



Cite this: DOI: 10.1039/d5ce00915d

Comprehensive structural insights into nitro-substituted azines as potential antioxidant additives for biodiesel

Ronaldo G. F. Junior, ^{*a} Vitor S. Duarte, ^a Leonardo R. Almeida, ^a
 Patrícia R. S. Wenceslau, ^a Gilberto L. B. Aquino, ^{ab}
 Clodoaldo Valverde ^{*ac} and Hamilton B. Napolitano ^{*a}

Fossil fuels remain the primary global energy source, but their finite nature and environmental impact drive the search for renewable alternatives. Biodiesel is a promising candidate, though its oxidative instability limits widespread adoption. This work provides a comprehensive structural and computational analysis of two nitro-substituted azine derivatives to evaluate their potential as biodiesel additives. Single-crystal X-ray diffraction and Hirshfeld surface analysis revealed supramolecular stabilization through C–H⋯O, C–H⋯N, and C–H⋯ π interactions, highlighting distinct packing motifs associated with nitro substitution. Topological and electronic descriptors showed that additional nitro and methyl groups reduced reactivity in the gas phase, while in the solid state the molecular energy gap (HOMO–LUMO) remained comparable. Also, a non-centric azine molecular structure exhibited an exceptionally high second-order nonlinear optical response, more than 30-fold higher than centric azine. Machine learning models were employed to predict the oxidation rate constants in the presence of $\cdot$ OH radicals and to predict the optical activity parameters. The results indicated a better absorption and emission response for azine with asymmetric electronic distribution and high dipole moment. Predictions of the oxidation rate in the presence of $\cdot$ OH radicals indicate superior antioxidant performance for the azine with the fewest nitro groups, with reaction rates comparable to those observed in diesel and the main components of biodiesel. These findings demonstrate that crystal packing, molecular symmetry, and substitution patterns govern both solid-state properties and antioxidant performance, underscoring the value of molecular-based approaches in designing next-generation biodiesel stabilizers.

Received 22nd September 2025,
Accepted 27th November 2025

DOI: 10.1039/d5ce00915d

rsc.li/crystengcomm

1. Introduction

Fossil fuels such as coal, natural gas, and petroleum have been the foundation of industrial and economic development throughout history. Although abundant, these resources are finite and directly linked to air pollution, environmental degradation, and the greenhouse effect.^{1–5} More than 80% of the global energy matrix comes from non-renewable sources,^{6,7} increasing the demand for alternative resources and sustainable solutions.⁸ In this context, biofuels emerge as an attractive option due to their renewable nature and lower environmental impact.^{8,9} Biofuels are biodegradable fuels produced from biomass,^{8,9} with biodiesel standing out as a

notable example due to its ability to reduce emissions of atmospheric pollutants, such as unburned hydrocarbons and carbon dioxide,¹⁰ its lower toxicity,¹¹ and its capacity to improve the lubrication of moving parts in the fuel supply system of motor vehicles.¹² Although biodiesel is consumed during combustion, it is regarded as a renewable fuel because it is produced from biological sources, such as vegetable oils and animal fats, that can be replenished within human timescales. Unlike fossil fuels, its continuous production makes it a sustainable and environmentally favorable alternative.^{13,14}

Biodiesel offers several advantages such as renewable origin, environmental benefits and lower toxicity. However, certain limitations hindered its consolidation in the global energy matrix, such as lower oxidative stability and reduced energy availability compared to fossil fuels.^{13–16} Biodiesel is an alkyl ester of fatty acids, obtained from animal fats, vegetable oils, algae, and greasy waste.^{8,17–21} According to Da Silva and co-workers²² its oxidative stability is related to its fatty acid composition, where a higher amount of

^a Grupo de Química Teórica e Estrutural de Anápolis, Universidade Estadual de Goiás, Anápolis, GO, Brazil. E-mail: ronaldogf135@gmail.com, valverde@ueg.br, hbnapolitano@gmail.com

^b Instituto Nacional de Criminalística, Diretoria Técnico Científica, Polícia Federal, Brasília, DF, Brazil

^c Universidade Paulista, Goiânia, GO, Brazil

polyunsaturated fatty acids leads to greater oxidative degradation compared to samples with a prevalence of saturated fatty acids. Other factors that may contribute to biodiesel oxidation include exposure to air, light, high temperatures, and the presence of catalytic enzymes or metals in the fuel.²³ In this sense, one or a combination of these factors can compromise its quality and render it unsuitable for commercial use. Another factor that contributes to biodiesel degradation is the proliferation of microorganisms, such as fungi and bacteria.^{24–26} These organisms, together with oxidative processes, promote the formation of hydroperoxides (primary oxidation products) that compromise the quality and stability of the biofuel.^{27,28} In motor vehicles, these sediments clog filters, block injectors, and form deposits in the fuel supply system, resulting in damage to the mechanical components of the engine.^{29–31}

Biodiesel esters have lower energy availability compared to the hydrocarbons present in petroleum-derived fuels, reducing their calorific value. Studies show that engines powered by biodiesel lose between 1 and 8% of their power,¹⁴ which can lead to increased fuel consumption.¹³ Also, the development of compounds with antioxidant, antibacterial properties and good energy availability is essential to increase the stability and efficiency of biodiesel.²⁴ This added compound acts as a shield, preventing or delaying oxidative degradation by interrupting the oxidation reaction through chain breaking and decomposition of hydroperoxides.^{32,33} As a result, it helps inhibit polymerization and avoid the precipitation of oxidized compounds, which are undesirable final stages of oxidation that promote the formation of abiotic sediments.

Several classes of compounds have been investigated as biodiesel additives, mainly for their antioxidant activity.^{34–36} However, azines remain little explored, despite having simple synthesis, efficient purification, and conjugated systems capable of favoring electron delocalization and stabilizing free radicals.^{37,38} Therefore, investigating their potential may reveal new strategies to improve biodiesel stability and efficiency. Azines are organic molecules formed by the reaction of hydrazine with ketones or aldehydes,^{39,40} featuring two imine groups (C=N) linked by a nitrogen bridge, forming the structure $R_1R_2C=N-N=CR_3R_4$. Although this synthetic route is the most common, they can also be obtained from ammonia, hydrogen peroxide⁴¹ or from the reaction between chalcones and hydrazones.⁴² Depending on the nature of the R substituent, azines can be classified as symmetric ($R_1R_2 = R_3R_4$), asymmetric ($R_1R_2 \neq R_3R_4$), aldazines ($R_1 = R_3 = H$), ketazines ($R_1R_2R_3R_4 \neq H$), mixed ($R_1 = H, R_2R_3R_4 \neq H$), aromatic, aliphatic, cyclic, and acyclic.⁴³ The structural versatility of azines gives these molecules diverse physicochemical and biological properties, encouraging their application in health, materials science, and energy. The biological potential of azines is widely recognized, including antibacterial,^{43–45} antifungal^{43,46} and antioxidant activities.^{38,40,47,48} In addition, their optical^{49–51}

and conductive properties indicate potential for applications in optoelectronics.^{52,53} Specifically, the ability to engineer their extensive π -conjugated systems has made azines a target for nonlinear optical (NLO) materials.^{54,55} Research in this area includes the development of new asymmetric azine derivatives whose second-order NLO responses were characterized in solution to evaluate their performance.

Furthermore, the strong inductive electronic effect of nitro groups, combined with the structural versatility of azines, enables precise modulation of molecular electronic distribution, redox behavior, and overall reactivity.^{37,56,57} Consequently, the enhanced electron-withdrawing capacity influences molecular polarity and dipole moment, favoring single electron transfer (SET) mechanisms and increasing radical-scavenging efficiency even in the absence of classical OH or NH donor groups.⁵⁸ In this context, the present work compares two new azines, (1*E*,2*E*)-1-benzylidene-2-[1-(4-nitrophenyl)-ethylidene]-hydrazine (AZN1) and (1*E*,2*E*)-bis[1-(4-nitrophenyl)-ethylidene]-hydrazine (AZN2), with potential application as antioxidant additives for biodiesel. Structural characterization was carried out by X-ray diffraction, Hirshfeld surfaces (HS)⁵⁹ and 2D fingerprint plots⁶⁰ to evaluate intermolecular interaction patterns. The electronic study employed density functional theory (DFT),⁶¹ along with Fukui functions. Additionally, the quantum theory of atoms in molecules (QTAIM)⁶² was used to analyze the topology of the electron density and characterize the interactions responsible for stabilizing the crystal packing. To evaluate the antioxidant potential, machine learning models were employed to predict the reaction rate against $\cdot OH$ radicals. In addition, the first hyperpolarizability (hyper-Rayleigh scattering) was calculated to assess the NLO properties, considering their relationship with electronic structures that enhance antioxidant activity. Given the crucial role of antioxidants in enhancing biodiesel stability and performance, we explore how nitro substitution and molecular symmetry in azine derivatives affect their supramolecular arrangements, electronic reactivity, and antioxidant potential, integrating experimental crystallography, quantum-chemical descriptors, and machine learning predictions.

2. Experimental and computational procedures

2.1 Solid-state analysis

The two azines AZN1 and AZN2 were synthesized by the reaction of hydrazone (1) with benzaldehyde (2) and 4-nitroacetophenone (2) respectively, in ethanol according to Figueredo and co-workers,⁶³ as depicted in Supplementary Information (Scheme S1 and Fig. S1–S10). X-ray diffraction data for the samples were collected at the MANACA beamline of Sirius, the National Synchrotron Light Laboratory, at 120 K, using paratone as a cryoprotectant and a wavelength of $\lambda = 0.67019$. The data were processed using the MNCAutoproc pipeline with XDS.⁶⁴ Both

structures were solved using SHELXS⁶⁵ and refined with SHELXL⁶⁶ on the Olex2 platform.⁶⁷ Crystallographic information files were deposited in the Cambridge Structural Database⁶⁸ under the deposition number 2484685 (AZN1) and 2484683 (AZN2). Graphical representations and supramolecular interactions were generated using the Mercury software.⁶⁹

Hirshfeld surfaces were generated to investigate intermolecular interactions in the crystal packing. The normalized d_{norm} function was employed to locate contact regions on the molecules based on the internal (d_i) and external (d_e) distances to the surface, normalized by the respective van der Waals radii (r^{vdw}),^{59,70,71} as shown in eqn (1).

$$d_{\text{norm}} = \frac{d_i - r_i^{\text{vdw}}}{r_i^{\text{vdw}}} + \frac{d_e - r_e^{\text{vdw}}}{r_e^{\text{vdw}}} \quad (1)$$

In this configuration, red regions indicate contacts with distances shorter than the sum of the van der Waals radii, highlighting stronger interactions, while white and blue areas correspond to separations close to or greater than this value, associated with weaker or absent contacts.⁷¹ The shape index was employed as a complementary tool to identify interactions involving π systems (such as C-H $\cdots\pi$ and $\pi\cdots\pi$), evidenced by red concave regions over the aromatic rings and blue convex regions over the C-H atoms.^{59,70,72}

The contribution of each contact to the stabilization of the supramolecular arrangement was measured through the fingerprint plot, a two-dimensional graph generated from the combined distribution of d_i and d_e , which allowed visualization of the relative frequency of each type of contact.⁶⁰ All analyses were performed using the Crystal Explorer software⁷³ with the crystallographic information files obtained from structure solution and refinement serving as input data for the calculations.

2.2 Molecular modeling analysis

The electronic study of the compounds was conducted using DFT⁶¹ employing the hybrid functional M06-2X⁷⁴ and the 6-311++G(d,p) basis set.^{75,76} This theoretical level was chosen for providing satisfactory results in accounting for electron correlation,^{77,78} as well as being recommended for describing non-covalent interactions.^{74,79} Calculations were initially performed in the solid state, followed by geometry optimizations in the gas phase to investigate possible electronic variations. Structural modeling was carried out using the Gaussian09 (ref. 80) and GaussView programs.⁸¹

Based on the obtained results, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) were calculated to understand the electronic properties and reactivity of the compounds.^{82,83} Using the energies of these orbitals, the global chemical hardness (η) was calculated, a parameter that quantifies the system's resistance to changes in electron density,⁸⁴ as presented in eqn (2).

$$\eta = \frac{I - A}{2} \quad (2)$$

Additionally, the chemical potential (μ) was determined, a parameter that indicates the tendency of compounds to donate electrons, from the species with higher potential to the one with lower potential,⁸⁴ as represented in eqn (3).

$$\mu = -\frac{I + A}{2} = -\chi \quad (3)$$

To assess the energetic stability associated with the addition of electronic charge to the system, the global electrophilicity index was calculated according to the definition by Parr and co-workers,⁸⁵ as presented in eqn (4).

$$\omega = \frac{\mu^2}{2\eta} \quad (4)$$

In eqn (2) and (3) $I \approx -E_{\text{HOMO}}$ corresponds to the ionization energy, while $A \approx -E_{\text{LUMO}}$ represents the electron affinity. The most reactive regions of the molecules were identified through the molecular electrostatic potential (MEP) map,^{86–88} constructed from the potential generated by the nuclei and the electron density on the molecular surface. The calculation was performed according to eqn (5), where the first term represents the nuclear potential and the second the electronic potential,⁸⁷ enabling the identification of areas associated with probable molecular interactions.

$$V(\mathbf{r}) = \sum_{\alpha} \frac{Z_{\alpha}}{|\mathbf{r}_{\alpha} - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' \quad (5)$$

Complementarily, the Fukui functions $F(\mathbf{r})$ were calculated to identify the sites most susceptible to nucleophilic, electrophilic, and radical attacks.^{89,90} Formally, $F(\mathbf{r})$ is defined as the first derivative of the electron density $\rho(\mathbf{r})$ with respect to the number of electrons N , at constant external potential V , in order to evaluate the local variation of the electron density caused by the addition or removal of electrons,⁹¹ thus allowing the relationship between electronic distribution and local reactivity. From the electronic densities of the neutral, anionic ($N + 1$), and cationic ($N - 1$) species, optimized in the gas phase, the reactivity indicators for each type of attack were calculated using the following equations.

$$f^+(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N} \right)_v^+ : \text{Nucleophilic attack} \quad (6)$$

$$f^-(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N} \right)_v^- : \text{Electrophilic attack} \quad (7)$$

$$f^0(\mathbf{r}) = \left(\frac{\partial \rho(\mathbf{r})}{\partial N} \right)_v^0 : \text{Radical attack} \quad (8)$$

Using the finite difference approximation, the above equations were rewritten in the form:

$$f^+(\mathbf{r}) = \rho_{N+1}(\mathbf{r}) - \rho_N(\mathbf{r}) \quad (9)$$

$$f^-(\mathbf{r}) = \rho_N(\mathbf{r}) - \rho_{N-1}(\mathbf{r}) \quad (10)$$

$$f^0(\mathbf{r}) = \frac{\rho_{N+1}(\mathbf{r}) - \rho_{N-1}(\mathbf{r})}{2} \quad (11)$$

QTAIM is a quantum mechanics approach^{92,93} that employs the topological analysis of the electron density $\rho(\mathbf{r})$ to describe structural properties and interactions,^{62,94,95} allowing the identification of critical points (CPs) along the bonding paths between adjacent nuclei. To characterize hydrogen bonds of the D-H...A type, Popelier and Koch^{96–98} proposed eight criteria, grouped into two subsets: four local topological parameters of $\rho(\mathbf{r})$ and four associated with the hydrogen atom.

