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Synthesis of and theoretical research on some azine derivatives and investigation of their antimicrobial activities

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Abstract: This study includes experimental, theoretical and antimicrobial investigations on 1-(diphenylmethylene)-2-(4-methoxybenzylidene)hydrazine (**5**), 1-(3,5-dimethoxybenzylidene)-2-(diphenylmethylene)hydrazine (**6**) and 1-(diphenylmethylene)-2-(2,3,4-trimethoxybenzylidene)hydrazine (**7**). The structures of the compounds, synthesized by the microwave method, were determined by spectroscopic methods and elemental analysis. Conformational analysis, ground state structure, Fourier-transform infrared spectra (FT-IR) and nuclear magnetic resonance (NMR) spectra of the compounds were determined using density the functional theory (DFT) calculations in the theoretical research. Based on the B3LYP/6-31G(d,p) level, the conformers from the torsional barrier scanning were optimized. The B3LYP/6-311++G .(d,p) was used to determine the harmonic vibrational frequencies, potential energy distribution (PED), infrared intensities, and NMR chemical shifts of the most stable conformers. The experimental findings were compared with the theoretically expected spectral data. The antibacterial activity of the prepared compounds was tested *in vitro* against nine bacteria and one yeast species. The antimicrobial activity of the compounds was tested by minimum inhibitory concentration (*MIC*) and agar well diffusion method. Compound **7** showed good activity against the bacteria and yeast, while **5** and **6** showed no antimicrobial activity. Compound **7** showed zone of inhibition values in the range of 10–15 mm against *Klebsiella pneumonia, Pseudomonas aeruginosa* and *Salmonella typhimurium* The results indicated that compound **7** was effective against bacteria.

Keywords: heterocyclic compounds; microwave; microorganisms; DFT.

INTRODUCTION

Combating microorganisms that cause infections is of great importance for human health. For this purpose, there is increasing interest in the synthesis of new and effective antimicrobial agents.[1,2] The biological potential of hetero-

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cyclic nitrogen-containing compounds against diverse bacteria has been documented.[3] There are many types of synthetic organic compounds with antimicrobial properties. Azines, sometimes called N–N-linked diimines (C=N-N=C), are among them and are 2,3-diaza analogues of 1,3-butadiene.[4] The conventional method for the synthesis of azines is the treatment of carbonyl compounds with hydrazine.[5] Several techniques for the preparation of these compounds under different conditions have been described in the literature, but most of them require high temperatures and complex catalysts.[6] In addition to the conventional synthesis technique, it has been reported that the synthesis of azines also employs microwave energy[7], ultrasonic radiation[8] and grinding[9] techniques. The short reaction time, low by-product formation, low solvent consumption and high efficiency are the most important advantages of these techniques over the classical technique.[10–12]

Azines are of great interest in organic synthesis, and they have important biological properties such as antibacterial, antifungal, antiviral, anticancer and antiinflammatory.[1] They are also good synthons for obtaining many pharmacologically interesting heterocyclic compounds such as pyrazoles, purines and pyrimidines.[6,13] They are an important agent for reducing the antimicrobial activities of common pathogenic bacteria such as *Bacillus subtilis*, *Streptococcus faecalis* and *Enterococcus faecalis*.[14,15]

The objective of the present study was to synthesize, characterize and theoretically analyse azine molecules and investigate their antimicrobial properties. For the first time, compounds **6** and **7** were synthesized using microwave irradiation, which is a fast, inexpensive, highly effective and environmentally friendly method.[12,16,17] Compound **5** has been reported in the literature. It is known from the literature that this compound was synthesized by the grinding method using 1-(diphenyl methylene) hydrazine and 4-methoxybenzaldehyde compounds.[6,18] However, in the present study for the re-synthesis of compound **5**, the microwave method was also used for the first time. Structures of compounds **5**–**7** were determined by NMR, FT-IR spectroscopy and elemental analysis techniques. The present study also includes the theoretical outcomes of a thorough investigation of the torsional barrier analysis, vibrational spectra, and NMR spectra of **5**–**7** using density functional theory (DFT) calculations. The antibacterial properties of **5–7** against selected microorganisms were examined applying the agar well diffusion and microdilution broth technique.

EXPERIMENTAL

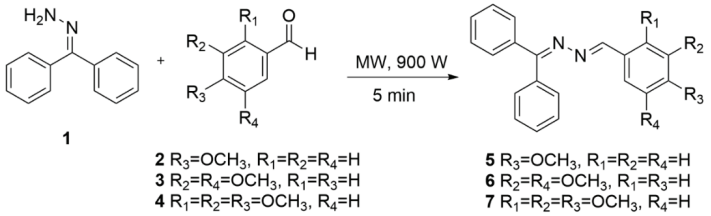
General chemistry

All chemicals are commercially available and purchased from Merck and Sigma–Aldrich. Analytical-grade solvents were used without further purification. Reactions were performed *via* domestic microwave oven (Vestel MD 20 DB, 230 V-50 Hz, 900 W). Thin-layer chromatography (TLC) was employed to monitor the reactions. ^{1}H-NMR (400 MHz) and ^{13}C--NMR (100 MHz) spectra were recorded with a Varian spectrometer using $CDCl_3$. The FT-IR

spectra were recorded with a Perkin Elmer spectrophotometer in the range of 4000–600 cm^{-1}. A capillary melting device was used to determine melting points (Buchi 530). On a Leco CHNS-932 instrument, elemental analysis was carried out.

