A REVIEW: THE BIOLOGICAL ACTIVITIES OF SCHIFF BASES

VISHESH CHAUHAN[1], VIKAS KUMAR[1], SANDEEP KUMAR TYAGI[2], DHARMENDRA KUMAR[3], KULDEEP KUMAR[4]

[1]Department of Chemistry, IIMT University, Meerut-250 004 (U.P.), India
[2]Department of Environment Science, IIMT University, Meerut-250 004 (U.P.), India
[3]Department of Physics, IIMT University, Meerut-250 004 (U.P.), India
[4]Department of Agriculture, IIMT University, Meerut-250 004 (U.P.), India
Tel : + 91-7417265056, email : vikas_sobst@iimtindia.net

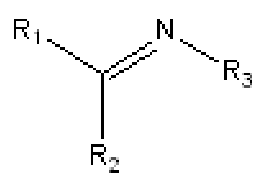
ABSTRACT

An imine ($R_1C=NR_2$) functional group, which is produced when an amine condenses with an aldehyde or a ketone, is a component of chemcial compounds known as schiff bases. Numerous industries, including industry, agriculture, and medicine, frequently use Schiff bases. They are widely recognized for their ability to form stable compounds with metal ions, which makes them useful as catalysts, sensors, and dyes. One of the most important uses of Schiff bases is in the chemistry of medicine. Schiff bases exhibit a wide range of biological characteristics, including anticancer, antibacterial, antifungal, antiviral, anti-inflammatory, and antioxidant action. They have been used as the basis for the creation of several medicines, including antibiotics, cancer treatments, and antimalarial. The chemistry of medicine is one of the most significant applications for Schiff bases.

Keywords: Schiff base, antimicrobial, antiviral, anti-inflammatory, antitumor activity etc.

Introduction

A family of organic compounds known as schiff bases has received a lot of interest because of how adaptable they are and the potential uses they may have in a variety of areas. They are produced when an aldehyde or ketone reacts with a primary amine to initiate a condensation process that forms a carbon-nitrogen double bond with an attached azomethine group (-C=N-). Hugo Schiff, a German scientist, originally created these compounds in 1864 by condensing an aldehyde or ketone with a primary amine. These compounds bear his name.



The specific structure fragment characteristic of Schiff bases, where R_1, R_2 and R_3 are alkyl or (more often) aryl groups. R_1 or/and R_2 may also be hydrogen atoms.

One of the unique features of Schiff bases is their ability to be easily modified by varying the substituents on the aromatic ring or the imine nitrogen. This property makes them a versatile class of compounds that can be tailored to meet specific requirements for various applications.

International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 07 Issue: 05 | May - 2023 SJIF 2023: 8.176 ISSN: 2582-3930

Schiff bases have a wide range of applications in various fields, including organic synthesis, coordination chemistry, medicinal chemistry, and biochemistry[1-3]. They are commonly used as ligands in metal complexation, as intermediates in organic reactions, and as fluorescent probes in biological studies. In addition, Schiff bases are interesting candidates for drug development since they have been shown to display a wide range of biological actions, including antibacterial, antiviral, anti-inflammatory, anticancer, and antidiabetic characteristics[4-10].

Despite their versatility and potential applications, Schiff bases also have some limitations. One of the challenges in the synthesis of Schiff bases is the formation of unwanted by-products due to side reactions. In addition, the stability of Schiff bases can be affected by various factors such as pH, temperature, and the presence of water, which can result in the decomposition of the compound [11,12].

Chemistry of Schiff Base

Schiff bases are synthesized by the reaction of an aldehyde or ketone with a primary amine in the presence of a dehydrating agent. The reaction mechanism involves the formation of an imine intermediate, which is then converted to the final Schiff base product by the elimination of water. The reaction is usually catalyzed by an acid or a base, depending on the nature of the starting materials. Schiff bases can also be prepared by the reaction of an amine with a carbonyl compound in the presence of a Lewis acid catalyst.

One of the most important properties of Schiff bases is their ability to coordinate with metal ions, forming metal complexes that have various applications in catalysis, sensing, and materials science. The imine nitrogen atom in Schiff bases can act as a donor ligand, forming a coordination bond with the metal ion. The coordination chemistry of Schiff bases has been extensively studied, and various metal complexes have been synthesized with different geometries and electronic properties [13].