The electron density at the bond critical point (BCP) expresses the strength of the interaction and serves as the basis for descriptors that define its nature. The Laplacian $\nabla^2\rho$ represents the curvature of the electron density and indicates regions of charge accumulation or depletion. Negative values of $\nabla^2\rho$ indicate electron density accumulation, associated with the covalent character of the interaction, while positive values reveal charge depletion along the bonding path, typical of closed-shell interactions.^{94,98} The mutual penetration (MP) between the involved atoms is considered a sufficient criterion to predict the formation of hydrogen bonds (HB).^{97,98} It is quantified by the expression $MP = (R_H + R_A) - D_{H...A}$, where R_H and R_A are the radii of the hydrogen and acceptor atoms, respectively, and $D_{H...A}$ is the distance between them. When there is no penetration, the electron densities of these atoms do not significantly overlap, and the interaction tends to be predominantly electrostatic.

The interaction energy can be estimated from the electron density at the BCP using the equation proposed by Emamian and co-workers⁹⁹ $BE = -233.08 \times \rho(\mathbf{r}) + 0.7423$, in kJ mol^{-1} . The ellipticity (ε), defined as $\varepsilon = \lambda_1/\lambda_2 - 1$, indicates the anisotropy of the electron density in the plane perpendicular to the bond. High ε values suggest π character or greater susceptibility to local distortions, while values close to zero indicate σ bonds, with a cylindrical and symmetrical electron distribution.^{92,96,100} These parameters, together with other structural descriptors, were used in the analysis of the C-H...O and C-H...N interactions of the compounds evaluated in this study. For this purpose, a partial optimization was applied using the *opt=readfreeze* option, keeping the geometric parameters of the non-hydrogen atoms fixed and adjusting only the positions of the hydrogens. The analysis was conducted using the Multiwfn program.¹⁰¹ For the investigation of NLO properties, the structures were considered in an *n*-hexane solution, a solvent chosen for its low polarity and compatibility with biodiesel lipids, providing a representative medium to analyze the performance of antioxidant additives.^{102–104}

The initial geometry used in the calculations was obtained from X-ray data and subsequently optimized by DFT using the

CAM-B3LYP functional.¹⁰⁵ This hybrid functional includes long-range corrections and is suitable for accurate calculations of polarizability in long chains, as well as Rydberg and charge-transfer excitations. The 6-311++G(d,p)^{75,76} basis set was employed for all calculations. The supermolecule approach adopted in this study employs an interactive process that simulates the effect of medium polarization on the molecule's electrical properties.¹⁰⁶ This methodology was applied to calculate the total dipole moment (μ), the average dynamic linear polarizability ($\langle\alpha(-\omega;\omega)\rangle$), as described by eqn (12) and (13).

$$\mu = (\mu_x^2 + \mu_y^2 + \mu_z^2)^{\frac{1}{2}} \quad (12)$$

$$\langle\alpha(-\omega;\omega)\rangle = \frac{1}{3} \sum_{i=x,y,z} \alpha_{ii}(-\omega;\omega) \quad (13)$$

The hyperpolarizability (β_{HRS}) for hyper-Rayleigh scattering was calculated from the components defined as¹⁰⁷

$$\beta_{\text{HRS}} = \sqrt{\beta_{\text{ZZZ}}^2 + \beta_{\text{XZZ}}^2} \quad (14)$$

In this context, the laboratory frame is defined by the X, Y, and Z coordinates. The X-axis is considered the direction of propagation of the fundamental light beam, with polarization occurring along the Z-axis. The macroscopic averages β_{ZZZ}^2 and β_{XZZ}^2 are calculated based on the components of the first β_{HRS} using the eqn (15) and (16), in which the coefficients δ_n are defined in Table 1.

$$\langle\beta_{\text{ZZZ}}^2\rangle = \frac{1}{210} (30\delta_1 + 12(\delta_2 + \delta_3 + \delta_5) + 6(\delta_4 + \delta_6) + 2(\delta_7 + \delta_8 + \delta_{11})) \quad (15)$$

$$\langle\beta_{\text{XZZ}}^2\rangle = \frac{1}{210} (6(\delta_1 - \delta_3 - \delta_5 + \delta_7) + 8\delta_2 + 18\delta_4 + 4\delta_6 - \delta_8 - 2\delta_9 + 3\delta_{10}) \quad (16)$$

All of the NLO numerical calculations were performed at DFT/SMD/CAM-B3LYP/6-311++G(d,p) level using the Gaussian 09 software package.⁸⁰

2.3 Machine learning

The prediction of optical properties, such as absorption and emission wavelengths as well as the Stokes shift of the AZN1 and AZN2 molecules, was carried out based on the machine learning approach described by Verissimo and co-workers,¹⁰⁸ which employs molecular fingerprints to encode structural information and enable the prediction of optical properties from structural patterns. In the present study, the extreme gradient boosting (XGBoost) algorithm was adopted, as it is widely used in chemical predictions due to its robustness and interpretability.¹⁰⁹ Model interpretation was performed using shapley additive explanations (SHAP) analysis, which allowed the identification of the molecular substructures most influential on the predicted optical properties.¹⁰⁸ The

Table 1 First β_{HRS} coefficients (δ_n)

$$\begin{aligned}
 \delta_1 &= \sum_i \beta_{iii}^2, & \delta_2 &= \sum_{i,j} \beta_{iii} \beta_{jjj}, & \delta_3 &= \sum_{i,j} \beta_{iii} (\beta_{jjj} + \beta_{jji}), \\
 \delta_4 &= \sum_{i,j} \beta_{ijj}^2, & \delta_5 &= \sum_{i,j} \beta_{ijj} (\beta_{jjj} + \beta_{jji}), & \delta_6 &= \sum_{i,j} (\beta_{jjj} + \beta_{jji})^2, \\
 \delta_7 &= \sum_{i,j,k} \beta_{ijj} \beta_{ikk}, & \delta_8 &= \sum_{i,j,k} (\beta_{jjj} + \beta_{jji}) (\beta_{kik} + \beta_{kki}), & \delta_9 &= \sum_{i,j,k} \beta_{ijj} (\beta_{kik} + \beta_{kki}), \\
 \delta_{10} &= \sum_{i,j,k} (\beta_{ijk} + \beta_{ikj})^2, & \delta_{11} &= \sum_{i,j,k} (\beta_{ijk} + \beta_{ikj}) (\beta_{jik} + \beta_{jki}).
 \end{aligned}$$

similarity between the studied molecules and the training database was calculated using the Tanimoto index,¹¹⁰ obtained from the comparison of molecular fingerprints. Based on this model, the maximum absorption (λ_{abs}), maximum emission (λ_{em}) and Stokes shift values were estimated for AZN1 and AZN2 in *n*-hexane, complementing the electronic analyses obtained by DFT and providing a comparative basis between structural parameters and optical response.

The free radical oxidation reaction rates were predicted using pySIRC,¹¹¹ a machine learning computational platform. The 'OH radical was chosen because it is one of the most reactive oxidizing species and is widely involved in the degradation processes of organic compounds. The predictions employed the Morgan and MACCS structural descriptors and the XGBoost algorithm to get the reaction constants (k_{OH}) in B20 biodiesel mixtures¹¹² in an aqueous environment. The Tanimoto index¹¹⁰ assessed the similarity of the study compounds, while the applicability domain (AD%) measured their proximity to the database, reinforcing the model's reliability.¹¹¹ The k_{OH} parameters were calculated for diesel (decene) and for the main biodiesel (BD) components: methyl 9-octadecenoate (BD M9OD, 19.98%), methyl palmitate (BD MPAL, 12.87%), and methyl 8,11-octadecenoate (BD M8OD, 10.22%).¹¹³ Furthermore, for comparative purposes, the k_{OH} indices of five nitro-substituted azines were determined,¹¹⁴ selected based on their similarities to the compounds in this study (see SI, Fig. S11), as well as the kinetic parameters of commercial additives such as BHT, BHA, TBHQ, PG, and GA were also estimated.¹¹⁵

3. Results and discussion

3.1 Crystal structure and supramolecular synthons

The compound AZN1 crystallized in the triclinic system, in the space group $P\bar{1}$, while AZN2 crystallized in the orthorhombic system, in the space group $Pbcn$. The crystallographic data and refinement parameters for both structures are presented in Table 2. Further crystallographic parameters are presented in Tables S1–S10. The molecules are structurally similar, with nitro groups (NO_2) in the *para* position of aromatic ring 1 in AZN1 (Fig. 1a) and on rings 1 and 2 in AZN2 (Fig. 1b). In both compounds, the imine group is located between atoms C₇ and C₉.

From a conformational standpoint, AZN2 exhibits greater planarity compared to AZN1, with an angle of 16.22° between rings 1 and 2, while AZN1 shows a significantly higher value of 57.77°. This conformational distinction is even more evident in the structural overlay (Fig. 1c), revealing pronounced deviations in the regions of nitrogen atoms N₂ (30.80°) and the methyl group attached to carbon C₈ (15.88°). The largest deviation was observed in ring 2, with an angular variation of 38.36°, suggesting greater conformational flexibility in AZN1, which may reflect differences in supramolecular packing as well as structural and physicochemical properties.

Structural analysis revealed that the supramolecular arrangement of both structures is mainly supported by C–H⋯O, C–H⋯N and C–H⋯ π interactions. In AZN1, the

Table 2 Crystallographic data and structural refinement parameters for AZN1 and AZN2

Crystallographic parameters	AZN1	AZN2
Empirical formula	C ₁₅ H ₁₃ N ₃ O ₂	C ₁₆ H ₁₄ N ₄ O ₄
Formula weight	267.28	326.31
Temperature (K)	120(2)	120(2)
Crystal system	Triclinic	Orthorhombic
Space group	$P\bar{1}$	$Pbcn$
<i>a</i> (Å)	9.3240(17)	12.680(5)
<i>b</i> (Å)	9.3840(11)	11.488(8)
<i>c</i> (Å)	9.5750(10)	20.223(11)
α (°)	105.669(5)	90
β (°)	105.283(8)	90
γ (°)	116.786(4)	90
Volume (Å ³)	643.68(16)	2946(3)
<i>Z</i> , <i>Z'</i>	2, 1	8, 1
ρ_{calc} (g cm ^{−3})	1.379	1.472
μ (mm ^{−1})	0.084	0.096
<i>F</i> (000)	280	1360
Radiation	$\lambda = 0.67019$	$\lambda = 0.67019$
2 θ range for data collection (°)	2.330 to 30.000	1.899 to 30.032
Index ranges	−13 ≤ <i>h</i> ≤ 13, −13 ≤ <i>k</i> ≤ 13, −13 ≤ <i>l</i> ≤ 13	−14 ≤ <i>h</i> ≤ 14, −15 ≤ <i>k</i> ≤ 15, −26 ≤ <i>l</i> ≤ 26
Reflections collected	32 769	48 828
Independent reflections	3767	4136
Data/restraints/parameters	3767/0/191	4136/0/224
Goodness-of-fit on <i>F</i> ²	1.099	1.064
Final <i>R</i> indexes [<i>I</i> ≥ 2 σ (<i>I</i>)]	<i>R</i> ₁ = 0.0501, <i>wR</i> ₂ = 0.1286	<i>R</i> ₁ = 0.0434, <i>wR</i> ₂ = 0.1248
Final <i>R</i> indexes [all data]	<i>R</i> ₁ = 0.0504, <i>wR</i> ₂ = 0.1290	<i>R</i> ₁ = 0.0446, <i>wR</i> ₂ = 0.1259
Largest diff. peak/hole/e Å ^{−3}	0.395/−0.597	0.500/−0.346

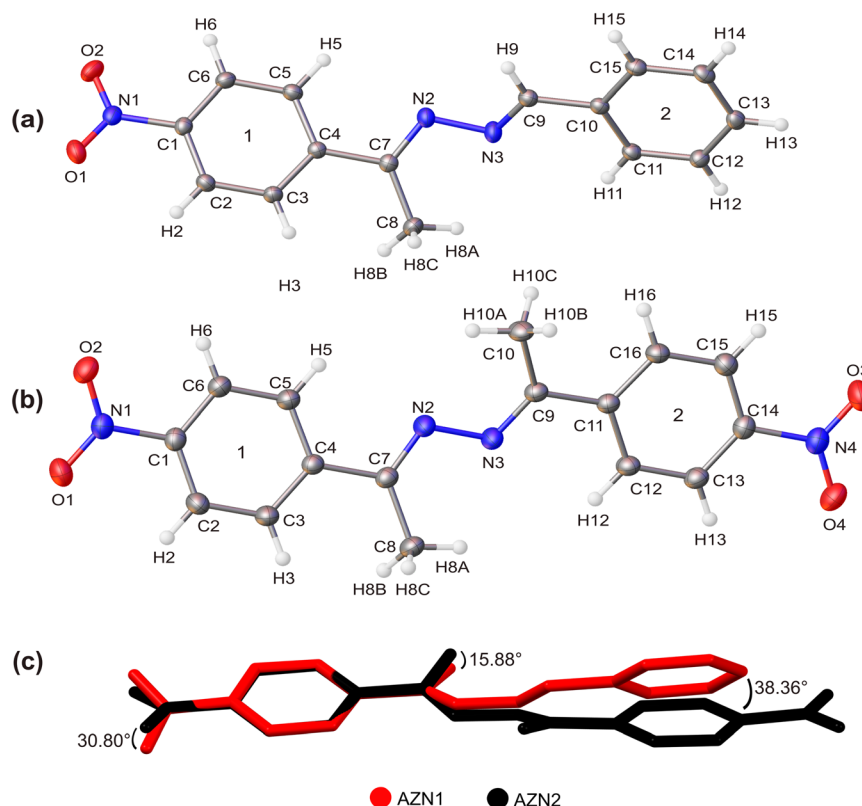


Fig. 1 ORTEP diagram with 50% probability ellipsoids and atomic numbering scheme indicated for (a) AZN1 and (b) AZN2. Hydrogen atoms are represented as spheres with arbitrary radii. (c) Overlay of the AZN1 (red) and AZN2 (black) structures.