General synthesis of azines ***5****–****7***

Compounds **5**–**7** were synthesized according to the procedure described in the literature.[12,16,17] The general synthetic pathway is given Scheme 1.



Scheme 1. The general synthetic pathway of azine derivatives.

Computational details

The software Gaussian 09 was used to carry out the DFT calculations.[19] In all calculations, the DFT/B3LYP functional was applied.[20-22] With the B3LYP functional, the basis sets 6-31G(d,p) and 6-311++G(d,p) were used. The 6-311++G(d,p) basis set was used in all other computations, whereas the conformer optimization was carried out on the 6-31G(d,p) basis set.[23]

Before beginning the computations of the other molecular characteristics of the system studied, the stable conformers of the molecular system must be identified. The conformational analysis must be completed first for these calculations. The software Spartan 08 is used to perform conformational analysis by examining the conformational distribution.[24] In this approach, calculations are performed using molecular mechanical methods, and then possible conformer structures are identified. In the present study, the Merck molecular force field (MMFF) method[25] was used for analysing conformational distribution. These conformers are then optimized using Gaussian 09.

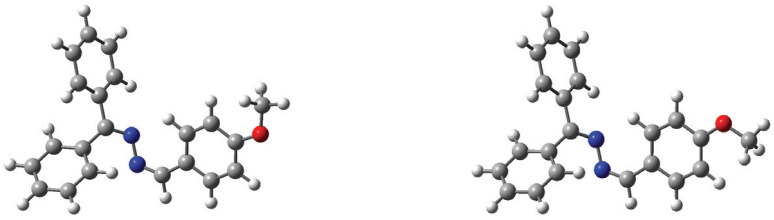
The gauge independent atomic orbital (GIAO) approach was used to predict the theoretical NMR data of **5**–**7**. The IEF-PCM model was used for these calculations in chloroform solution. The predicted ^{1}H- and ^{13}C-NMR measurements were compared to the experimental results. This matching could help with more detailed identification and characterization of the compounds. Chemical shifts were measured from absolute isotropic magnetic shielding constants. This conversion was carried out using tetramethylsilane (TMS), which was employed as a standard.[26,27]

Conformational analysis and molecular structure

Fig. 1 shows the optimized molecular structure of compounds **5**–**7**. The bonds described for **1**–**3** in Fig. 2 were taken into consideration while performing the conformational analysis of **5**–**7**. Changing the dihedral angle in 10° steps from 0 to 360° allowed the potential energy surface (*PES*) scan to be performed on the dihedral angles around the bonds of C–OCH_3 (**1**), C-phenyl groups (**2**) and C–N-phenyl groups (**3**). According to the PES scan results in Fig. 1, the Spartan determined two conformers of **5**, six conformers of **6** and twelve conformers of **7**, using the MMFF.

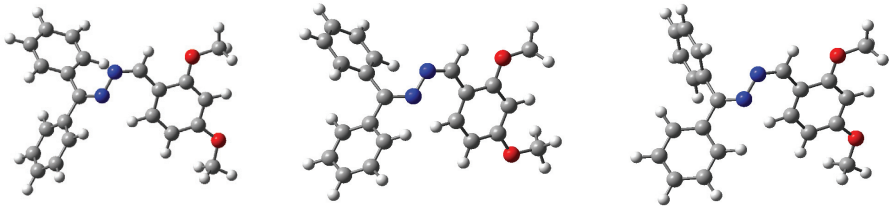
These conformers were optimized by B3LYP/6-31G(d,p) level in Gaussian 09. The optimized geometric structure, optimized energies and relative energies of the conformers are given in Table I. These findings indicate that the first conformer (conformer-1) of **5**–**7** has the most stable molecular structure. Fig. 2 shows molecular structure and atomic numbering of the most stable geometries of **5**–**7**. All future calculations will be performed with these most stable conformers.

