

Biological Activity of Azo Compounds: A Comprehensive Review

Manar Ghyath Abd-Almutalib

Department of Pharmacy Techniques, Kufa, Technical Institute, Al-Furat Al-Awsat Technical University, 31001, Kufa, Al-Najaf, Iraq.

ABSTRACT: Azo compounds, defined by the characteristic azo ($-N=N-$) functional group, represent one of the largest classes of synthetic organic compounds with extensive industrial and biomedical applications. This review provides a comprehensive analysis of their synthesis methods, structural diversity, physicochemical properties, and biological activities. Emphasis is placed on their evolving role in medicinal chemistry, particularly in the development of antimicrobial, anticancer, antioxidant, and anti-inflammatory agents. Advances in synthetic techniques—including green chemistry approaches—have improved their functional versatility and environmental safety. Furthermore, applications in photodynamic therapy, laser dyes, and dye-sensitized solar cells highlight their importance in emerging technologies. The review also discusses environmental concerns and the need for sustainable degradation strategies. This work aims to serve as a reference point for researchers exploring the multifunctional potential of azo compounds in both industrial and biomedical domains.

KEYWORDS: Diazotization and coupling reactions, Chromophore and auxochrome, Anticancer azo compounds, Antibacterial azo derivatives, Anti-inflammatory azo compounds.

1. INTRODUCTION TO AZO COMPOUNDS

Azo compounds are a prominent class of synthetic organic molecules characterized by the presence of a diazenyl group ($-N=N-$) connecting two sp^2 -hybridized carbon atoms, typically within aromatic or heterocyclic systems. This azo linkage acts as a chromophore, conferring intense coloration and enabling widespread use in the dye and pigment industries [1,2]. As early as the 19th century, azo dyes have been central to textile coloration, and they currently account for more than 60% of all dyes used globally [3,4].

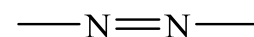
Beyond coloration, the structural flexibility of azo compounds allows for the incorporation of various functional groups, leading to tailored properties for advanced applications. Modern developments have expanded their utility into diverse areas such as photodynamic therapy, nonlinear optics, molecular electronics, solar energy harvesting, and biomedical engineering [5–7].

Azo compounds are typically synthesized via diazotization followed by electrophilic aromatic substitution, known as azo coupling. This approach provides synthetic accessibility and adaptability, especially when designing compounds for specific biological or electronic functions [8]. The ability to fine-tune substituents on either side of the azo group offers control over key characteristics such as light absorption, solubility, redox potential, and biological activity [9,10].

Recent research has underscored the biomedical relevance of azo derivatives, particularly as potential antimicrobial, anticancer, anti-inflammatory, and antioxidant agents [11–13]. Their biological activity is often attributed to their ability to interact with DNA, enzymes, and cellular redox systems, as well as their role as prodrugs that release active metabolites under specific physiological conditions.

Despite these promising features, azo compounds also pose environmental and toxicological challenges. Under reductive or acidic conditions, azo bonds can cleave to release aromatic amines, some of which are known to be mutagenic or carcinogenic [14]. Consequently, recent studies focus on designing safer azo systems, applying green chemistry approaches, and developing eco-friendly degradation techniques [15,16].

This review aims to provide a detailed and up-to-date summary of the structural features, synthetic methodologies, physicochemical properties, and bioactivities of azo compounds. Special attention is given to their pharmaceutical potential, mechanisms of action, and emerging roles in advanced materials science.



Schem (1) azo compound

Biological Activity of Azo Compounds: A Comprehensive Review

2. GENERAL PROPERTIES OF AZO COMPOUNDS

2.1. Bonding and Chemical Structure

Azo compounds typically possess at least one nitrogen-nitrogen ($-N=N-$) double bond associated with heterocyclic or aromatic systems. This conjugated structure enhances stability and facilitates visible light absorption, contributing to their intense coloration [12,13].

2.2. Optical Properties

Due to their conjugated structures, azo compounds exhibit strong absorption in the visible spectrum. Their optical properties can be fine-tuned by modifying substituents on the aromatic rings, making them valuable in dye and photochemical applications [14,15].