$C_9-H_9 \cdots O_2$ interaction ($D \cdots A = 3.294(2) \text{ \AA}$) forms a stable dimer with an $R_2^2(22)$ motif. A second dimer, with an $R_4^4(20)$ motif, arises when this interaction occurs together with $C_{13}-H_{13} \cdots O_1$ ($D \cdots A = 3.383(2) \text{ \AA}$) (Fig. 2b). On the Hirshfeld surface, these interactions stand out as red regions and defined contact areas (Fig. 2a), representing 18.5% of the total mapped contacts (Fig. 2c).

Similarly, AZN2 exhibits interactions that form dimers, highlighting the $C_{13}-H_{13} \cdots O_1$ ($D \cdots A = 3.311(3) \text{ \AA}$) and $C_{12}-H_{12} \cdots O_2$ ($D \cdots A = 3.496(2) \text{ \AA}$) bonds, which together compose a dimeric unit with an $R_2^2(7)$ motif (Fig. 2e), a pattern also observed in the $C_6-H_6 \cdots O_3$ and $C_5-H_5 \cdots O_4$ set. Other $C-H \cdots O$ interactions (Table 3), such as $C_{10}-H_{10C} \cdots O_1$ ($D \cdots A = 3.233(3) \text{ \AA}$) favor connectivity between molecular units, contributing to dimer formation. In the HS analysis, only the $C_{13}-H_{13} \cdots O_1$ interaction exhibits red regions and well-defined contacts (Fig. 2d), indicating closer proximity and greater strength, even compared to $C_{10}-H_{10C} \cdots O_1$ (Fig. 2f), whose narrower $D-H \cdots A$ angle ($117.81(2)^\circ$) reduces interaction effectiveness, explaining its lesser visual prominence on the HS despite its shorter distance $O \cdots H$ contacts represent 35.8% of the mapped contacts (Fig. 2g), reinforcing their influence in sustaining the supramolecular arrangement.

$C-H \cdots N$ interactions were identified in both structures, exhibiting a recurring pattern. In AZN1, these bonds favor dimer formation, notably the $C_{12}-H_{12} \cdots N_1$ interaction

[$D \cdots A = 3.361(2) \text{ \AA}$] between aromatic ring 2 and the nitrogen of the nitro group (NO_2). The interactions $C_8-H_{8A} \cdots N_2$ [$D \cdots A = 3.666(2) \text{ \AA}$] and $C_8-H_{8B} \cdots N_3$ [$D \cdots A = 3.474(2) \text{ \AA}$] occur between iminic nitrogens and hydrogens of methyl groups, as shown in Fig. 3b. In AZN2, the interactions $C_{16}-H_{16} \cdots N_2$ [$D \cdots A = 3.420(2) \text{ \AA}$] and $C_{15}-H_{15} \cdots N_3$ [$D \cdots A = 3.358(3) \text{ \AA}$] concentrate between the nitrogens of the imine portion and hydrogens of aromatic ring 2 (Fig. 3e). Notably, in both structures, interactions involving the nitrogens of the imine portion exhibit the lowest observed bond angles, with $102.40(2)^\circ$ and $111.94(2)^\circ$ in AZN1 and $108.32(2)^\circ$ and $102.44(3)^\circ$ in AZN2. This similarity is reflected in the d_{norm} HS, where regions corresponding to these interactions show white and bluish coloring (Fig. 3a and d). Overall, these interactions represent 7.4% of the mapped contacts in AZN1 and 4.5% in AZN2 (Fig. 3c and f).

Interactions involving π systems follow a complementary pattern in the structures. In AZN1, the $C_{11}-H_{11} \cdots Cg_1$ interaction [$D \cdots A = 3.512(2) \text{ \AA}$] is responsible for forming the only dimer involving ring 1 (Fig. 4b), while $C_3-H_3 \cdots Cg_2$ [$D \cdots A = 3.499(2) \text{ \AA}$] is related to a sequential molecular arrangement, with the aromatic rings positioned adjacently (Fig. 4c). In AZN2, the interactions $C_{10}-H_{10B} \cdots Cg_1$ [$D \cdots A = 3.624(2) \text{ \AA}$] and $C_8-H_{8B} \cdots Cg_2$ [$D \cdots A = 3.681(2) \text{ \AA}$] together create a staggered arrangement in which each molecule is positioned laterally to the previous one, advancing along the b axis and forming a continuous

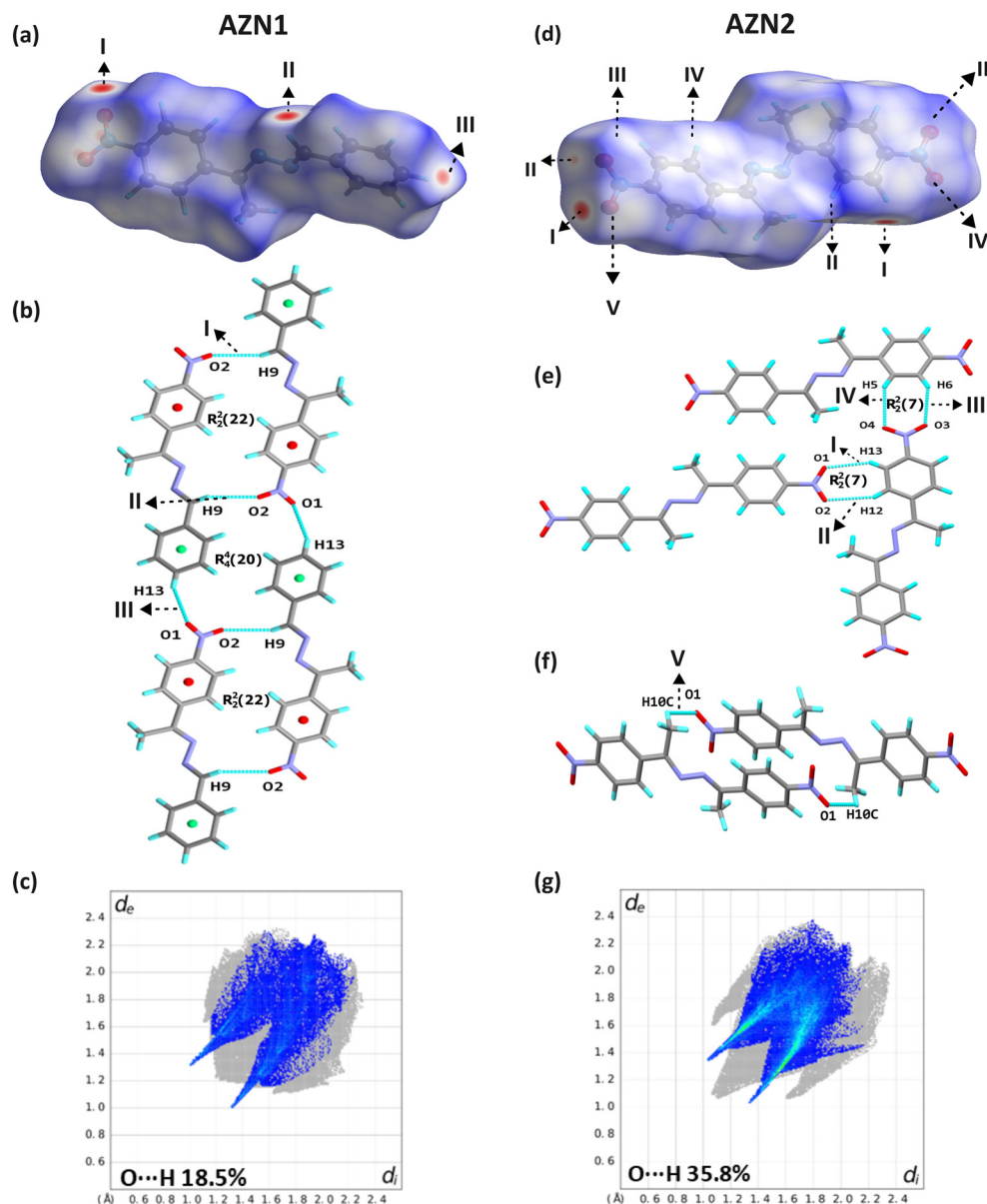


Fig. 2 HS with the d_{norm} property mapped and a detailed view of the C–H $\cdots$ O interactions in the supramolecular arrangement of AZN1 and AZN2. (a) d_{norm} surface mapped for AZN1. (b) Representation of the C₁₃–H₁₃ $\cdots$ O₁ and C₉–H₉ $\cdots$ O₂ interactions. (c) 2D fingerprint plot of O $\cdots$ H contacts, representing 18.5% of the total mapped contacts in AZN1. (d) d_{norm} surface mapped for AZN2. (e) Representation of the C₁₃–H₁₃ $\cdots$ O₁, C₁₂–H₁₂ $\cdots$ O₂, C₆–H₆ $\cdots$ O₃, and C₅–H₅ $\cdots$ O₄ interactions. (f) Representation of the C₁₀–H_{10C} $\cdots$ O₁ interaction. (g) 2D fingerprint plot of O $\cdots$ H contacts, representing 35.8% of the total mapped contacts in AZN2.

stacking pattern (Fig. 4f). In the shape index HS, these interactions are observed as red concave regions over the aromatic rings and blue convex regions over the methyl groups (Fig. 4a and e), corresponding to 33.1% of the mapped interactions in AZN1 (Fig. 4d) and 15% in AZN2 (Fig. 4g).

Additionally, in AZN2, π – π stacking, typical of energetic crystals,¹¹⁶ is observed between aromatic rings 1 (Cg₁) and 2 (Cg₂) (Fig. 5b) of neighboring molecules (Cg₁ $\cdots$ Cg₁ = 3.561 Å, Cg₂ $\cdots$ Cg₂ = 3.539 Å). In the Hirshfeld surface, these interactions appear as two complementary triangular spots, red and blue, over the ring region, forming a characteristic

“bow-tie” pattern (Fig. 5a). These contacts account for 7.3% of the total mapped interactions (Fig. 5c).

3.2 Electronic properties and reactivity descriptors

The analysis of frontier molecular orbitals is fundamental to understanding the electronic properties of the compounds. In general, the HOMO is associated with a bonding orbital, and the higher its energy, the more prone the molecule is to donate electrons in interactions, indicating a greater tendency toward oxidation. A similar argument applies to the LUMO, which is antibonding in nature; its energy reflects the

Table 3 Hydrogen bond geometry obtained from structural analysis for AZN1 and AZN2

Interaction	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)	Symmetry code
AZN1					
C ₁₃ –H ₁₃ ···O ₁	0.930	2.575(2)	3.383(2)	145.56(1)	2 + x, 1 + y, z
C ₉ –H ₉ ···O ₂	0.930	2.451(1)	3.294(2)	150.73(3)	1 – x, 2 – y, –z
C ₁₂ –H ₁₂ ···N ₁	0.930	2.958(1)	3.666(2)	134.09(2)	1 – x, 2 – y, 1 – z
C ₈ –H _{8A} ···N ₂	0.960	3.021(2)	3.361(2)	102.40(2)	1 – x, 2 – y, 1 – z
C ₈ –H _{8B} ···N ₃	0.960	3.000(2)	3.474(2)	111.94(2)	1 – x, 2 – y, 1 – z
C ₃ –H ₃ ···Cg ₂	0.930	2.803(8)	3.499(2)	132.42(4)	1 + x, y, z
C ₁₁ –H ₁₁ ···Cg ₁	0.930	2.846(5)	3.512(2)	129.52(5)	1 – x, 2 – y, 1 – z
AZN2					
C ₁₃ –H ₁₃ ···O ₁	0.930	2.498(2)	3.311(3)	146.16(2)	x, 1 – y, 1/2 + z
C ₁₂ –H ₁₂ ···O ₂	0.930	2.660(2)	3.496(2)	149.85(2)	x, 1 – y, –1/2 + z
C ₁₀ –H _{10C} ···O ₁	0.960	2.672(2)	3.233(3)	117.81(2)	–x, 1 – y, –z
C ₆ –H ₆ ···O ₃	0.930	2.664(4)	3.390(3)	135.40(4)	x, 2 – y, 1/2 + z
C ₅ –H ₅ ···O ₄	0.930	2.805(1)	3.574(4)	140.69(2)	x, 2 – y, 1/2 + z
C ₁₆ –H ₁₆ ···N ₂	0.959	2.995(2)	3.420(2)	108.32(2)	1/2 – x, –1/2 + y, z
C ₁₅ –H ₁₅ ···N ₃	0.930	3.032(3)	3.358(3)	102.44(3)	1/2 – x, –1/2 + y, z
C ₁₀ –H _{10B} ···Cg ₁	0.960	2.979(4)	3.624(2)	125.69(4)	1/2 – x, –1/2 + y, z
C ₈ –H _{8B} ···Cg ₂	0.960	3.098(5)	3.681(2)	120.62(4)	1/2 – x, 1/2 + y, z