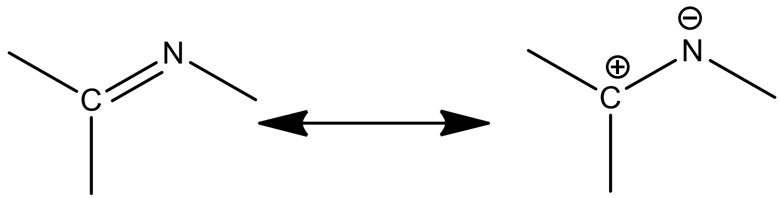
The applications of Schiff bases in various fields are numerous. In medicine, Schiff bases have been used as antimicrobial agents, anticancer agents, and enzyme inhibitors. In materials science, Schiff bases have been used as photochromic dyes, fluorescent probes, and catalysts. In analytical chemistry, Schiff bases have been used as colorimetric and fluorescent probes for the detection of metal ions and biomolecules [14].

Schiff bases are versatile compounds that exhibit unique properties, such as their ability to coordinate with metal ions, exhibit photochromism, and act as fluorescent probes. Their chemistry has been extensively studied, and their applications in various fields are numerous. The development of new Schiff bases with tailored properties will continue to be an active area of research, leading to new and innovative applications in the future.

Physical properties of Schiff bases

Schiff bases are often solids that are colored and transparent. Due to their exact melting points, they are used to quantify metal concentrations and identify carbonyl compounds.

Because the carbon-nitrogen double bond in Schiff bases spins more easily than the carbon-carbon double bond, stereoisomers can transform into one another. Because nitrogen has a higher electronegative charge than carbon, the azomethine bond is polarised.



In general, the isolation of stereoisomers of Schiff bases is challenging due to their relatively small energy differences. However, exceptions exist. When the nitrogen atom is hindered by an electronegative group, the rotation around the azomethine bond becomes restricted, allowing for the separation of stereoisomers. The presence of an electronegative group on the azomethine group pushes the negative charges on the nitrogen atom towards the carbon, resulting in a decrease in polarization and an enhancement of the covalent double bond character. This contributes to the stability and distinct properties of the stereoisomers.

Due to the nitrogen atom's unshared electron pairs and the double bond's capacity to donate electrons, compounds with an azomethine group exhibit fundamental properties. However, compared to their equivalent amines, Schiff bases typically show worse basicity. This is a result of the nitrogen atom's transition from sp3 hybridization in amines to sp2 hybridization in the imine structure of Schiff bases.

The increase in the s character of the hybrid orbital as a result of sp2 hybridization leads to a decrease in basicity. The higher s character reduces the availability of the lone pair of electrons on the nitrogen atom for donation, resulting in diminished basic characteristics of Schiff bases compared to amines[15].

The C-N system in Schiff bases shows absorption in the UV region, although it is considered a weak chromophore. Conjugation with phenyl groups shifts the absorption to the visible spectrum, resulting in a shorter wavelength of absorption. Additionally, the presence of deactivating substituents, like halogens, on the attached aromatic ring can further influence the absorption properties, causing a decrease in the absorption wavelength.

In the infrared (IR) spectrum, the C-N bond stretching vibrations in Schiff bases are typically observed in the range of 1610-1635 cm-1. However, if the C-N bond is positively charged, the IR stretch bands are shifted to higher frequencies, typically observed at 1665-1690 cm-1. These spectral characteristics provide valuable information about the structural features and bonding nature of Schiff bases[16].

Overall, the absorption and IR properties of Schiff bases are influenced by the conjugation of the C-N system with aromatic groups, the presence of electron-donating or electron-withdrawing substituents, and the nature of the C-N bond itself.