2.3. Chemical and Thermal Stability

Azo compounds, particularly those with aromatic substituents, demonstrate high chemical and thermal stability. Their stability can be further enhanced by incorporating electron-donating or electron-withdrawing groups. However, under reductive or acidic conditions, azo compounds may degrade into amines [5,16].

2.4. Polarity and Solubility

The solubility of azo compounds depends on their structural modifications. While many are soluble in organic solvents, some require functionalization to improve water solubility. The introduction of polar functional groups, such as hydroxyl ($-OH$) or sulfonates ($-SO_3H$), enhances hydrophilicity [7,18,19].

2.5. Redox Behavior

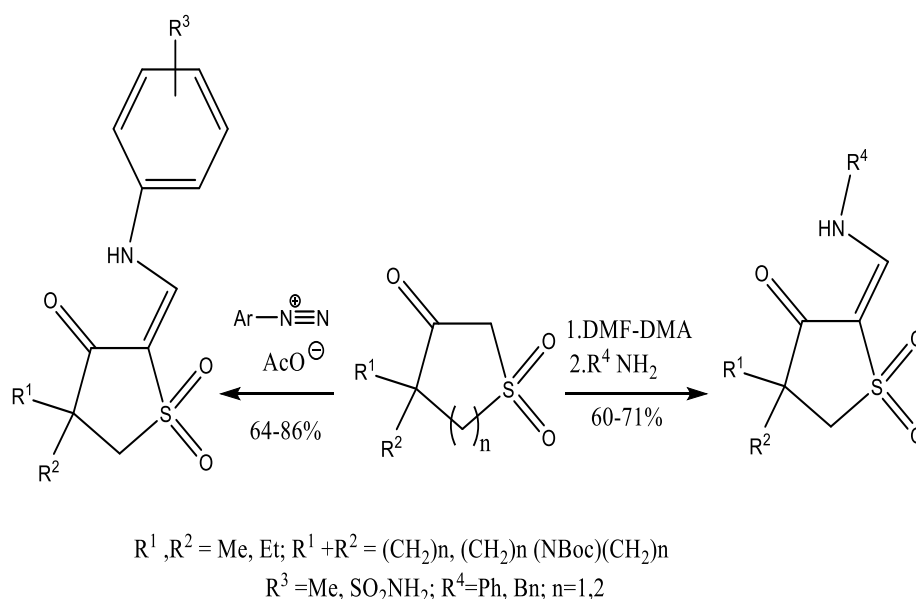
Azo compounds exhibit redox activity, making them useful in electrochemical applications. They can undergo reduction to hydrazines ($-NH-NH-$) or cleavage into aromatic amines under reductive conditions. This property is relevant in biological and medicinal applications but also raises environmental concerns [9,20,21].

3. BIOLOGICAL AND PHARMACOLOGICAL ACTIVITY

3.1. Anti-cancer and anti-bacterial

Recent studies highlight the synthesis of cyclic β -keto sulfone derivatives containing azo groups, demonstrating significant biological activity:

- Antibacterial Activity:** These compounds effectively inhibit *Staphylococcus aureus*, likely through interactions with dihydropteroate synthase (DHPS), a crucial bacterial enzyme [22].
- Anticancer Activity:** Certain azo derivatives exhibit selective cytotoxicity against the MDA-MB-231 breast cancer cell line while sparing normal cells. Their strong binding affinity to therapeutic targets such as CDC-like kinase 4 (CLK4) and indoleamine 2,3-dioxygenase 1 (IDO1) suggests potential anticancer applications [22].