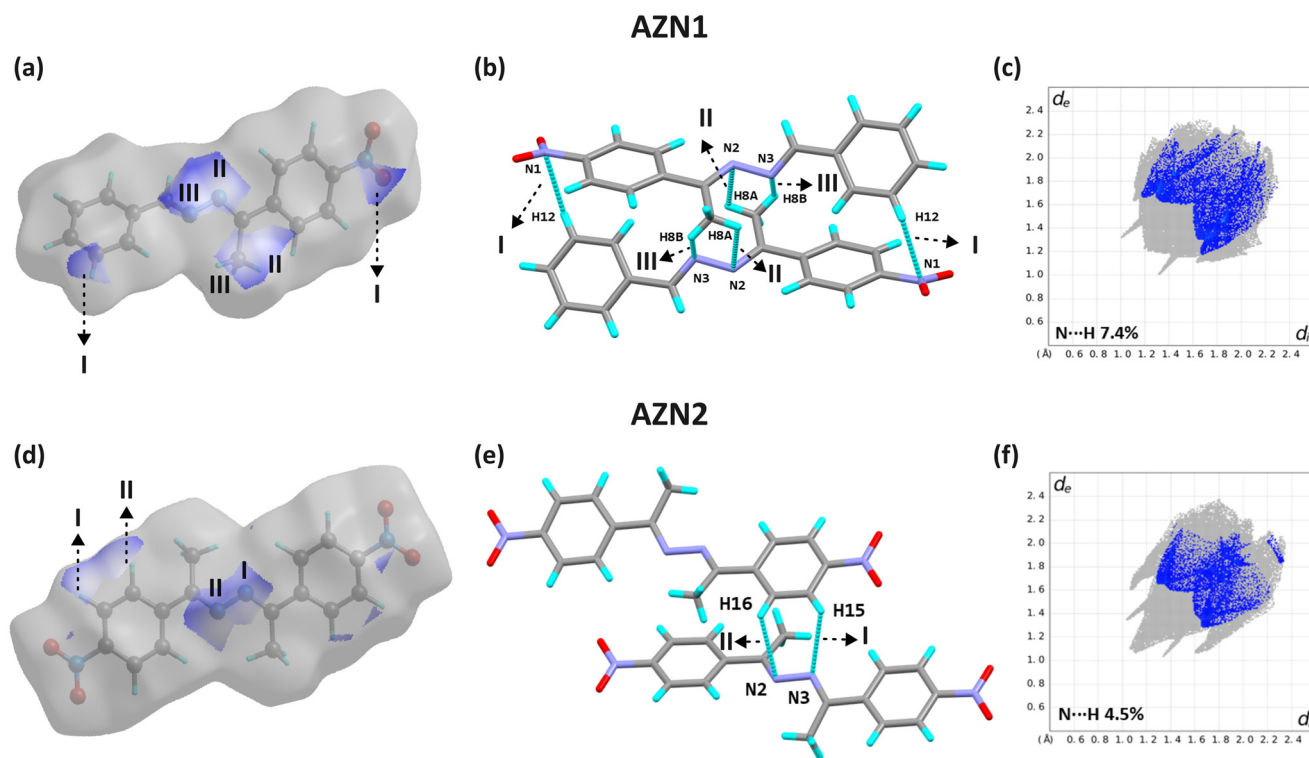


Fig. 3 HS with the d_{norm} property mapped and a detailed view of the C–H···N interactions in the supramolecular arrangement of AZN1 and AZN2. (a) d_{norm} surface mapped for AZN1. (b) Representation of the C₁₂–H₁₂···N₁, C₈–H_{8A}···N₂, and C₈–H_{8B}···N₃ interactions. (c) 2D fingerprint plot of N···H contacts, representing 7.4% of the total mapped contacts in AZN1. (d) d_{norm} surface mapped for AZN2. (e) Representation of the C₁₆–H₁₆···N₂ and C₁₅–H₁₅···N₃ interactions. (f) 2D fingerprint plot of N···H contacts, representing 4.5% of the total mapped contacts in AZN2.

molecule's ability to accept electrons, indicating a tendency toward reduction. The energy difference between the HOMO and LUMO, defined as the gap ($\Delta E_{\text{L-H}} = E_{\text{LUMO}} - E_{\text{HOMO}}$), is an important indicator of chemical stability and reactivity. Higher gap values indicate that more energy is required for electronic excitation, which is associated with lower reactivity and greater kinetic stability.^{82,117} In this context, the energy

difference discussed here corresponds to the molecular HOMO–LUMO separation obtained from DFT calculations. Although often referred to simply as gap, it reflects intrinsic electronic excitation behavior within isolated molecules, distinct from the band structure of extended materials.

In Fig. 6, the isosurfaces of the frontier orbitals show the distribution of electron density in the regions corresponding

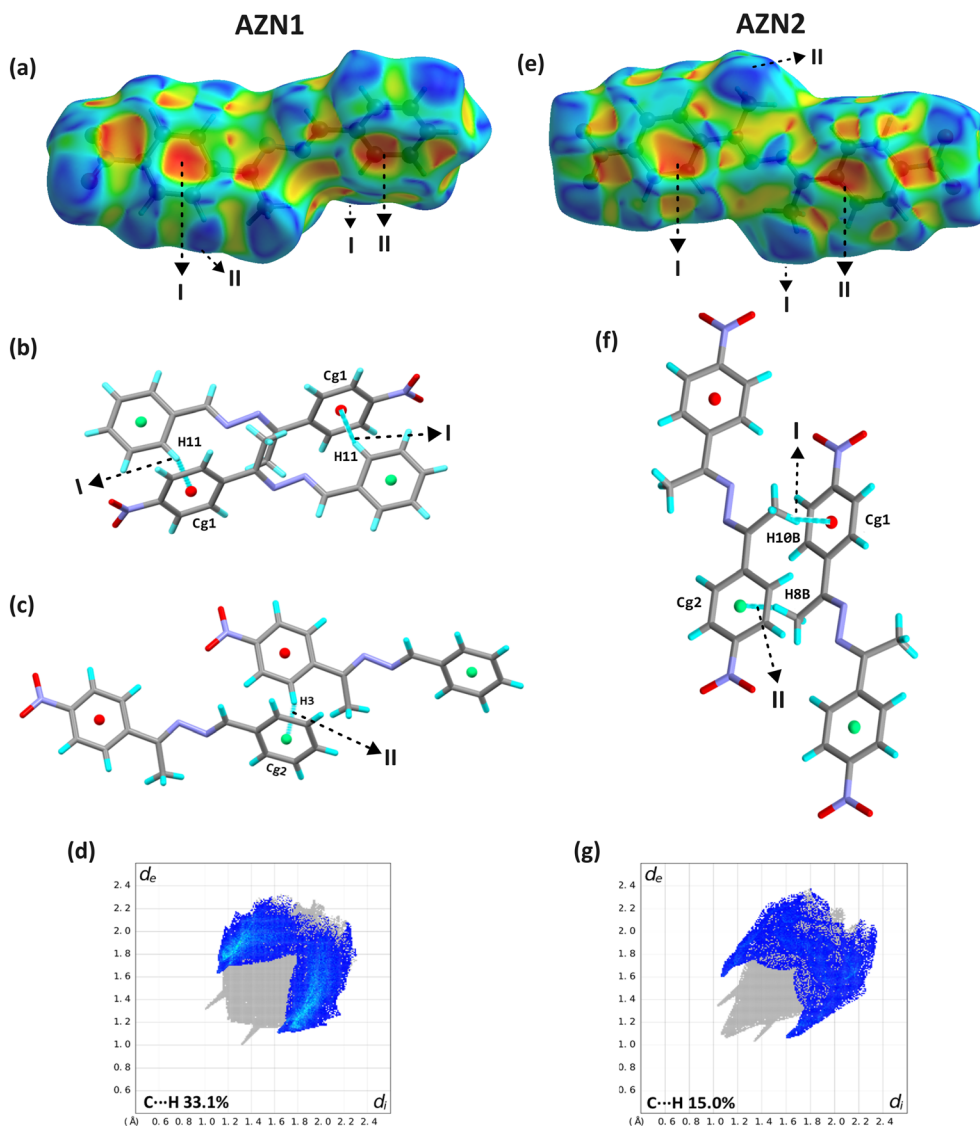


Fig. 4 HS with the shape index property mapped, highlighting the red concave and blue convex regions where C–H $\cdots$ π interactions occur, along with details of these interactions in the supramolecular arrangement of AZN1 and AZN2. (a) Shape index surface mapped for AZN1. (b) Representation of the C₁₁–H₁₁ $\cdots$ Cg₁ interaction in AZN1. (c) Representation of the C₃–H₃ $\cdots$ Cg₂ interaction in AZN1. (d) 2D fingerprint plot of C $\cdots$ H contacts, representing 33.1% of the total mapped contacts in AZN1. (e) Shape index surface mapped for AZN2. (f) Representation of the C₁₀–H_{10B} $\cdots$ Cg₁ and C₈–H_{8B} $\cdots$ Cg₂ interactions in AZN2. (g) 2D fingerprint plot of C $\cdots$ H contacts, representing 15% of the total mapped contacts in AZN2.

to the HOMO and LUMO. Each compound was evaluated in both solid and gas phases, allowing the identification of electronic variations between them. Despite minor changes in orbital energies after optimization, the electronic profile of AZN1 (Fig. 6a) remained stable, with no significant alteration in the energy gap. In contrast, AZN2 exhibited notable changes in these parameters (Fig. 6b). The data indicate that, compared to AZN1 in the gas phase, the additional presence of a nitro and a methyl group in AZN2 reduces molecular reactivity by approximately 5.38%, while this property remains unchanged in the solid state.

When compared to commercial additives (Table 4), the molecules in this study exhibit distinct electronic characteristics. High ionization energy values indicate a lower

tendency to donate electrons in molecular interactions. Furthermore, low HOMO and LUMO values result in a smaller energy gap compared to other additives, making them more reactive, as also indicated by more negative μ values and lower η values. According to the analyzed parameters, AZN1 and AZN2 show greater polarizability and electronic reactivity, while their more negative E_{HOMO} values indicate a reduced oxidation capacity compared to the other additives, since the removal of an electron becomes energetically less favorable.

The observed differences between the energy values of the frontier orbitals of azines and commercial antioxidants stem from the fact that these compounds belong to distinct chemical classes. While conventional antioxidants are

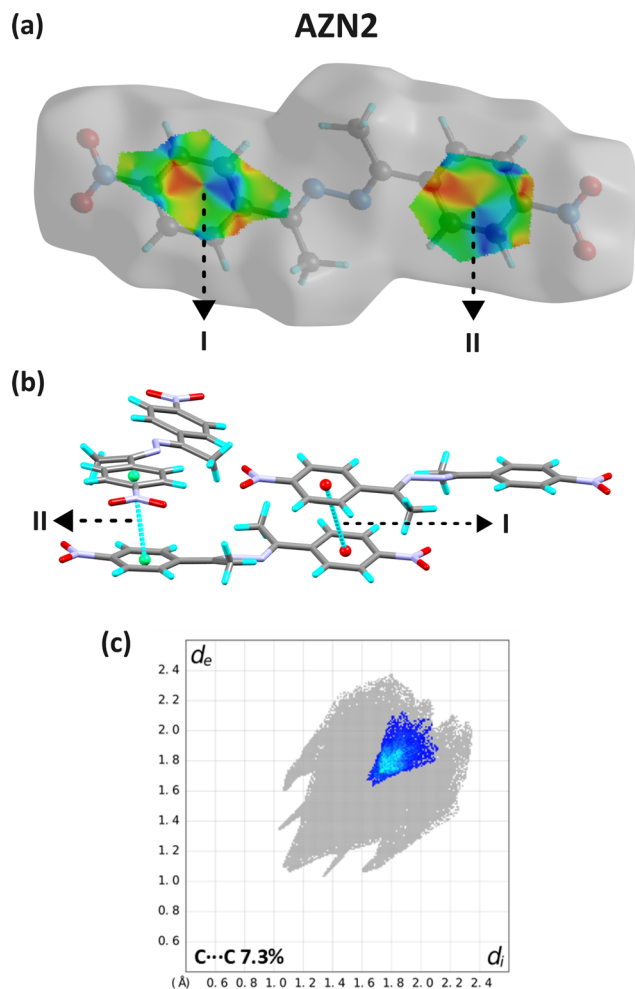


Fig. 5 HS with the shape index property mapped, highlighting the complementary spots (red and blue) where $\pi\cdots\pi$ interactions occur in AZN2. (a) Shape index surface mapped for AZN2. (b) Representation of the $Cg_1\cdots Cg_1$ and $Cg_2\cdots Cg_2$ interactions in AZN2. (c) 2D fingerprint plot of $C\cdots C$ contacts, representing 7.3% of the mapped contacts in AZN2.

predominantly phenolic and act through hydrogen atom transfer (HAT) mechanisms, azines exert their antioxidant activity through SET processes and radical stabilization *via* electronic delocalization in the π -conjugated system. Despite these structural differences, both classes share the same purpose: to increase the oxidative stability of biodiesel, reinforcing the potential of azines as non-phenolic alternatives to traditional antioxidant additives and expanding the perspectives for formulating new stabilizers based on electronic parameters.

The high electrophilicity index (ω) and electronic affinity (A) values for AZN1 and AZN2 reflect their greater ability to accept electrons, indicating instability toward nucleophiles. This behavior is consistent with the presence of nitro groups and the extended π -conjugated system of azines, which increase electron-withdrawing character and charge delocalization. Compared to phenolic antioxidants, which exhibit lower ω and A values due to the hydroxyl group donor

effect, azines show a greater tendency to stabilize radicals through SET mechanisms rather than HAT mechanisms. The electrostatic potential surfaces of the compounds are shown in Fig. 7, with colors indicating nucleophilic (red) and electrophilic (blue) sites. Both molecules share similarities in the locations of reactive sites, and the addition of the nitro group in AZN2 caused a 1.25% increase in electron density at O_1 and a 7.61% decrease at O_2 . The most significant change occurred in the bond region between C_9 and the methyl group added in AZN2, corresponding to a 47.37% reduction in electron density.

Table 5 presents the main topological parameters obtained for AZN1 and AZN2. As shown in Fig. 8, both structures display BCPs along their bond paths, with densities within the expected range (0.002 to 0.035 au). In AZN1, the $C_9-H_9\cdots O_2$ interaction shows the highest electron density at the BCP (0.0115 au); the $\nabla^2\rho$ (0.0416 au) and H (0.0015) values indicate a weak interaction with electrostatic character.^{118,119} Nevertheless, its mutual penetration (0.8105) indicates better overlap of the electron densities,^{97,98} with a bond energy ($BE = -1.8231$ kJ mol⁻¹) stronger than the others.