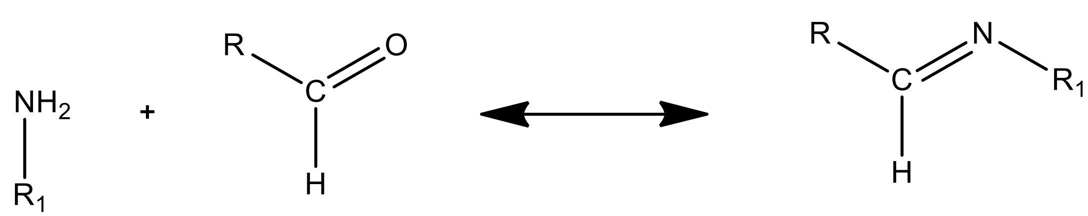
Chemical properties of Schiff bases

The characteristics of Schiff bases are influenced by the substituents attached to the azomethine (C=N) group. When the nitrogen atom is connected to an electronegative group, the stability of the Schiff base molecule increases. This is best exemplified by the fact that Schiff bases with alkyl or aryl substituents on the nitrogen atom are more prone to hydrolysis compared to oximes with hydroxyl groups on the nitrogen atom, as well as phenylhydrazones and semicarbazones with NH groups. While Schiff bases exhibit resistance to alkaline conditions, they undergo hydrolysis in an acidic environment, breaking down into amine and carbonyl compounds. This hydrolysis reaction is facilitated by the protonation of the nitrogen atom, which makes it more susceptible to nucleophilic attack by water, leading to the cleavage of the C=N bond. Therefore, the stability and susceptibility to hydrolysis of Schiff bases are influenced by the nature of the substituents attached to the nitrogen atom of the azomethine group[17].

Reversibility is an inherent characteristic of the Schiff base formation reaction. The reaction involves the condensation of an aldehyde or ketone with an amine, resulting in the formation of a Schiff base and the release of one mole of water. The presence of water in the surroundings can drive the equilibrium of the reaction to the left, favoring the hydrolysis of the Schiff base back into its starting components.

Furthermore, the choice of amines with electronegative atoms and unpaired electrons, such as aromatic amines, can also enhance the efficiency of Schiff base formation. The presence of these electron-donating substituents on the nitrogen atom stabilizes the Schiff base and makes it less prone to hydrolysis. This allows for the separation and isolation of Schiff bases with a high degree of efficiency, as hydrolysis is minimized.

By carefully controlling the reaction conditions, including solvent choice and reactant selection, the reversibility and hydrolysis of Schiff bases can be effectively managed, leading to efficient synthesis and isolation of the desired products.

