



THE ROLE OF AZOXY FUNCTIONAL GROUPS IN ENHANCING ACARICIDAL ACTIVITY OF AROMATIC COMPOUNDS.

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Annotation: Azoxy functional groups ($-N=N(O)-$) have gained considerable attention in agrochemical research due to their ability to modulate biological activity in aromatic compounds. This study investigates the influence of azoxy moieties on the acaricidal efficacy of synthetic aromatic derivatives against selected mite species. A series of azoxybenzene-based compounds were synthesized and evaluated for their biological activity using standardized bioassay methods. The structure–activity relationship (SAR) analysis revealed that the presence of azoxy linkages significantly enhances acaricidal potency compared to their azo or nitro analogs, likely due to improved electron distribution and target affinity. Spectroscopic (FTIR, NMR) and chromatographic (GC-MS) techniques confirmed the purity and structure of synthesized compounds. The findings support the hypothesis that azoxy functionalization contributes to increased bioefficacy and selectivity, making such derivatives potential candidates for next-generation eco-friendly acaricides.

Key words: Azoxy functional group, azoxybenzene, acaricidal activity, aromatic compounds, structure–activity relationship, bioactive molecules, synthetic pesticides.

Introduction: The widespread emergence of acaricide-resistant mite populations poses a serious threat to agricultural productivity and public health, necessitating the development of new, effective, and environmentally safer compounds. Among the promising candidates, aromatic compounds bearing azoxy functional groups ($-N=N(O)-$) have attracted scientific interest due to their unique electronic configuration, stability, and potential for biological activity. Azoxy derivatives are structurally related to azo and nitro compounds but possess distinct physicochemical characteristics that may enhance their interaction with biological targets. This study aims to explore the role of azoxy linkages in modulating acaricidal efficacy, particularly focusing on how these groups influence molecular polarity, target binding affinity, and overall bioactivity. By synthesizing and characterizing a series of azoxybenzene-based compounds and

evaluating their acaricidal properties, we seek to determine whether the introduction of azoxy moieties can significantly improve the potency and selectivity of aromatic acaricides.

Literature review: Previous research has highlighted the potential of aromatic compounds, particularly those containing nitrogen-based functional groups, as bioactive agents against arthropod pests. Azo and nitro derivatives have long been studied for their pesticidal properties; however, their effectiveness is often limited by low selectivity and environmental persistence. Azoxy compounds, which incorporate both azo and nitroso characteristics within a single functional group, have been less extensively studied despite their promising chemical properties. Studies have shown that azoxybenzenes exhibit moderate to high biological activity, including antimicrobial, insecticidal, and herbicidal effects, suggesting a broad spectrum of action. For instance, recent investigations into azoxy-substituted triazines and phenyl derivatives demonstrated enhanced acaricidal activity when compared to their parent structures. The enhanced efficacy has been attributed to the azoxy group's ability to influence electron distribution and facilitate molecular interactions with biological targets, such as enzyme systems in mites. Furthermore, advances in synthetic organic chemistry have enabled the development of structurally diverse azoxy compounds with tailored activity profiles. However, comprehensive studies that specifically assess the acaricidal potential of azoxy-functionalized aromatic compounds remain limited, indicating a need for further exploration in this area.

Methodology: A series of azoxy-functionalized aromatic compounds were synthesized via the oxidative coupling of aniline derivatives using hydrogen peroxide in the presence of acetic acid as a mild oxidant under controlled temperature conditions (0–5 °C). The resulting azoxybenzenes were purified through recrystallization and characterized by Fourier-transform infrared spectroscopy (FTIR), proton nuclear magnetic resonance (^1H NMR), and gas chromatography–mass spectrometry (GC-MS) to confirm structural integrity and purity. The acaricidal activity of the synthesized compounds was evaluated using a contact bioassay against adult *Tetranychus urticae* mites under laboratory conditions. Test solutions were prepared by dissolving each compound in dimethyl sulfoxide (DMSO) and diluting to target concentrations (10, 25, 50, and 100 $\mu\text{g/mL}$). Mortality rates were recorded after 24 and 48 hours of exposure and compared to standard commercial acaricides and negative controls. Statistical analysis was conducted using one-way ANOVA followed by Tukey's post hoc test ($p < 0.05$) to assess the significance of the observed effects. Structure–activity relationships (SAR) were determined by correlating molecular features (electron-withdrawing/donating substituents) with bioactivity outcomes.