Among the interactions mapped in AZN2, $C_{10}-H_{10C}\cdots O_1$ shows the lowest values of $\rho(r)$ (0.0070 au), penetration ($MP = 0.3753$), and interaction energy (-0.8193 kJ mol⁻¹). The $\nabla^2\rho$ (0.0253 au), H (0.0009), and η (0.1514) values indicate low covalent tendency.^{118,119} Furthermore, its ellipticity (0.2045) suggests pronounced anisotropy, possibly with π -orbital contribution.⁹⁶ On the other hand, the $C_{13}-H_{13}\cdots O_1$ and $C_{12}-H_{12}\cdots O_2$ interactions present low ellipticity values (0.0294 and 0.0274, respectively), indicating σ character, with more regular geometry and symmetrical electron density.¹⁰⁰ The AZN1 and AZN2 structures exhibit all $C-H\cdots O$ interactions with $|V(r)|/G(r)$ around 0.8, consistent with hydrogen bonds. Similarly, the BD values observed for these interactions are close to 0.1, reinforcing this characteristic.¹²⁰

The study of molecular electric properties, like dipole moment (μ) and mean linear polarizability ($\langle\alpha\rangle$), can be useful for predicting the behavior of molecules with potential applications in optical properties and antioxidant activity. The compound AZN1 shows a large total dipole moment (μ) of 6.94 D, with the vector oriented mostly in the XY plane of the molecule. This high value is consistent with the structural asymmetry of the compound, where the single nitro-substituent acts as a strong electron acceptor, making the charge separation bigger along the molecular structure. In contrast, AZN2 has a much smaller dipole moment, 2.64 D, with a different orientation, almost completely aligned with the Z axis, see Table 6.

The presence of two nitro groups in positions that are relatively symmetric causes a partial compensation of the charge distributions, which results in a smaller total dipole moment. This molecular structure symmetry is not perfect because of conformational torsions, and this explains the non-zero value. This makes AZN1 a strongly polar molecule, while AZN2 is a moderately polar molecule. The analysis of

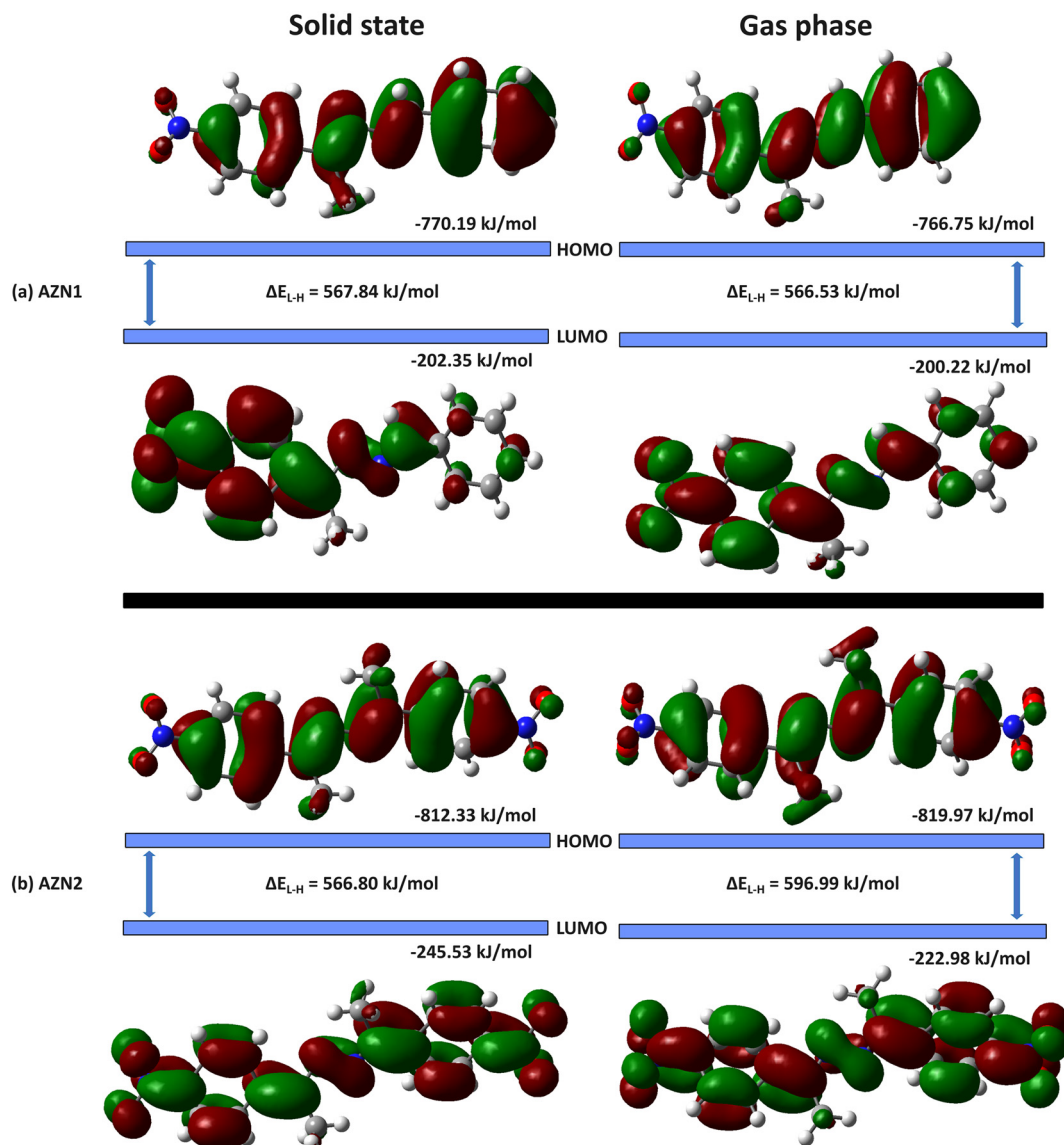


Fig. 6 Frontier molecular orbitals HOMO (above) and LUMO (below) for the solid state (left) and gas phase (right) of (a) AZN1 and (b) AZN2, calculated at the M06-2X/6-311++G(d,p) level of theory.

Table 4 Chemical reactivity descriptors of AZN1 and AZN2 in solid (s) and gas (g) phases compared to commercial additives in kJ mol^{-1}

Descriptor	AZN1 _s	AZN1 _g	AZN2 _s	AZN2 _g	BHT	BHA	TBHQ	PG	GA
E_{HOMO}	-770.19	-812.33	-766.75	-819.97	-689.04	-673.76	-685.41	-758.98	-763.44
E_{LUMO}	-202.35	-245.53	-200.22	-222.98	-17.59	-16.51	-22.63	-47.60	-62.25
Gap (ΔE_{L-H})	567.84	566.80	566.53	596.99	671.45	657.25	662.78	711.38	701.19
Ionization energy (I)	770.19	812.33	766.75	819.97	689.04	673.76	685.41	758.98	763.44
Electronic affinity (A)	202.35	245.53	200.22	222.98	17.59	16.51	22.63	47.60	62.25
Electronegativity (χ)	486.27	528.93	483.49	521.48	353.32	345.14	354.02	403.29	412.85
Chemical hardness (η)	283.92	283.40	283.27	298.50	335.73	328.63	331.39	355.69	350.60
Chemical potential (μ)	-486.27	-528.93	-483.49	-521.48	-353.32	-345.14	-354.02	-403.29	-412.85
Electrophilicity index (ω)	416.42	493.59	412.61	455.51	185.91	181.24	189.10	228.63	243.07

the dynamic mean linear polarizability, $\langle\alpha(-\omega;\omega)\rangle$, shows an expected dispersive behavior for both compounds, with the values decreasing as the incident wavelength (λ) increases

from 400 to 1900 nm. The compound AZN2 was more polarizable than AZN1 in the entire spectral range we evaluated, see Fig. 9.

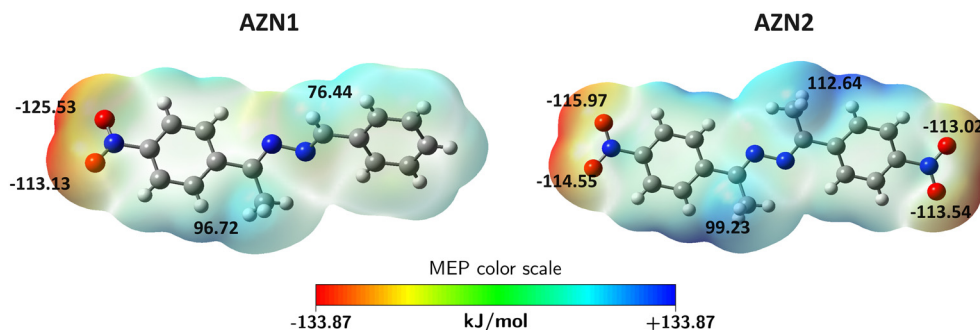


Fig. 7 Molecular electrostatic potential surfaces at $\rho(r) = 4.0 \times 10^{-4}$ electrons per bohr³ contour of the total electronic density for AZN1 and AZN2.

Table 5 QTAIM topological parameters for AZN1 and AZN2 obtained at the M06-2x/6-311++G(d,p) level of theory

Interaction	$\rho(r)$	$\nabla^2\rho$	MP	BE	ϵ	$G(r)$	$V(r)$	$H(r)$	$\eta(r)$	BD	$ V(r) /G(r)$
AZN1											
C ₁₃ -H ₁₃ ...O ₁	0.0093	0.0314	0.6127	-1.3323	0.0690	0.0067	-0.0057	0.0010	0.1883	0.1075	0.8507
C ₉ -H ₉ ...O ₂	0.0115	0.0416	0.8105	-1.8231	0.1132	0.0088	-0.0072	0.0015	0.1844	0.1304	0.8182
C ₈ -H _{8B} ...N ₃	0.0052	0.0183	0.4512	-0.4177	0.8461	0.0038	-0.0031	0.0007	0.1091	0.1346	0.8158
AZN2											
C ₆ -H ₆ ...O ₃	0.0074	0.0259	0.4558	-0.9085	0.1250	0.0055	-0.0045	0.0010	0.1823	0.1351	0.8182
C ₁₀ -H _{10C} ...O ₁	0.0070	0.0253	0.3753	-0.8193	0.2045	0.0054	-0.0044	0.0009	0.1514	0.1286	0.8148
C ₁₃ -H ₁₃ ...O ₁	0.0103	0.0367	0.6813	-1.5554	0.0294	0.0078	-0.0064	0.0014	0.1826	0.1359	0.8205
C ₁₂ -H ₁₂ ...O ₂	0.0079	0.0258	0.6233	-1.0200	0.0274	0.0056	-0.0047	0.0009	0.1843	0.1139	0.8393
C ₅ -H ₅ ...O ₄	0.0059	0.0196	0.4291	-0.5739	0.0600	0.0042	-0.0035	0.0007	0.1767	0.1186	0.8333

For example, at 532 nm, the $\langle\alpha\rangle$ of AZN2 ($\approx 342.8 \times 10^{-24}$ esu) is about 7% higher than AZN1 ($\approx 319.8 \times 10^{-24}$ esu). This polarizability is connected to its diffuse electron cloud, influenced by having two nitro groups and one extra methyl substituent. The results for the linear properties show a dichotomy between the static and dynamic electric properties of the two compounds. AZN1, because of its clear asymmetry, maximizes the permanent charge separation, resulting in a dipole moment (μ) almost three times larger than AZN2. On the other hand, AZN2 has a more reactive electron cloud for oscillating fields, which reflects in a higher mean linear polarizability ($\langle\alpha\rangle$). The high dipole of AZN1 is a fundamental prerequisite for a good first β_{HRS} response. At the same time, the higher polarizability of AZN2 suggests a bigger susceptibility to oscillating electric fields. This can favor both the linear response (refractive index) and the third-order response (γ).

The evaluation of the first dynamic hyperpolarizability, $\beta_{\text{HRS}}(-2\omega;\omega,\omega)$, shows a superiority of AZN1 over AZN2 in the analyzed spectral range. The ratio $\beta_{\text{HRS}}(\text{AZN1}/\text{AZN2})$ is ~ 2.7 at 400 nm, reaches ~ 7.3 at 450 nm, is ~ 4.7 at 532 nm, and grows sharply in the near-infrared (NIR). From 700 nm on, AZN1 stays ~ 33 – 41 times higher than AZN2, see Fig. 10.

This stability is maintained across the near-infrared (NIR), a region relevant for many technologies. The high ratio persists at the widely used 1064 nm laser wavelength and also within the standard optical telecom windows (1300–1550 nm). Both show a peak at 450 nm (resonant enhancement). Away from resonance, AZN1 decays gradually but remains

significant (23.04×10^{-30} esu at 1900 nm), while AZN2 reduces almost to a residual value (0.694×10^{-30} esu at 1900 nm). The reason for the difference is linked to symmetry and charge distribution; β is sensitive to non-centrosymmetry and to dipole differences between states. The greater electronic asymmetry of AZN1 (consistent with its high μ) reduces tensorial cancellations and favors a large β . AZN2, even with a higher $\langle\alpha\rangle$ (linear response), behaves almost centrosymmetrically from a 2nd order point of view, which suppresses β , especially away from resonance. To better interpret our results, we compared them with the reference material *p*-nitroaniline (pNA). According to the literature, pNA exhibits a β value for pNA of 23×10^{-30} esu in chloroform,¹²¹ which is also an apolar solvent.