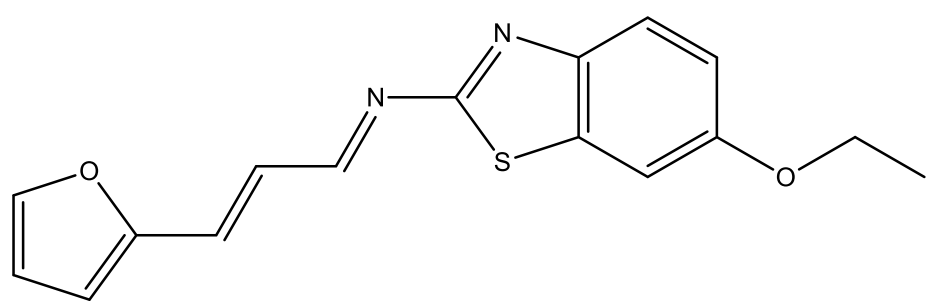


BIOLOGICAL ACTIVITY SCHIFF BASE

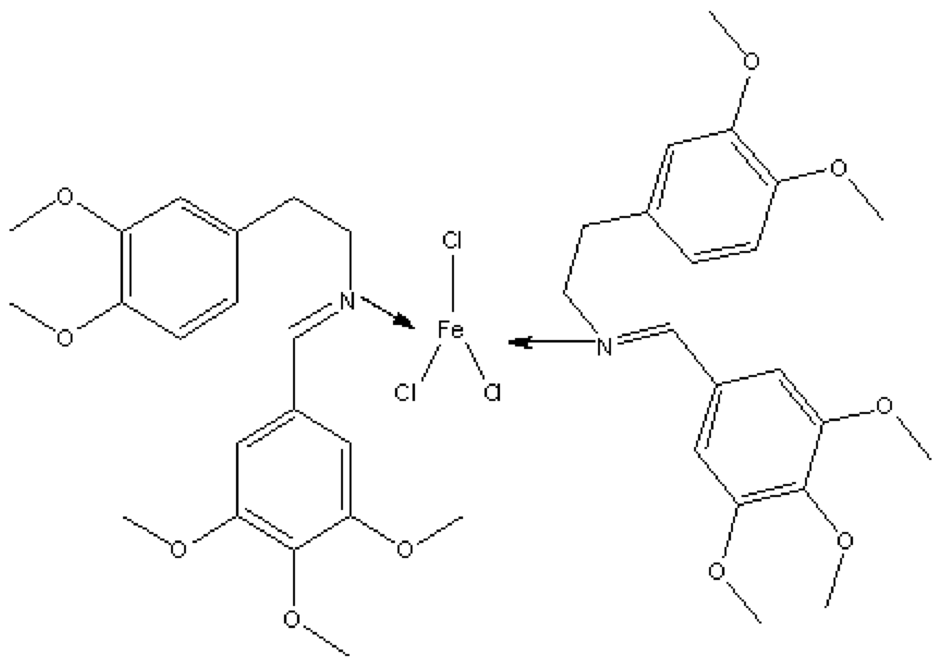
A variety of biological activity, including antibacterial, antiviral, anticancer, anti-inflammatory, and antioxidant characteristics, have been linked to schiff bases. The existence of functional groups that may interact with biological molecules through hydrogen bonds, electrostatic interactions, and covalent bonds is thought to be the cause of the Schiff bases' biological activity. The presence of a conjugated system in Schiff bases also contributes to their biological activity by enabling electron transfer and free radical scavenging.

One of the most significant biological functions of Schiff bases is antimicrobial activity. It has been demonstrated that Schiff bases have antibacterial action against a variety of pathogens, such as bacteria, fungus, and viruses. The antimicrobial activity of Schiff bases is due to their ability to disrupt the cell membrane or cell wall of microorganisms, resulting in cell death. Schiff bases also inhibit the activity of enzymes involved in the biosynthesis of essential molecules, such as DNA, RNA, and proteins, leading to the inhibition of microbial growth. Another important biological activity of Schiff bases is their anticancer activity. Schiff bases have been shown to exhibit cytotoxicity against various cancer cell lines, including breast, lung, colon, and prostate cancer. Because they can cause cancer cells to undergo apoptosis (programmed cell death), suppress cell growth, and mess with the cell cycle, Schiff bases have anticancer properties. The activity of enzymes involved in the metabolism and signal transmission of cancer cells can also be inhibited by schiff bases, which will stop the proliferation of cancer cells. Additionally, it has been demonstrated that schiff bases have antiviral properties against a variety of viruses, including as the influenza virus, herpes simplex virus, and HIV. The antiviral activity of Schiff bases is due to their ability to interfere with the viral life cycle, inhibit viral replication, and block viral entry into host cells. Schiff bases can also activate the immune system, leading to the clearance of viral infections. In addition to their antimicrobial, anticancer, and antiviral activities, Schiff bases exhibit antioxidant and anti-inflammatory properties. Schiff bases can scavenge free radicals and inhibit oxidative stress, leading to the prevention of cellular damage. Schiff bases can also inhibit the production of pro-inflammatory cytokines, leading to the inhibition of inflammation.

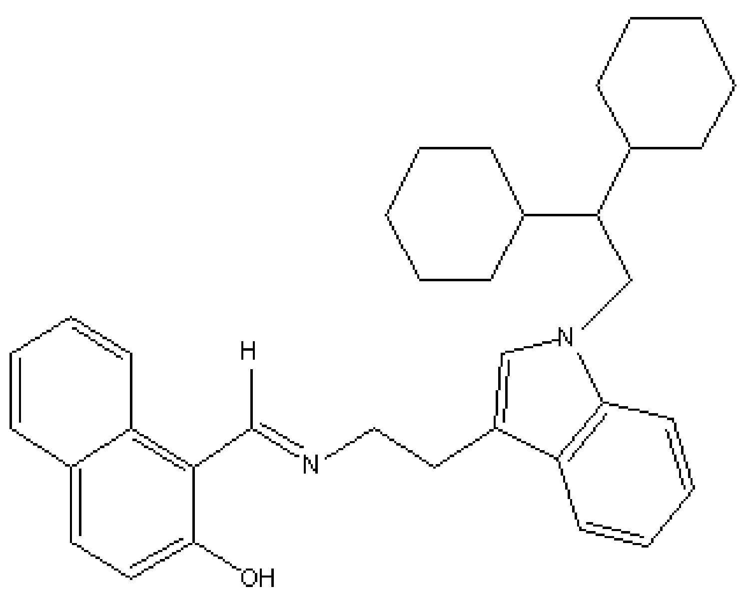
The new Schiff baseAccording to Abu-Yamin [18], this compound is N-(6-ethoxybenzo[d]thiazol-2-yl)-3-(furan-2-yl)prop-2-en-1-imine. Screening was done on the Schiff base and its complexes to look for things like antibacterial, antifungal, antioxidant, and anticancer activity.