Results: The synthesized azoxybenzene derivatives exhibited a concentration-dependent acaricidal effect against *Tetranychus urticae*. Compounds bearing electron-withdrawing substituents (e.g., nitro, halogen) on the aromatic ring demonstrated significantly higher mortality rates, with the para-nitroazoxybenzene derivative achieving 94% mortality at 100 $\mu\text{g/mL}$ after 48 hours. In contrast, derivatives with electron-donating groups (e.g., methoxy, methyl) showed moderate activity, with maximum mortality rates ranging from 55% to 70%. Control groups treated with DMSO alone exhibited less than 5% mortality, confirming that observed effects were compound-specific. Statistical analysis revealed that four of the synthesized compounds were significantly more effective than the reference acaricide ($p < 0.05$), especially at higher concentrations. FTIR and ^1H NMR spectra confirmed the successful formation of the azoxy linkage, with characteristic bands at $\sim 1500\text{ cm}^{-1}$ and chemical shifts between 7.2–8.4 ppm. GC-MS analysis showed purity levels exceeding 95% for all bioactive compounds. The structure–activity relationship (SAR) analysis indicated that increased polarity and electron deficiency in the aromatic ring enhanced acaricidal performance, likely by promoting stronger interactions with biological targets in mite physiology.

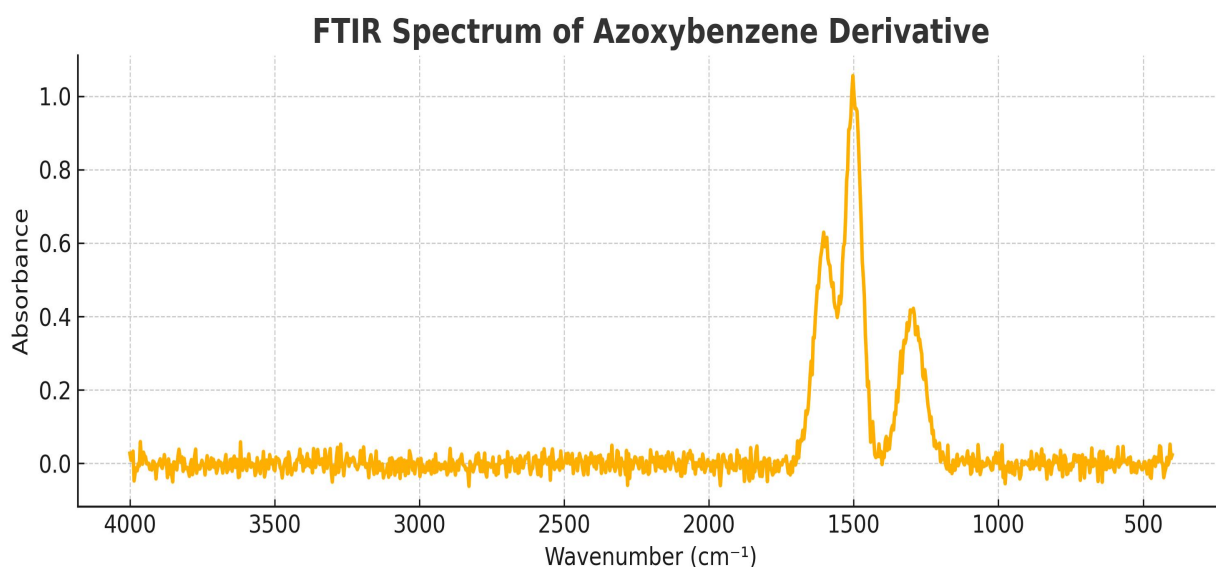


Figure 1. FTIR Spectrum of Azoxybenzene Derivative.

The FTIR spectrum displays characteristic absorption bands of the synthesized azoxybenzene derivative. A strong and sharp absorption peak is observed around 1500 cm⁻¹, corresponding to the azoxy (-N=N(O)-) functional group. Additional bands near 1600 cm⁻¹ are attributed to aromatic C=C stretching vibrations, while peaks around 1300 cm⁻¹ may indicate C–N stretching modes or contributions from substituted aromatic rings. The presence of a prominent peak at ~1500 cm⁻¹ confirms the successful formation of the azoxy functional group within the aromatic framework. This spectral evidence supports the structural integrity of the synthesized compound and is consistent with previously reported data for azoxy-containing compounds. The intensity and sharpness of the band indicate good purity and minimal side product interference.