At the resonance peak (450 nm), the β of AZN1 is approximately 875×10^{-30} esu. This value is almost 40 times larger than the pNA reference value, which demonstrates a very strong resonant effect. More importantly, the non-resonant value for AZN1 in the NIR region (23.04×10^{-30} esu at 1900 nm) is almost identical to the pNA reference value. For AZN2, the response is much smaller than the pNA reference, an expected result due to its molecular symmetry. Therefore, this comparison indicates that AZN1 is a high-performance NLO material, not only at resonance but also in the non-resonant NIR spectral region. AZN1 is a good candidate for 2nd order effects in solution (measured by HRS, *i.e.*, incoherent SHG), including in the NIR. AZN2, with a suppressed β , is likely more interesting for linear response and possibly 3rd order processes ($\chi^{(3)}$). Significantly, the

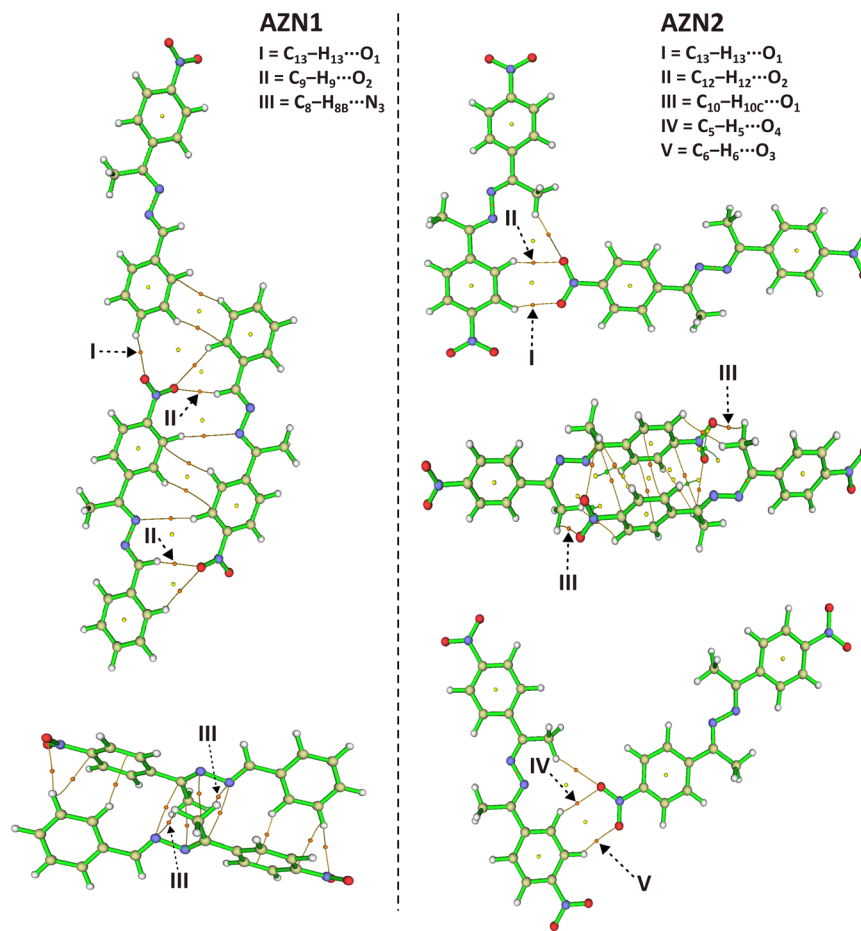


Fig. 8 BCPs identified for the interactions of AZN1 and AZN2 through QTAIM.

same intramolecular charge-transfer character that drives the high hyperpolarizability of AZN1 also reduces its adiabatic ionization potential (IP_{ad}). Thus, NLO properties and antioxidant activity not only coexist but stem from the same fundamental electronic feature: the asymmetry and delocalization of electron density along the π -system.

The molecules AZN1 and AZN2 exhibit similar luminescent behavior, with variations arising from their structural and symmetry differences. According to the results predicted by machine learning, the maximum absorptions occur at 390.770 nm (AZN1) and 380.231 nm (AZN2), while the emissions are observed at 472.422 and 474.218 nm, resulting in Stokes shifts of 81.651 and 93.987 nm, respectively. The larger Stokes shift of AZN2 indicates a more pronounced electronic reorganization between the ground

and excited states, attributed to the presence of the second nitro group, which enhances the electron-withdrawing character and promotes a more significant structural reorganization upon excitation. AZN1, on the other hand, with a more asymmetric structure and higher dipole moment, exhibits slightly more energetic transitions. The similarities of 46.71% (AZN1) and 47.86% (AZN2) with

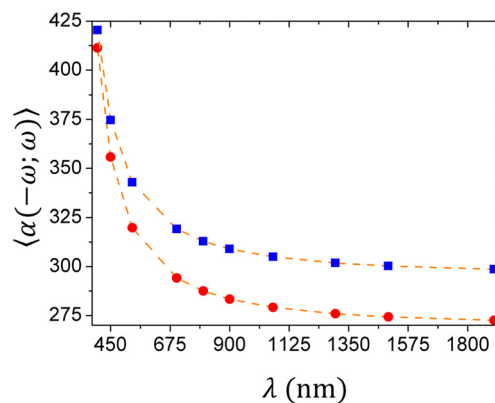


Fig. 9 Average linear polarizability $\langle \alpha(-\omega; \omega) \rangle$, as a function of wavelength (λ). The red circles represent AZN1 and the blue square represent AZN2.

Table 6 Dipole moment components and total value (μ , in Debye) for AZN1 and AZN2

Dipole moment	AZN1	AZN2
μ_x	-6.68	0.01
μ_y	1.88	-0.18
μ_z	-0.00	-2.63
μ	6.94	2.64

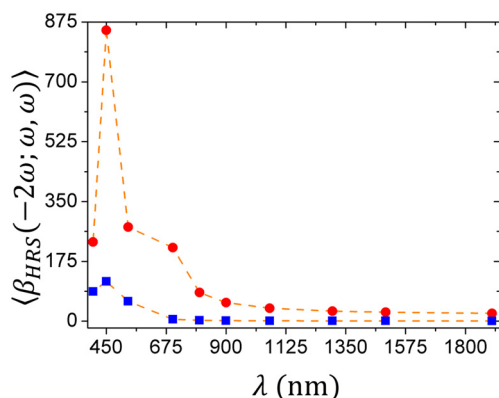


Fig. 10 First β_{HRS} as a function of wavelength (λ). The red circles represent AZN1 and the blue squares represent AZN2.

respect to the training database demonstrate consistency with the reference set, supporting the validity of the predictions obtained. These well-defined absorption and emission values indicate that AZN1 and AZN2 could be detected in fuels such as biodiesel or diesel/biodiesel blends by fluorescence or absorbance spectroscopic techniques, using λ_{abs} and λ_{em} as specific optical signatures for monitoring oxidative stability and identifying antioxidant additives during fuel use and storage.

3.3 Antioxidant performance

The Fukui indices mapped the regions most susceptible to nucleophilic, electrophilic, and radical attacks. In Fig. 11a, it is observed that the C=N bonds and the *para* and *ortho* positions of ring 2 in AZN1 present high electron density, favoring electrophilic attacks; in AZN2, the addition of the nitro group reduces the density in ring 2, favoring attacks on the iminic nitrogens (Fig. 11d). Despite the difference in centricity, AZN1 and AZN2 exhibit similar regions susceptible to nucleophilic attacks, located between the nitro group and ring 1, in the C₄–C₇ bond, and in the O₁ and O₂ oxygens (Fig. 11b). These reactive patterns are repeated in the equivalent regions of AZN2, as shown in Fig. 11e. The regions

susceptible to radical attacks are concentrated between the nitro group and ring 1, as well as in the C=N bonds in AZN1 (Fig. 11c). In AZN2, they are located in the iminic nitrogens, as shown in Fig. 11f. In light of this, the presence of nitro groups in the centric azine restricts the reactive sites for radical attacks to the N–N region, which may compromise the molecule's antioxidant activity, since radicals may be related to this process.

The reaction rate constant is a key kinetic parameter for evaluating the efficiency of the oxidative process mediated by hydroxyl radicals, where higher k_{OH} values indicate a greater degradation rate. In Table 7, the k_{OH} values for AZN1 and AZN2 are presented and compared with diesel, three biodiesel components (BD M9OD, BD MPAL and BD M8OD), and commercial additives. The results indicate AD% values above 76% for all molecules with the MACCS fingerprint, demonstrating greater accuracy of this descriptor compared with the Morgan descriptor in the training set.

The k_{OH} values obtained for the azines are 3.25×10^9 for AZN1 and 1.13×10^9 for AZN2, both within the same order of magnitude as the main biodiesel components: BD M9OD (5.94×10^9), BD MAPL (4.98×10^9) and BD M8OD (5.94×10^9), as well as commercial additives: BHT (4.34×10^9), BHA (4.31×10^9), TBHQ (7.63×10^9), and GA (1.48×10^9). The equivalence between BD M9OD and BD M8OD is due to the limitation of the MACCS fingerprint, which uses a predefined set of fragments, making it difficult to differentiate similar structures. In contrast, the Morgan descriptor, which considers more details of the atomic neighborhood, better distinguished the structures, with k_{OH} values of 6.39×10^9 (AZN1) and 4.70×10^9 (AZN2), close to those of diesel (6.05×10^9) and biodiesel (5.90×10^9 for BD M9OD and BD M8OD, 5.70×10^9 for MPAL) and higher than the additives BHT (4.16×10^9) and GA (4.09×10^9).

When the comparison is extended to the other azines, the same trend observed for AZN1 and AZN2 is maintained. Azines with a lower number of nitro groups exhibit better performance in neutralizing $\cdot OH$ radicals, as evidenced by the higher k_{OH} value observed for AZN3 (9.42×10^9). This relationship reinforces that nitro groups, by acting as

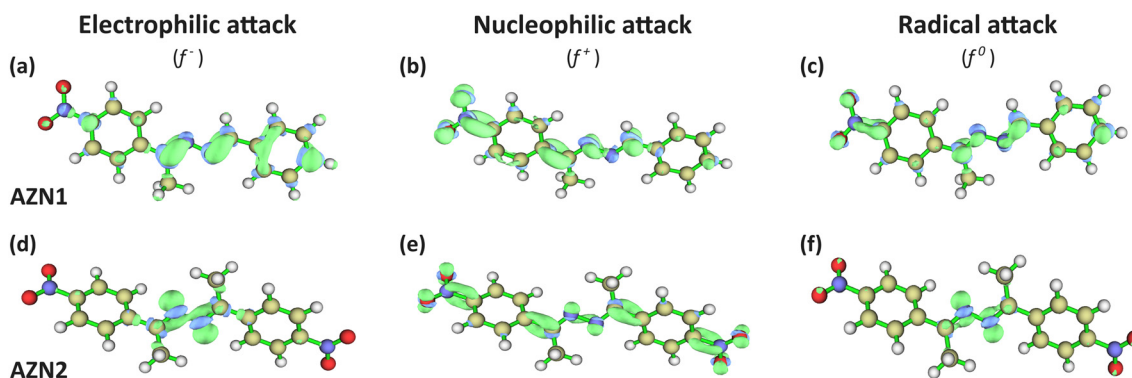


Fig. 11 Isosurfaces of the Fukui functions indicating the sites of electrophilic (left a and d), nucleophilic (center b and e), and radical (right c and f) attacks for AZN1 (top) and AZN2 (bottom), obtained at the M06-2X/6-311++G(d,p) level of theory.

Table 7 Reaction rate (k_{OH} in $\text{M}^{-1} \text{s}^{-1}$) for compounds AZN1 and AZN2 (this work), major diesel and biodiesel (BD) components, and other commercial additives obtained using the XGBoost algorithm model, separated into two types of fingerprints: Morgan and MACCS. AD is the percentage of similarity within the applicability domain

Molecule	Molecular formula	Morgan	AD (%)	MACCS	AD (%)	References
Diesel ¹¹³	$\text{C}_{10}\text{H}_{20}$	6.05×10^9	50.00	1.14×10^{10}	76.92	Duarte <i>et al.</i> ¹¹²
BD M9OD (19.98%) ¹¹³	$\text{C}_{19}\text{H}_{38}\text{O}_2$	5.90×10^9	48.21	5.94×10^9	85.00	Duarte <i>et al.</i> ¹¹²
BD MPAL (12.87%) ¹¹³	$\text{C}_{17}\text{H}_{34}\text{O}_2$	5.70×10^9	58.70	4.98×10^9	89.47	Duarte <i>et al.</i> ¹¹²
BD M8OD (10.22%) ¹¹³	$\text{C}_{19}\text{H}_{34}\text{O}_2$	5.90×10^9	40.32	5.94×10^9	85.00	Duarte <i>et al.</i> ¹¹²
AZN1	$\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2$	6.39×10^9	37.74	3.25×10^9	82.76	This work
AZN2	$\text{C}_{16}\text{H}_{14}\text{N}_4\text{O}_4$	4.70×10^9	55.56	1.13×10^9	79.41	This work
AZN3 (ref. 57)	$\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_2$	9.42×10^9	33.33	1.38×10^9	77.42	This work
AZN4 (ref. 114)	$\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_4$	5.70×10^9	36.96	1.02×10^9	84.38	This work
AZN5 (ref. 114)	$\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_4$	2.89×10^9	30.91	6.88×10^8	85.71	This work
AZN6 (ref. 114)	$\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_4$	5.31×10^9	44.74	1.02×10^9	84.38	This work
AZN7 (ref. 114)	$\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_4$	5.70×10^9	40.00	1.02×10^9	84.38	This work
CA BHT ¹¹⁵	$\text{C}_{15}\text{H}_{24}\text{O}$	4.16×10^9	100.00	4.34×10^9	100.00	Duarte <i>et al.</i> ¹¹²
CA BHA ¹¹⁵	$\text{C}_{22}\text{H}_{32}\text{O}_4$	7.27×10^9	66.67	4.31×10^9	77.78	Duarte <i>et al.</i> ¹¹²
CA TBHQ ¹¹⁵	$\text{C}_{10}\text{H}_{14}\text{O}_2$	7.57×10^9	100.00	7.63×10^9	100.00	Duarte <i>et al.</i> ¹¹²
CA PG ¹¹⁵	$\text{C}_6\text{H}_6\text{O}_3$	1.11×10^{10}	100.00	1.22×10^{10}	100.00	Duarte <i>et al.</i> ¹¹²
CA GA ¹¹⁵	$\text{C}_7\text{H}_6\text{O}_5$	4.09×10^9	40.62	1.48×10^9	100.00	Duarte <i>et al.</i> ¹¹²

electron-withdrawing centers, reduce the ability of azines to donate electrons or hydrogens, which compromises their antioxidant efficiency. Furthermore, the position of the nitro groups on the aromatic ring significantly influences the efficiency of the azines. Molecules with substituents in the *para* position (such as AZN4 and AZN7) showed greater potential compared to those with groups in the *meta* position (such as AZN6), as indicated by the results of the Morgan fingerprint descriptor, with values of 5.31×10^9 for AZN6 and 5.70×10^9 for AZN4 and AZN7. When comparing the *meta* and *ortho* positions, the reduction in antioxidant potential becomes even more evident: relative to AZN6, AZN5, which has the nitro group on the second ring in the *ortho* position, showed a 45.6% decrease in the k_{OH} value, according to the Morgan model. In the MACCS model, however, the identical values observed among AZN4, AZN6, and AZN7 result from the lower sensitivity of this descriptor to subtle structural differences, since it uses a limited set of information and therefore does not adequately distinguish variations in the position of substituents. Complementarily, the structural similarity analysis revealed a high degree of correlation between the studied azines and the molecules from the reference database. Among the analyzed azines, AZN1 and AZN2 showed the highest similarity to each other (97%), as well as a strong correspondence with AZN7 (74% and 72%, respectively) and AZN4 (61% and 60%), indicating that small variations in the position and number of substituents may be decisive for the antioxidant behavior (see SI, Fig. S12).