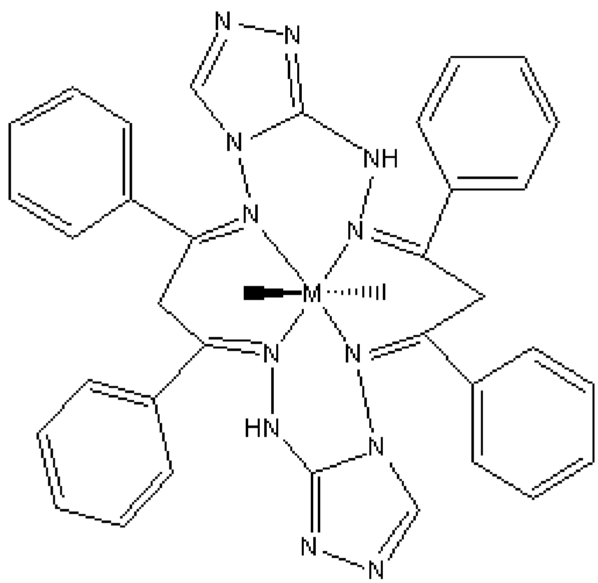
Schiff bases were used in the work published by Nureen et al [19], and their iron and zinc metal complexes were synthesised. Several spectroscopic methods, including Ultraviolet-visible spectroscopy (UV-Vis), Fourier-transform infrared spectroscopy (FTIR), Nuclear magnetic resonance spectroscopy (NMR), and Mass spectrometry (MS), were used to characterise the ligands and their metal complexes.



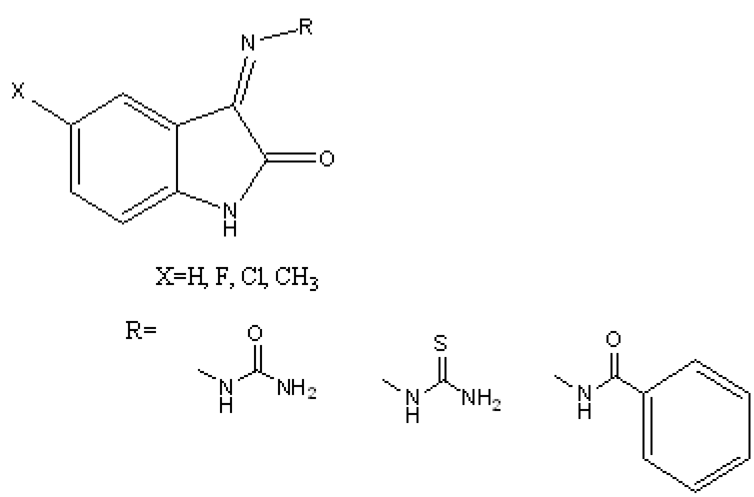
By reacting 1[2[(1H]Indol3yl)ethylimino] methyl naphthalen-2-ol with dicyclohexyl amine, Zoubi et al. created a novel Schiff base in 2018 called 1[(2[(dicyclohexylamino)methyl]1Hindol3ylmethyl]naphthalen-2-ol (HL)] [19].



Six unique Co(II) and Ni(II)-triazole Schiff base complexes were successfully synthesised in a work by Nassar et al. from 2017. Techniques including elemental analysis, FT-IR, UV-Vis spectroscopy, magnetic moment, conductivity, and thermal analysis were used to characterise these complexes. [20].