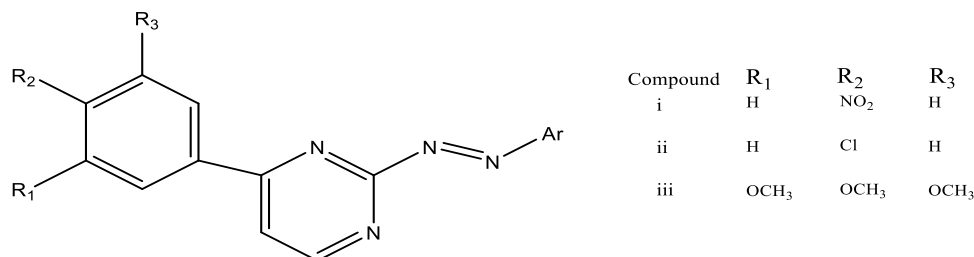
Scheme 2. Structures of bioactive azo-based cyclic β -keto sulfones

3.2. Antioxidant and anti-inflammatory properties:

Azo compounds have also been explored for their antioxidant and anti-inflammatory potential:

Biological Activity of Azo Compounds: A Comprehensive Review

1. Antioxidant Activity: Azo-based pyrimidine derivatives exhibit strong free radical scavenging properties, as demonstrated in DPPH assays [23].
2. Anti-inflammatory Activity: These compounds show promising anti-inflammatory effects in heat hemolysis assays, indicating their potential for inflammation control [23].

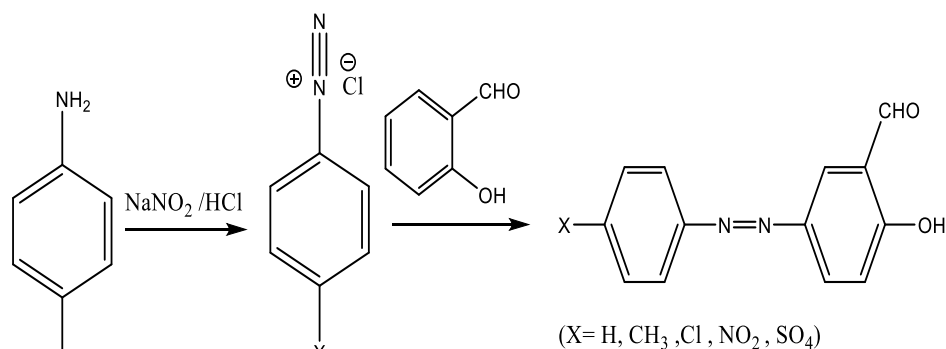


Scheme (3) 6-aryl substituted pyrimidine azo dyes

4. PRODUCTION AND APPLICATIONS OF AZO COMPOUNDS

4.1. Microwave-Assisted Azo-Schiff Base Synthesis

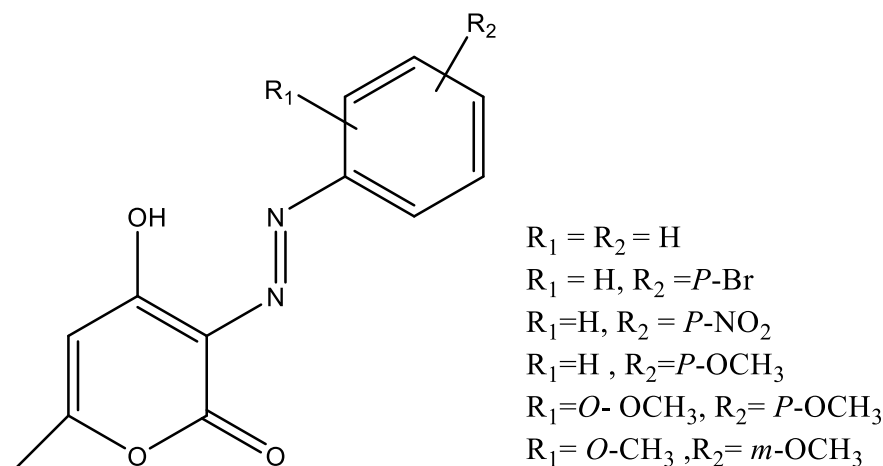
A recent study employed microwave-assisted synthesis to produce novel tetra-Schiff bases (M2–M9) and azo-Schiff bases (M16–M20). This method offers a cleaner, more efficient alternative to conventional synthesis. IR and NMR spectroscopy confirmed the structures of these derivatives, which show potential as photosensitizers in photochemical reactions [2].