These results indicate that azines with fewer nitro substituents are better candidates for additives, as the nitro groups on the aromatic rings act as localized, non-conjugated electron-withdrawing centers.¹²² In the case of AZN2, the additional nitro group intensifies this effect, resulting in a lower k_{OH} value. To complement the machine learning predictions, a more direct assessment of the electron-donating capacity of the azines was performed. This analysis focuses on the SET mechanism, a key antioxidant pathway

for molecules that, like AZN1 and AZN2, lack the traditional O–H or N–H groups required for HAT. The viability of the SET pathway can be effectively evaluated by calculating the IP_{ad} , where a lower value indicates a greater propensity for the molecule to donate an electron and neutralize radical species.

The SET trend can be checked by IP_{ad} , which we get from the difference between the Gibbs energies at 298 K of the radical cation and the neutral molecule, using the same solvent and theory level,

$$\text{IP}_{\text{ad}} = G(\text{A}^{\cdot+}) - G(\text{A}) \quad (17)$$

The calculations were done with CAM-B3LYP/6-311++G(d,p) and SMD (*n*-hexane). We did geometry optimization and vibrational analysis (freq) for the neutral and radical cation (duplet) forms. This gives us good thermochemical corrections at 298 K.

Following this protocol, we got IP_{ad} for AZN1 (7.183 eV/693.0 kJ mol^{−1}) and AZN2 (7.250 eV/699.5 kJ mol^{−1}). This means AZN1 has a bit lower IP_{ad} than AZN2, which in SET-based mechanisms, a lower IP_{ad} means it is easier to oxidize. From these results, AZN1 should have a small advantage over AZN2 as an electron donor in *n*-hexane. The difference (0.067 eV/6.46 kJ mol^{−1}) is small, which suggests both compounds are in the same range of redox reactivity. So, other things can affect the practical result in biodiesel, like: (i) the stabilization and delocalization of the radical cation that is formed (we can describe this with spin/charge density analysis), and (ii) phase affinity (how it partitions into the lipid matrix).

In addition, it is important to note that the reactivity of these molecules depends not only on the ionization potentials but also on specific structural features. The azine bridge is known to act as a “conjugation stopper”, which limits the full electronic delocalization, a property discussed in many works by the Glaser group and reviewed by Safari

and co-workers.³⁷ The introduction of nitro groups creates a push–pull effect, changing the charge density distribution. This is relevant because it influences the electron availability for SET processes and the capacity for proton exchange, as observed in studies on azine-hydrazone tautomerism.¹²³ This electronic versatility of azines is well documented in several applications, ranging from organocatalysis, where they act in substrate activation,^{124,125} to recent applications in chemosensors that rely on electron and proton transfer mechanisms.^{126,127} Looking only at the IP_{ad} in SMD (*n*-hexane), AZN1 is a slightly favorable for the SET mechanism than AZN2. However, the values are very close, indicating that azines may serve as additive candidates if nitro groups are absent, primarily due to their electron-withdrawing character observed for the nitro-azines in this work, which reduces the compound's antioxidant potential in a non-polar medium.

4. Conclusion

The growing use of biodiesel as a renewable fuel highlights the urgent need for additives that can enhance oxidative stability and performance. In this study, two nitro-substituted azine derivatives were structurally and computationally characterized to probe the relationship between molecular design, supramolecular organization, and functional properties. Both compounds are stabilized by C–H $\cdots$ O, C–H $\cdots$ N, and C–H $\cdots\pi$ interactions, forming dimers with $R_2^2(22)$ and $R_4^4(20)$ motifs in AZN1 and $R_2^2(7)$ in AZN2. The additional nitro group (NO_2) in AZN2 did not cause a significant difference in the HOMO–LUMO gap compared to AZN1 in the solid state. However, in the gas phase, AZN2 shows a larger gap than AZN1, indicating a 5.38% increase in stability.

While the additional nitro group in AZN2 did not significantly alter solid-state HOMO–LUMO gaps, it reduced reactivity in the gas phase and shifted frontier orbital distributions. The Fukui functions revealed that the additional nitro and methyl groups in AZN2 cause a change in the reactive sites, relocating the electrophilic and radical attack sites solely to the imine nitrogens and extending the nucleophilic attack to regions corresponding to an inversion center. The topological analysis showed that the interactions in both compounds are predominantly closed-shell type, with the $C_{10}-H_{10C}\cdots O_1$ interaction in AZN2 exhibiting greater π character, and $C_{13}-H_{13}\cdots O_1$ and $C_{12}-H_{12}\cdots O_2$ showing greater σ character.

Also, an analysis of the SET mechanism showed that AZN1 has a slightly lower ionization potential than AZN2. The study of the electric properties found a clear difference: AZN1 is strongly polar with a high dipole moment, but AZN2 has a higher linear polarizability. Most important, the asymmetric AZN1 showed a much bigger second-order NLO response (β_{HRS}), more than 30 times higher than the symmetric AZN2 in the NIR region. This makes AZN1 a high-performance NLO material, comparable to the *p*-nitroaniline reference.

The results obtained from the oxidation rate predictions against $\cdot OH$ radicals revealed a slightly superior antioxidant performance for the azine with a lower number of nitro groups. This is attributed to the reducing capacity provided by the nitro group, which influences the reactivity of azines toward free radicals. Consequently, AZN1 demonstrated a slightly better antioxidant potential than AZN2, with reaction rates comparable to those of diesel and the main components of biodiesel, in addition to surpassing some commercial additives. These findings illustrate how detailed structural insights can guide the rational design of antioxidant additives for biodiesel stabilization and reinforce the potential of AZN1 as an additive of renewable fuels, particularly biodiesel.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The datasets supporting the findings of the manuscript titled “Comprehensive structural insights into nitro-substituted azines as potential antioxidant additives for biodiesel” are available within the article and its supplementary information (SI). Crystallographic data for the reported structures have been deposited with the Cambridge Crystallographic Data Centre under the deposition numbers 2484685 (AZN1) and 2484683 (AZN2).

Supplementary information: the SI is available at DOI: <https://doi.org/10.1039/d5ce00915d>. ^1H NMR, ^{13}C NMR spectra, associated HSQC, HMBC and COSY plots of AZN1 and AZN2. Fig. S1–S12, Tables S1–S10. Crystallographic information files of AZN1 (deposition number: 2484685) and AZN2 (deposition number: 2484683) were deposited in the CSD.

CCDC 2484685 (AZN1) and 2484683 (AZN2) contain the supplementary crystallographic data for this paper.^{128a,b}

Acknowledgements

The authors thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) – Project: 130350/2024-9; Project: 401425/2023-1 (L. R. A.), and the Fundação de Amparo à Pesquisa do Estado de Goiás (FAPEG) – Process: 202310267000442 (L. R. A./H. B. N.) for the financial and institutional support that made this work possible. This research utilized facilities at the National Synchrotron Light Laboratory, part of the Brazilian Center for Research in Energy and Materials (CNPEM), a private non-profit organization under the supervision of the Ministry of Science, Technology, and Innovations (MCTI). The MANACA beamline/facility team is recognized for their assistance during the experiments (proposal number: 20233032). C. V. is also grateful to the High-Performance Computing Laboratory of the Universidade Federal de Goiás (LAMCAD/UFG).

References

- 1 A. Zecca and L. Chiari, *Energy Policy*, 2010, **38**, 1–3.
- 2 L. Chiari and A. Zecca, *Energy Policy*, 2011, **39**, 5026–5034.
- 3 T. Levander, *Atmos. Environ.*, 1990, **24**, 2707–2714.
- 4 M. Hoel and S. Kvemdokk, *Resour. Energy Econ.*, 1996, **18**, 115–136.
- 5 F. C. Drumm, A. E. Gerhardt, G. D. Fernandes, P. Chagas, M. S. Sucolotti and P. D. D. C. Kemerich, *Rev. Eletr. Gest. Educ. Tecnol. Ambient.*, 2014, **18**, 66–78.
- 6 Planete Energies, What Is the Energy Mix?, <https://www.planete-energies.com/en/media/article/what-energy-mix>, (accessed 12 February 2025).
- 7 F. Junior, “Série Energia”: Mais de 80% da matriz energética vêm de recursos fósseis, <https://jornal.usp.br/campus-ribeirao-preto/serie-energia-mais-de-80-da-matriz-energetica-vem-de-recursos-fosseis/>, (accessed 12 February 2025).
- 8 R. C. Rial, *Renewable Sustainable Energy Rev.*, 2024, **196**, 114369.
- 9 N. Gaurav, S. Sivasankari, G. S. Kiran, A. Ninawe and J. Selvin, *Renewable Sustainable Energy Rev.*, 2017, **73**, 205–214.
- 10 E. R. Rene, J. Ge, G. Kumar, R. P. Singh and S. Varjani, *Environ. Sci. Pollut. Res.*, 2020, **27**, 17435–17437.
- 11 A. G. Souza, M. L. Medeiros, A. M. M. T. Cordeiro, N. Queiroz, L. E. B. Soledade and A. L. Souza, *Energy Fuels*, 2014, **28**, 1074–1080.
- 12 K. Varatharajan and D. S. Pushparani, *Renewable Sustainable Energy Rev.*, 2018, **82**, 2017–2028.
- 13 O. Awolu, *Am. Chem. Sci. J.*, 2015, **7**, 168–174.
- 14 N. Kinnal, G. Sujaykumar, S. W. D'Costa and G. S. Girishkumar, *IOP Conf. Ser.: Mater. Sci. Eng.*, 2018, **376**, 012012.
- 15 Z. Yaakob, B. N. Narayanan, S. Padikkaparambil, S. K. Unni and M. P. Akbar, *Renewable Sustainable Energy Rev.*, 2014, **35**, 136–153.
- 16 J. Pullen and K. Saeed, *Renewable Sustainable Energy Rev.*, 2012, **16**, 5924–5950.
- 17 P. Maheshwari, M. B. Haider, M. Yusuf, J. J. Klemeš, A. Bokhari, M. Beg, A. Al-Othman, R. Kumar and A. K. Jaiswal, *J. Cleaner Prod.*, 2022, **355**, 131588.
- 18 D. M. de Oliveira, D. P. Ongaratto, L. A. M. Fontoura, F. F. Naciuk, V. O. B. dos Santos, J. D. Kunz, M. V. Marques, A. O. de Souza, C. M. P. de Pereira and D. Samios, *Quim. Nova*, 2013, **36**, 734–737.
- 19 S. N. Naik, V. V. Goud, P. K. Rout and A. K. Dalai, *Renewable Sustainable Energy Rev.*, 2010, **14**, 578–597.
- 20 M. Naqvi and J. Yan, in *Handbook of Clean Energy Systems*, Wiley, 2015, pp. 1–18.
- 21 Y. F. Lin, J. H. Chen, S. H. Hsu and T. W. Chung, *CrystEngComm*, 2013, **15**, 6506–6510.
- 22 C. C. Da Silva, B. S. Pacheco, S. C. de Freitas, L. M. Berneira, M. A. Z. dos Santos, L. Pizzuti and C. M. P. de Pereira, in *Green Energy and Technology*, Springer Verlag, 2018, pp. 81–110.
- 23 J. Xin, H. Imahara and S. Saka, *Fuel*, 2009, **88**, 282–286.
- 24 C. A. Martins, P. S. Fernández and G. A. Camara, in *Green Energy and Technology*, Springer, 2018, pp. 159–186.
- 25 B. W. Stamps, C. L. Bojanowski, C. A. Drake, H. S. Nunn, P. F. Lloyd, J. G. Floyd, K. A. Emmerich, A. R. Neal, W. J. Crookes-Goodson and B. S. Stevenson, *Front. Microbiol.*, 2020, **11**, 167.
- 26 F. J. Passman, *Int. Biodeterior. Biodegrad.*, 2013, **81**, 88–104.
- 27 L. Longanesi, A. P. Pereira, N. Johnston and C. J. Chuck, *Biofuels, Bioprod. Biorefin.*, 2022, **16**, 265–289.
- 28 P. Sharma, A. Chhillar, Z. Said, Z. Huang, V. N. Nguyen, P. Q. P. Nguyen and X. P. Nguyen, *Energy Sources, Part A*, 2022, **44**, 5929–5950.
- 29 R. K. Saluja, V. Kumar and R. Sham, *Renewable Sustainable Energy Rev.*, 2016, **62**, 866–881.
- 30 F. Sundus, M. A. Fazal and H. H. Masjuki, *Renewable Sustainable Energy Rev.*, 2017, **70**, 399–412.
- 31 X. Liu, C. L. Bull, A. K. Kleppe, P. J. Dowding, K. Lewtas and C. R. Pulham, *CrystEngComm*, 2019, **21**, 4427–4436.
- 32 E. C. Zuleta, L. Baena, L. A. Rios and J. A. Calderón, *J. Braz. Chem. Soc.*, 2012, **23**, 2159–2175.
- 33 R. Bharti and B. Singh, *Fuel*, 2020, **262**, 116658.
- 34 V. S. Duarte, R. F. Naves, A. J. Bortoluzzi, E. C. M. Faria, A. M. da Silva, V. Mori, C. G. Alonso, G. R. Oliveira and H. B. Napolitano, *Biofuels*, 2023, **14**, 279–292.
- 35 L. R. de Almeida, A. S. N. Aguiar, A. B. R. M. da Anunciação, G. D. C. d'Oliveira, W. F. Vaz, J. M. F. Custódio, C. N. Pérez and H. B. Napolitano, *ACS Omega*, 2024, **9**, 49188–49204.
- 36 D. F. Vieira, I. D. Borges, A. S. N. Aguiar, V. S. Duarte, G. D. C. d'Oliveira, W. F. Vaz, R. F. Costa, C. N. Perez and H. B. Napolitano, *J. Mol. Struct.*, 2023, **1276**, 134736.
- 37 J. Safari and S. Gandomi-Ravandi, *RSC Adv.*, 2014, **4**, 46224–46249.
- 38 W. S. Hamama, M. A. Gouda, H. A. Kamal El-din and H. H. Zoorob, *J. Heterocyclic Chem.*, 2020, **57**, 257–267.
- 39 S. S. Chourasiya, D. Kathuria, A. A. Wani and P. V. Bharatam, *Org. Biomol. Chem.*, 2019, **17**, 8486–8521.
- 40 M. Bingul, S. Ercan, M. Boga and A. A. Bingul, *Polycyclic Aromat. Compd.*, 2024, **44**, 1326–1347.
- 41 J. Schirmann and P. Bourdauducq, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley, 2001.
- 42 J. Lasri and A. I. Ismail, *Indian J. Chem.*, 2018, **57**, 362–373.
- 43 V. B. Kurteva, S. P. Simeonov and M. Stoilova-Disheva, *Pharmacol. Pharm.*, 2011, **2**, 1–9.
- 44 I. Timtcheva, A. Pentchev, S. Metsov, S. Bakalova, V. Kolevab and P. Nikolov, *Dyes Pigment.*, 1995, **28**, 131–138.
- 45 C. Chiter, A. Bouchama, T. N. Mouas, H. Allal, M. Yahiaoui, I. Warad, A. Zarrouk and A. Djedouani, *J. Mol. Struct.*, 2020, **1217**, 128376.
- 46 J. Lasri, M. M. Aly, N. E. Eltayeb and B. A. Babgi, *J. Mol. Struct.*, 2018, **1164**, 1–8.
- 47 M. N. Ristić, N. S. Radulović, B. R. Dekić, V. S. Dekić, N. R. Ristić and Z. Stojanović-Radić, *Chem. Biodiversity*, 2019, **16**, 800486.