The synthesis and characterisation of Schiff base compounds produced from 5-substituted isatins and bioactive amines/hydrazides were the main objectives of the 2016 study by Tehrani et al. The objective was to investigate these chemicals' possible bioactivity. Spectroscopic methods such nuclear magnetic resonance, infrared spectroscopy, and mass spectrometry were used to confirm the structures of the synthesised Schiff bases [21].



CONCLUSION

A group of chemical compounds known as schiff bases have a variety of biological effects, such as antibacterial, antiviral, anticancer, and anti-inflammatory capabilities. The biological activity of Schiff bases is attributed to their ability to interact with biological molecules through hydrogen bonding, electrostatic interactions, and covalent bonding. Schiff bases have the potential to be developed into therapeutic agents for the treatment of various diseases, and the development of new Schiff bases with tailored properties will continue to be an active area of research. It is important to note that the biological activity of Schiff bases is influenced by their chemical structure, substituents, and other factors. Therefore, the specific properties and potential applications of Schiff bases may vary for different compounds. Further research and studies are necessary to explore the full range of biological activities and mechanisms of action of Schiff bases. Schiff bases offer a broad range of applications in diverse fields due to their synthetic versatility, coordination chemistry, and biological activities. Continued research on Schiff bases and their derivatives is expected to uncover further insights into their properties and enable the development of new and improved applications in the future.

REFERENCE

1. Ghanghas, P., Choudhary, A., Kumar, D., & Poonia, K. (2021). Coordination metal complexes with Schiff bases: Useful pharmacophores with comprehensive biological applications. Inorganic Chemistry Communications, 130, 108710. https://doi.org/10.1016/j.inoche.2021.108710
2. Collinson, S. L., & Fenton, D. E. (1996). Metal complexes of bibracchial Schiff base macrocycles. Coordination Chemistry Reviews, 148, 19–40. https://doi.org/10.1016/0010-8545(95)01156-0
3. Abdallah, S. A., Mohamed, G. G., Zayed, M. A., & El-Ela, M. S. A. (2009). Spectroscopic study of molecular structures of novel Schiff base derived from o-phthaldehyde and 2-aminophenol and its coordination compounds together with their biological activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 73(5), 833–840. https://doi.org/10.1016/j.saa.2009.04.005
4. Bentham Science Publishers. (n.d.). Advances in Research of Schiff-Base Metal Complexes as Potent Ant. . .: Ingenta Connect. https://www.ingentaconnect.com/content/ben/cmc/2013/00000020/00000036/art00010
5. Waziri, I., Kelani, M. T., Oyedeji-Amusa, M. O., Oyebamiji, A. K., Coetzee, L. C., Adeyinka, A. S., & Muller, A. J. (2023). Synthesis and computational investigation of N,N-dimethyl-4-[(Z)-(phenylimino)methyl]aniline derivatives: Biological and quantitative structural activity relationship studies. Journal of Molecular Structure, 1276, 134756. https://doi.org/10.1016/j.molstruc.2022.134756
6. Mukhtar, S. S., Hassan, A. A., Morsy, N. M., Hafez, T. S., Hassaneen, H. M., & Saleh, F. M. (2021). Overview on Synthesis, Reactions, Applications, and Biological Activities of Schiff Bases. Egyptian Journal of Chemistry, 0(0), 0. https://doi.org/10.21608/ejchem.2021.79736.3920
7. Gangani, B. J., & Parsania, P. H. (2007). Microwave-Irradiated and Classical Syntheses of Symmetric Double Schiff Bases of 1,1′-Bis(4-aminophenyl)cyclohexane and their Physicochemical Characterization. Spectroscopy Letters, 40(1), 97–112. https://doi.org/10.1080/00387010601091004
8. Kaushik, P. K., Varshney, V. K., Kumar, P., Bhatia, P., & Shukla, S. (2016). Microwave-assisted synthesis, characterization, and antimicrobial activity of some odorant Schiff bases derived from naturally occurring carbonyl compounds and anthranilic acid. Synthetic Communications. https://doi.org/10.1080/00397911.2016.1245749