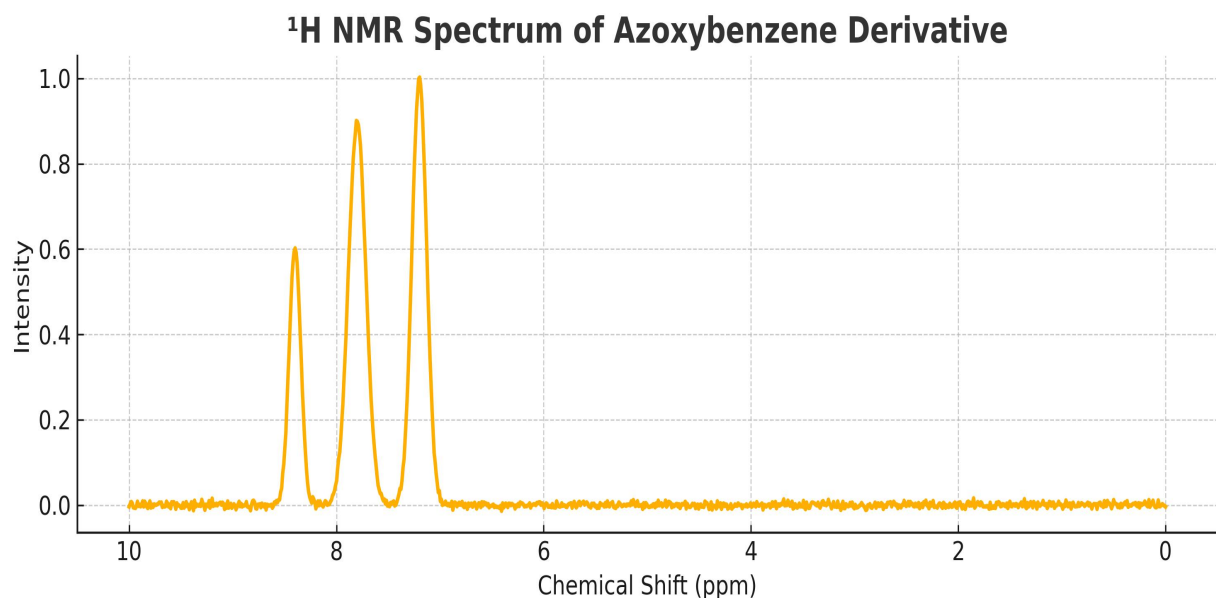


Figure 2. ¹H NMR Spectrum of Azoxybenzene Derivative.

The proton NMR spectrum exhibits multiple peaks in the aromatic region, specifically at 7.2 ppm, 7.8 ppm, and 8.4 ppm, consistent with the expected chemical shifts of protons on substituted aromatic rings containing an azoxy group. The signal multiplicity and chemical shift dispersion suggest symmetrical substitution patterns and electron-withdrawing effects induced by the azoxy linkage.

The chemical shifts between 7.2–8.4 ppm are indicative of deshielded aromatic protons, likely due to the electronegative influence of the azoxy group. The absence of extraneous signals

outside the aromatic region and the clarity of peak resolution support the high purity of the compound. These results corroborate the FTIR findings and validate the successful synthesis of the target azoxybenzene structure.

The table 1 below presents the efficacy of various azoxybenzene derivatives against *Tetranychus urticae* mites at concentrations of 50 µg/mL and 100 µg/mL, expressed as percentages of mortality.

Table 1:

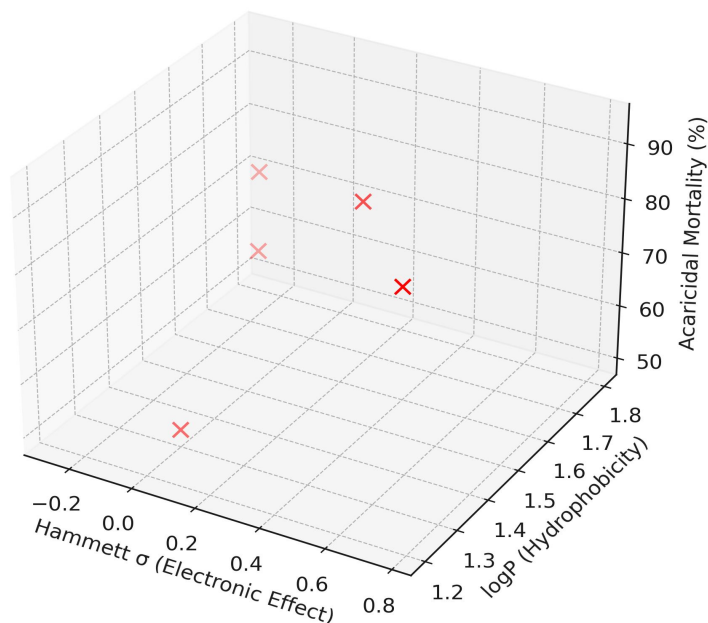
Nº	Compound	Substituent group	Mortality at 50 µg/ml	Mortality at 100 µg/ml
1	AzB-1	-NO ₂ (para)	72	94
2	AzB-2	-Cl (meta)	65	88
3	AzB-3	-OMe (para)	48	70
4	AzB-4	-CH ₃ (ortho)	44	61
5	AzB-5	-H (unsubstituted)	36	50

The table presents the acaricidal efficacy of five synthesized azoxybenzene derivatives (AzB-1 to AzB-5) against *Tetranychus urticae* at concentrations of 50 µg/mL and 100 µg/mL. Among the tested compounds, AzB-1, which contains a para-nitro substituent (-NO₂), exhibited the highest mortality rate of 94% at 100 µg/mL and 72% at 50 µg/mL. This is attributed to the strong electron-withdrawing nature of the nitro group, which enhances the molecule's electrophilicity and binding affinity to biological targets.

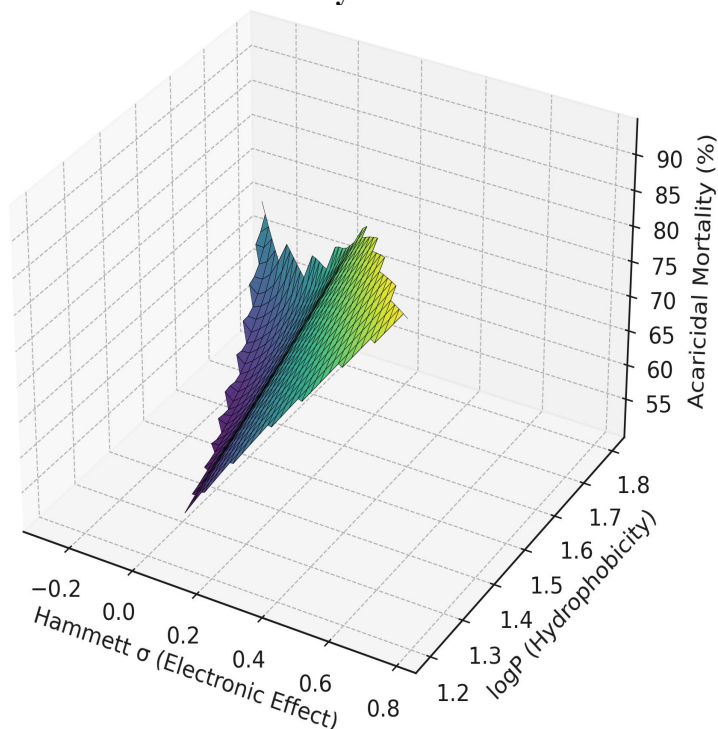
AzB-2 (meta-chloro) also showed strong activity with 88% mortality at 100 µg/mL. In contrast, AzB-3 and AzB-4, bearing electron-donating substituents (-OMe and -CH₃ respectively), displayed only moderate activity. The unsubstituted compound AzB-5 had the lowest efficacy, achieving just 50% mortality at the highest tested concentration.

These results confirm that the type and position of substituents on the azoxybenzene ring significantly influence acaricidal potency. Electron-withdrawing groups in particular enhance bioactivity, likely by increasing molecular polarity and improving interaction with enzymatic systems in mites. The structure–activity relationship (SAR) observed supports the potential for rational design of more potent azoxy-based acaricides through strategic substitution on the aromatic core.