- 48 T. Yamamura, K. Suzuki, T. Yamaguchi and T. Nishiyama, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 413–419.
- 49 N. Rajendiran and T. Balasubramanian, *Spectrochim. Acta, Part A*, 2007, **68**, 894–904.
- 50 W. Tang, Y. Xiang and A. Tong, *J. Org. Chem.*, 2009, **74**, 2163–2166.
- 51 R. Wei, P. Song and A. Tong, *J. Phys. Chem. C*, 2013, **117**, 3467–3474.
- 52 D. Sek, M. Siwy, K. Bijak, M. Grucela-Zajac, G. Malecki, K. Smolarek, L. Bujak, S. Mackowski and E. Schab-Balcerzak, *J. Phys. Chem. A*, 2013, **117**, 10320–10332.
- 53 J. Ardaraviciene, B. Barvainiene, T. Malinauskas, V. Jankauskas, K. Arlauskas and V. Getautis, *React. Funct. Polym.*, 2011, **71**, 1016–1022.
- 54 Y. Liang, H. Wang, D. Wang, H. Liu and S. Feng, *Dyes Pigm.*, 2012, **95**, 260–267.
- 55 J. M. F. Custodio, R. R. Ternavisk, C. J. S. Ferreira, A. S. Figueredo, G. L. B. Aquino, H. B. Napolitano, C. Valverde and B. Baseia, *J. Phys. Chem. A*, 2019, **123**, 153–162.
- 56 V. L. Rusinov, E. N. Ulomskii, O. N. Chupakhin, A. Yu. Petrov and E. A. Sharonov, *Chem. Heterocycl. Compd.*, 1989, **25**, 209–213.
- 57 L. R. de Almeida, P. S. Carvalho, H. B. Napolitano, S. S. Oliveira, A. J. Camargo, A. S. Figueredo, G. L. B. de Aquino and V. H. Carvalho-Silva, *Cryst. Growth Des.*, 2017, **17**, 5145–5153.
- 58 M. Platzter, S. Kiese, T. Herfellner, U. Schweiggert-Weisz, O. Miesbauer and P. Eisner, *Molecules*, 2021, **26**, 1244.
- 59 M. A. Spackman and D. Jayatilaka, *CrystEngComm*, 2009, **11**, 19–32.
- 60 M. A. Spackman and J. J. McKinnon, *CrystEngComm*, 2002, **4**, 378–392.
- 61 K. Burke, *J. Chem. Phys.*, 2012, **136**, 150901.
- 62 A. Becke, R. J. Boyd and C. F. Matta, *The Quantum Theory of Atoms in Molecules: From Solid State to DNA and Drug Design*, John Wiley & Sons, Chichester, 2007.
- 63 A. S. Figueredo, J. E. Queiroz, L. D. Dias, H. D. A. Vidal, I. V. Machado, G. M. Vila Verde and G. L. B. Aquino, *Pharm. Chem. J.*, 2019, **53**, 544–549.
- 64 W. Kabsch, *Acta Crystallogr., Sect. D: Biol. Crystallogr.*, 2010, **66**, 125–132.
- 65 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, **64**, 112–122.
- 66 G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, 2015, **71**, 3–8.
- 67 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339–341.
- 68 C. R. Groom, I. J. Bruno, M. P. Lightfoot and S. C. Ward, *Acta Crystallogr., Sect. B: Struct. Sci., Cryst. Eng. Mater.*, 2016, **72**, 171–179.
- 69 C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler and J. Van De Streek, *J. Appl. Crystallogr.*, 2006, **39**, 453–457.
- 70 J. J. McKinnon, D. Jayatilaka and M. A. Spackman, *Chem. Commun.*, 2007, 3814.
- 71 J. J. McKinnon, A. S. Mitchell and M. A. Spackman, *Chem. – Eur. J.*, 1998, **4**, 2136–2141.
- 72 J. J. McKinnon, M. A. Spackman and A. S. Mitchell, *Acta Crystallogr., Sect. B: Struct. Sci.*, 2004, **60**, 627–668.
- 73 C. F. Mackenzie, P. R. Spackman, D. Jayatilaka and M. A. Spackman, *IUCrJ*, 2017, **4**, 575–587.
- 74 Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215–241.
- 75 R. Krishnan, J. S. Binkley, R. Seeger and J. A. Pople, *J. Chem. Phys.*, 1980, **72**, 650–654.
- 76 A. D. McLean and G. S. Chandler, *J. Chem. Phys.*, 1980, **72**, 5639–5648.
- 77 K. B. Wiberg, *J. Comput. Chem.*, 2004, **25**, 1342–1346.
- 78 S. F. Sousa, P. A. Fernandes and M. J. Ramos, *J. Phys. Chem. A*, 2007, **111**, 10439–10452.
- 79 E. G. Hohenstein, S. T. Chill and C. D. Sherrill, *J. Chem. Theory Comput.*, 2008, **4**, 1996–2000.
- 80 A. Frisch, *Gaussian 09W Reference*, Gaussian Inc., Wallingford, CT, 2009, vol. 470.
- 81 R. D. Dennington, T. A. Keith and J. M. Millam, *GaussView 5.0*, Gaussian Inc., Shawnee Mission, KS, 2008.
- 82 D. H. Pereira, F. A. La Porta, R. T. Santiago, D. R. Garcia and T. C. Ramalho, *Rev. Virtual Quim.*, 2016, **8**, 425–453.
- 83 K. Fukui, *Angew. Chem., Int. Ed. Engl.*, 1981, **21**, 801–809.
- 84 R. G. Pearson, *J. Mol. Struct.: THEOCHEM*, 1992, **255**, 261–270.
- 85 R. G. Parr, L. V. Szentpály and S. Liu, *J. Am. Chem. Soc.*, 1999, **121**, 1922–1924.
- 86 P. Politzer, P. R. Laurence and K. Jayasuriya, *Environ. Health Perspect.*, 1985, **61**, 191–202.
- 87 P. Politzer, *J. Phys. Chem.*, 1990, **94**, 3959–3961.
- 88 J. S. Murray and P. Politzer, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.*, 2011, **1**, 153–163.
- 89 T. Lu, *J. Chem. Phys.*, 2024, **161**, 082503.
- 90 C. Lee, W. Yang and R. G. Parr, *J. Mol. Struct.: THEOCHEM*, 1988, **163**, 305–313.
- 91 R. G. Parr and W. Yang, *J. Am. Chem. Soc.*, 1984, **106**, 4049–4050.
- 92 R. Hilal, S. G. Aziz, A. O. Alyoubi and S. Elroby, *Procedia Comput. Sci.*, 2015, **51**, 1872–1877.
- 93 J. D. Osamura, Y. Schaefer, F. Iii, J. Am, R. F. W. Bader, T. T. Nguyen-Dang, T. T. Nguyen Dang, Y. Tal, H. Essen, G. A. Olah, G. K. Surya Prakash and M. Saunders, *Acc. Chem. Res.*, 1985, **18**, 914.
- 94 R. F. W. Bader, *Chem. Rev.*, 1991, **91**, 893–928.
- 95 R. F. W. Bader, M. T. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.*, 1987, **109**, 7968–7979.
- 96 P. L. A. Popelier, *J. Phys. Chem. A*, 1998, **102**, 1873–1878.
- 97 U. Koch and P. L. A. Popelier, *J. Phys. Chem.*, 1995, **99**, 9747–9754.
- 98 P. L. A. Popelier, F. M. Aicken and S. E. O'Brien, in *Atoms in molecules*, Manchester, 2000, vol. 188, pp. 143–198.
- 99 S. Emamian, T. Lu, H. Kruse and H. Emamian, *J. Comput. Chem.*, 2019, **40**, 2868–2881.
- 100 C. Silva López, O. Nieto Faza, F. P. Cossio, D. M. York and A. R. De Lera, *Chem. – Eur. J.*, 2005, **11**, 1734–1738.

- 101 T. Lu and F. Chen, *J. Comput. Chem.*, 2012, **33**, 580–592.
- 102 J. Cheng, R. Huang, T. Li, J. Zhou and K. Cen, *Bioresour. Technol.*, 2014, **170**, 69–75.
- 103 M. Mohadesi, G. Moradi, M. Ghanbari and M. J. Moradi, *Measurement*, 2019, **135**, 606–612.
- 104 Y. Zhang, Y. Li, X. Zhang and T. Tan, *Bioresour. Technol.*, 2015, **196**, 712–715.
- 105 T. Yanai, D. P. Tew and N. C. Handy, *Chem. Phys. Lett.*, 2004, **393**, 51–57.
- 106 T. L. Fonseca, J. R. Sabino, M. A. Castro and H. C. Georg, *J. Chem. Phys.*, 2010, **133**, 144103.
- 107 R. Bano, M. Arshad, T. Mahmood, K. Ayub, A. Sharif, S. Perveen, S. Tabassum, J. Yang and M. A. Gilani, *J. Phys. Chem. Solids*, 2022, **160**, 110361.
- 108 R. F. Verissimo, P. H. F. Matias, M. R. Barbosa, F. O. S. Neto, B. A. D. Neto and H. C. B. de Oliveira, *J. Chem. Inf. Model.*, 2025, **65**, 7874–7886.
- 109 T. Chen and C. Guestrin, in *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, ACM, New York, NY, USA, 2016, pp. 785–794.
- 110 D. Bajusz, A. Rácz and K. Héberger, *Aust. J. Chem.*, 2015, **7**, 20.
- 111 F. O. Sanches-Neto, J. R. Dias-Silva, L. H. Keng Queiroz Junior and V. H. Carvalho-Silva, *Environ. Sci. Technol.*, 2021, **55**, 12437–12448.
- 112 V. S. Duarte, I. D. Borges, G. D. C. d'Oliveira, E. C. M. Faria, L. R. de Almeida, V. H. Carvalho-Silva, C. Noda-Pérez and H. B. Napolitano, *New J. Chem.*, 2023, **47**, 10003–10015.
- 113 M. Maulidiyah, M. Nurdin, F. Fatma, M. Natsir and D. Wibowo, *Anal. Chem. Res.*, 2017, **12**, 1–9.
- 114 C. Glidewell, J. N. Low, J. M. S. Skakle and J. L. Wardell, *Acta Crystallogr., Sect. B: Struct. Sci.*, 2006, **62**, 666–675.
- 115 H. Hosseinzadeh-Bandbafha, D. Kumar, B. Singh, H. Shahbeig, S. S. Lam, M. Aghbashlo and M. Tabatabaei, *Fuel Process. Technol.*, 2022, **232**, 107264.
- 116 S. Li, R. Bu, R. J. Gou and C. Zhang, *Cryst. Growth Des.*, 2021, **21**, 6619–6634.
- 117 G. Zhang and C. B. Musgrave, *J. Phys. Chem.*, 2007, **111**, 1554–1561.
- 118 F. W. Biegler-König, R. F. W. Bader and T. H. Tang, *J. Comput. Chem.*, 1982, **3**, 317–328.
- 119 R. F. W. Bader, *Atoms in Molecules: A Quantum Theory*, Clarendon Press, Oxford, U. K., 1990.
- 120 E. Espinosa, I. Alkorta, J. Elguero and E. Molins, *J. Chem. Phys.*, 2002, **117**, 5529–5542.
- 121 K. Clays and A. Persoons, *Phys. Rev. Lett.*, 1991, **66**, 2980–2983.
- 122 V. A. Sauro and M. S. Workentin, *J. Org. Chem.*, 2001, **66**, 831–838.
- 123 S. S. Chourasiya, D. Kathuria, S. S. Nikam, A. Ramakrishnan, S. Khullar, S. K. Mandal, A. K. Chakraborti and P. V. Bharatam, *J. Org. Chem.*, 2016, **81**, 7574–7583.
- 124 A. A. Wani, S. S. Chourasiya, D. Kathuria and P. V. Bharatam, *Chem. Commun.*, 2021, **57**, 11717–11720.
- 125 K. Mehta, A. A. Wani and P. V. Bharatam, *Tetrahedron Lett.*, 2023, **122**, 154505.
- 126 A. A. Bhosle, M. Banerjee and A. Chatterjee, *Sens. Diagn.*, 2024, **3**, 745–782.
- 127 M. Gon, T. Kato, K. Tanimura, C. Hotta and K. Tanaka, *RSC Mechanochem.*, 2024, **1**, 322–327.
- 128 (a) CCDC 2484683: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc2pdj2q](https://doi.org/10.5517/ccdc.csd.cc2pdj2q); (b) CCDC 2484685: Experimental Crystal Structure Determination, 2025, DOI: [10.5517/ccdc.csd.cc2pdj4s](https://doi.org/10.5517/ccdc.csd.cc2pdj4s).