9. Iranmanesh, H., Behzad, M., Bruno, G., Rudbari, H. A., Nazari, H., Mohammadi, A., & Taheri, O. (2013). Cobalt(III) Schiff base complexes derived from mesostilbenediamine: Synthesis, characterization, crystal structure, electrochemistry and antibacterial studies. Inorganica Chimica Acta, 395, 81–88. https://doi.org/10.1016/j.ica.2012.10.030
10. Qin, W., Long, S., Panunzio, M., & Biondi, S. (2013). Schiff Bases: A Short Survey on an Evergreen Chemistry Tool. Molecules, 18(10), 12264–12289. https://doi.org/10.3390/molecules181012264
11. Bera, K., Mondal, A., Pal, U., & Maiti, N. C. (2020). Porphyrin-Armored Gold Nanospheres Modulate the Secondary Structure of α-Synuclein and Arrest Its Fibrillation. Journal of Physical Chemistry C, 124(11), 6418–6434. https://doi.org/10.1021/acs.jpcc.9b11503
12. Feng, L., Shi, W., Ma, J., Chen, Y., Kui, F., Hui, Y., & Xie, Z. (2016). A novel thiosemicarbazone Schiff base derivative with aggregation-induced emission enhancement characteristics and its application in Hg2+ detection. Sensors and Actuators B-chemical, 237, 563–569. https://doi.org/10.1016/j.snb.2016.06.129
13. Jin, Y., Zhu, Y., & Zhang, W. (2013). Development of organic porous materials through Schiff-base chemistry. CrystEngComm, 15(8), 1484–1499. https://doi.org/10.1039/c2ce26394g
14. Nath, M., & Saini, P. K. (2011). Chemistry and applications of organotin(iv) complexes of Schiff bases. Dalton Transactions, 40(27), 7077. https://doi.org/10.1039/c0dt01426e
15. Masteri-Farahani, M., Eghbali, P., & Şahin, E. (2019). SBA-16 supported amino acid Schiff base complexes of molybdenum as new heterogeneous molybdenum catalysts. Colloids and Surfaces A: Physicochemical and Engineering Aspects, 570, 347–353. https://doi.org/10.1016/j.colsurfa.2019.03.047
16. Hejchman, E., Kruszewska, H., Maciejewska, D., Sowirka-Taciak, B., Tomczyk, M., Sztokfisz-Ignasiak, A., Jankowski, J., & Mlynarczuk-Bialy, I. (2019). Design, synthesis, and biological activity of Schiff bases bearing salicyl and 7-hydroxycoumarinyl moieties. Monatshefte Fur Chemie, 150(2), 255–266. https://doi.org/10.1007/s00706-018-2325-5
17. Abu-Yamin, A. A., Abduh, M. S., Saghir, S. a. M., & Al-Gabri, N. A. (2022). Synthesis, Characterization and Biological Activities of New Schiff Base Compound and Its Lanthanide Complexes. Pharmaceuticals, 15(4), 454. https://doi.org/10.3390/ph15040454
18. Naureen, B., Miana, G. A., Shahid, K., Asghar, M., Tanveer, S., & Sarwar, A. (2021). Iron (III) and zinc (II) monodentate Schiff base metal complexes: Synthesis, characterisation and biological activities. Journal of Molecular Structure, 1231, 129946. https://doi.org/10.1016/j.molstruc.2021.129946
19. Zoubi, W. A., Al-Hamdani, A. a. S., Ahmed, S. W., & Ko, Y. G. (2018). Synthesis, characterization, and biological activity of Schiff bases metal complexes. Journal of Physical Organic Chemistry, 31(2), e3752. https://doi.org/10.1002/poc.3752
20. Nassar, M. Y., Aly, H. F., Abdelrahman, E. M., & Moustafa, M. S. (2017). Synthesis, characterization, and biological activity of some novel Schiff bases and their Co(II) and Ni(II) complexes: A new route for Co3O4 and NiO nanoparticles for photocatalytic degradation of methylene blue dye. Journal of Molecular Structure, 1143, 462–471. https://doi.org/10.1016/j.molstruc.2017.04.118
21. Tehrani, K. H. M. E., Hashemi, M., Hassan, M., Kobarfard, F., & Mohebbi, S. (2016). Synthesis and antibacterial activity of Schiff bases of 5-substituted isatins. Chinese Chemical Letters, 27(2), 221–225. https://doi.org/10.1016/j.cclet.2015.10.027