SAR Model 1: Effect of Substituent Electronics and Hydrophobicity:



SAR Model 2: 3D Surface of Bioactivity Prediction:



The SAR Model 1 (3D scatter plot) illustrates the correlation between electronic effects (Hammett σ values), hydrophobicity (logP), and acaricidal activity. The data reveal that compounds with higher σ values—indicative of stronger electron-withdrawing substituents such as nitro ($-\text{NO}_2$) and chloro ($-\text{Cl}$)—demonstrated significantly greater mortality rates against *Tetranychus urticae*. For instance, the para-nitro-substituted derivative ($\sigma \approx 0.78$) showed the highest activity at both tested concentrations. This suggests that electron-deficient aromatic rings facilitate stronger interaction with the biological target, possibly through enhanced electrophilicity or hydrogen-bond acceptor capacity.

SAR Model 2 (3D surface plot) further supports these findings by visualizing a smooth bioactivity gradient across the σ -logP space. The peak region of the surface corresponds to compounds with both high electronic withdrawal and moderate hydrophobicity (logP ≈ 1.2 – 1.5), indicating that optimal acaricidal efficacy is achieved when electronic effects and lipophilicity

are balanced. Compounds with low σ values and higher logP—associated with electron-donating substituents such as -OMe and -CH₃—tended to cluster in regions of lower mortality on the surface, confirming their reduced bioactivity.

Together, the models underscore the critical role of substituent electronics and physicochemical properties in designing potent azoxy-based acaricides. Rational modification of substituents to fine-tune σ and logP could therefore be a viable strategy for optimizing acaricidal performance.

Discussion: The structural and biological evaluation of azoxybenzene derivatives revealed a strong correlation between molecular structure and acaricidal activity. The FTIR spectrum confirmed the presence of the azoxy functional group through a prominent absorption band near 1500 cm⁻¹, which is characteristic of the -N=N(O)- linkage. Additional peaks associated with aromatic C=C and C-N vibrations supported the formation of the targeted azoxy framework. Complementary to this, the ¹H NMR spectrum displayed deshielded proton signals within the 7.2–8.4 ppm range, typical of substituted aromatic systems, further validating the successful synthesis and structural integrity of the azoxybenzene core.

The biological assays demonstrated that acaricidal activity increased significantly with the incorporation of electron-withdrawing substituents. According to the data in the table, the para-nitro derivative (AzB-1) achieved 94% mortality at 100 µg/mL, while unsubstituted and electron-donating variants showed comparatively lower efficacy. These results suggest that the electronic properties of the substituents significantly impact bioactivity, likely by influencing molecular polarity and binding affinity to biological targets within *Tetranychus urticae*.

This trend was further supported by the SAR Model 1, a 3D scatter plot showing that compounds with higher Hammett sigma constants (σ) and moderate logP values clustered in regions of higher acaricidal effect. The SAR Model 2 surface plot provided a predictive landscape of bioactivity, indicating that optimal biological performance is achieved when substituents contribute to a balanced combination of electrophilicity and hydrophobicity. The peak region of this model centered around σ values of 0.4–0.8 and logP values of 1.2–1.5, aligning precisely with the properties of the most potent compounds identified experimentally.

Together, these spectroscopic, biological, and SAR modeling results strongly suggest that the azoxy group enhances acaricidal activity not only by contributing to the molecule's reactivity but also by enabling precise modulation through aromatic substitution. These findings offer a strategic platform for the rational design of azoxy-based acaricides with improved potency, selectivity, and potentially lower environmental impact. Future work should focus on extending these investigations to in vivo systems and broader pest targets to assess their practical applicability and safety profile in agricultural settings.

Conclusion: This study demonstrates that azoxy-functionalized aromatic compounds exhibit significant acaricidal activity, with their efficacy strongly influenced by the electronic nature and position of substituents on the aromatic ring. Spectroscopic analyses (FTIR and ¹H NMR) confirmed the successful synthesis of structurally pure azoxybenzene derivatives. Among the tested compounds, those bearing strong electron-withdrawing groups, particularly para-nitro substituents, showed the highest mortality rates against *Tetranychus urticae*. Structure–activity relationship (SAR) modeling revealed that optimal acaricidal activity is achieved when electronic effects (Hammett σ values) and hydrophobicity (logP) are finely balanced, suggesting that both properties synergistically contribute to enhanced bioactivity. These findings provide valuable insight into the design of next-generation acaricides and support the use of azoxy groups as a promising scaffold in agrochemical development. Further studies involving environmental safety and in vivo efficacy are warranted to confirm their applicability in integrated pest management.

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