Scheme (4) azo-salicylaldehyde and aromatic amines with a bis-Schiff base

4.2. Azo Antibacterial Agents and Disperse Dyes

Researchers synthesized a new class of azo disperse dyes by coupling diazonium salts derived from aniline derivatives with triacetic acid lactone (TAL) or its dihydro derivative (DHTAL). These dyes exhibited strong antibacterial activity and high visible light absorption in organic solvents [3].



Scheme (5) Azo dye synthesis using aniline derivatives and TAL

CONCLUSION

Azo compounds are highly versatile chemicals with broad industrial, biological, and pharmacological applications. Their tunable optical properties, stability, and diverse functionalities make them invaluable in textile dyeing, cancer therapy, and advanced materials research. The development of environmentally friendly synthesis methods and multifunctional azo derivatives further

Biological Activity of Azo Compounds: A Comprehensive Review

enhances their potential. However, concerns about their environmental impact necessitate continued research into sustainable degradation strategies and assessments of biocompatibility. Future studies should focus on optimizing their pharmacological properties and exploring their use in emerging fields such as photodynamic therapy and solar energy conversion.

ACKNOWLEDGMENTS

I am particularly grateful to [Dr. Rusul Arif] for their financial support. Additionally. Finally, I appreciate the continuous encouragement and support from my family and friends.

REFERENCES

- 1) Singh, N., & Singh, R. *Mini Rev. Med. Chem.* 23, **2023**, 789–805.
- 2) Wang, L., & Liu, Y. *Molecules* 28, **2023**, 6741.
- 3) Alzain, H., & Ibrahim, S. *Int. J. Res. Rev.* 10, **2023**, 656–664.
- 4) Begum, S., Mishra, S. R., & Ahmaruzzaman, M. *Environ. Sci. Pollut. Res.* 29, **2022**, 4567–4581.
- 5) Kansal, S. K., Ali, A. H., & Kapoor, S. *Desalination* 259, **2010**, 147–155.
- 6) Chebli, D., Fourcade, F., Brosillon, S., Nacef, S., & Amrane, A. *J. Chem. Technol. Biotechnol.* 85, **2010**, 626–632.
- 7) Cooksey, C. J. *Biotech. Histochem.* 94, **2019**, 503–507.
- 8) Machado, K. M. G., Matheus, D. R., & Bononi, V. L. R. *Braz. J. Microbiol.* 36, **2005**, 246–252.
- 9) Priya, A. K., Kaith, B. S., Vipula, & Chandel, K. *Int. J. Biol. Macromol.* 206, **2022**, 456–467.
- 10) Machado, K. M. G., Matheus, D. R., & Bononi, V. L. R. *Braz. J. Microbiol.* 36, **2005**, 246–252.
- 11) Singh, N., & Singh, R. *Mini Rev. Med. Chem.* 23, **2023**, 789–805.
- 12) Wang, L., & Liu, Y. *Molecules* 28, **2023**, 6741.
- 13) Alzain, H., & Ibrahim, S. *Int. J. Res. Rev.* 10, **2023**, 656–664.
- 14) Begum, S., Mishra, S. R., & Ahmaruzzaman, M. *Environ. Sci. Pollut. Res.* 29, **2022**, 4567–4581.
- 15) Kansal, S. K., Ali, A. H., & Kapoor, S. *Desalination* 259, **2010**, 147–155.
- 16) Chebli, D., Fourcade, F., Brosillon, S., Nacef, S., & Amrane, A. *J. Chem. Technol. Biotechnol.* 85, **2010**, 626–632.
- 17) Cooksey, C. J. *Biotech. Histochem.* 94, **2019**, 503–507.
- 18) Priya, A. K., Kaith, B. S., Vipula, & Chandel, K. *Int. J. Biol. Macromol.* 206, **2022**, 456–467.
- 19) Machado, K. M. G., Matheus, D. R., & Bononi, V. L. R. *Braz. J. Microbiol.* 36, **2005**, 246–252.
- 20) Singh, N., & Singh, R. *Mini Rev. Med. Chem.* 23, **2023**, 789–805.
- 21) Wang, L., & Liu, Y. *Molecules* 28, **2023**, 6741.