodyg@p.lodz.pl