Conformers of compound **5**

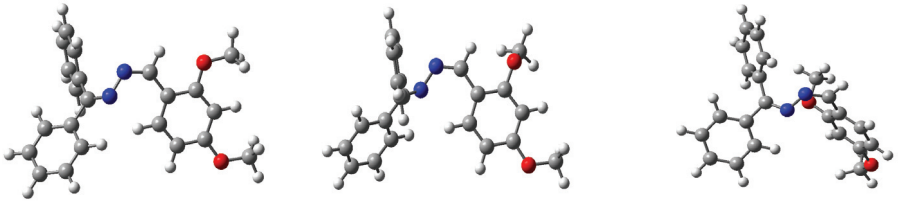


1 2

Conformers of compound **6**

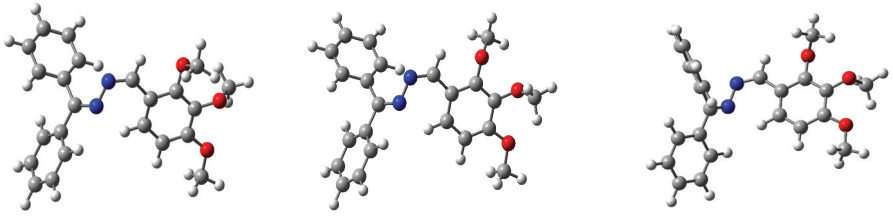


1 2 3



4 5 6

Conformers of compound **7**



1 2 3

Fig. 1. Conformers of **5**–**7**.

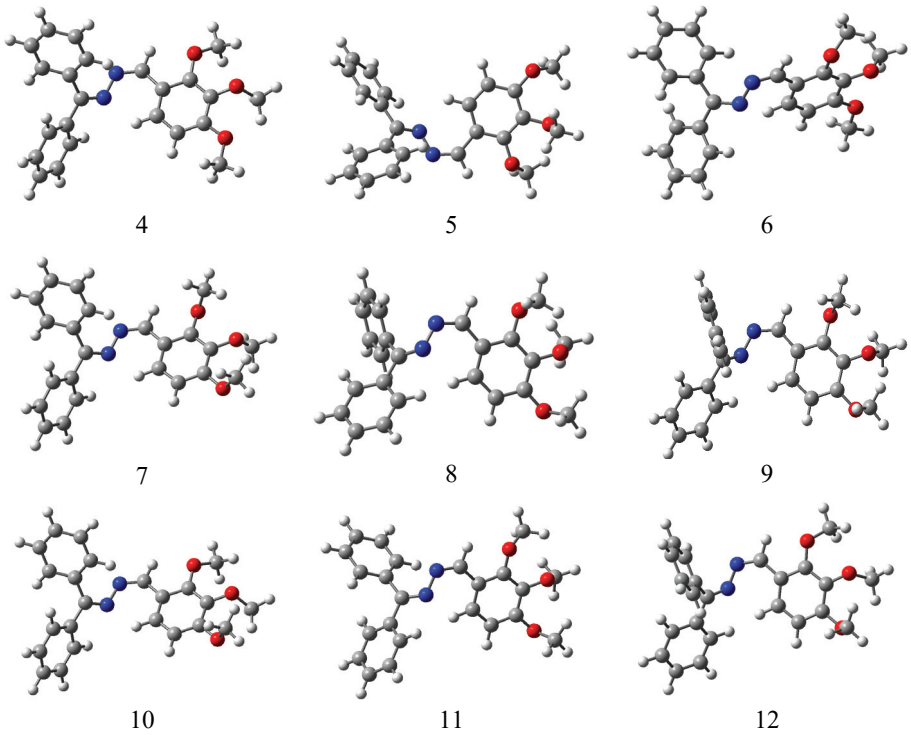


Fig. 1. (Continued).

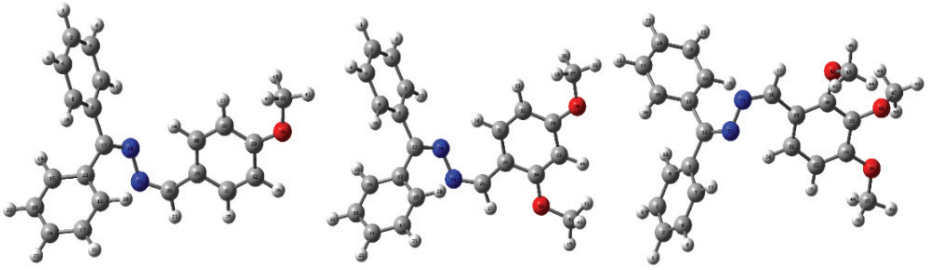


Fig. 2. Molecular structure and atomic numbering of the most stable geometries of **5**–**7**.

TABLE 1. Conformational analysis results of **5**–**7**

Compound		Opt. energy, a.u.	Rel. energy, kJ mol^{-1}	Pop. (298 K), %
5	Conformer–1	–995.779808398	0.00	55
	Conformer–2	–995.779618562	0.50	45
6	Conformer–1	–1110.30422576	0.00	68.56
	Conformer–2	–1110.30307700	3.02	20.30
	Conformer–3	–1110.30224177	5.21	8.38
	Conformer–4	–1110.30117394	8.01	2.71

TABLE 1. Conformational analysis results of **5**–**7**

Compound		Opt. energy, a.u.	Rel. energy, kJ mol^{-1}	Pop. (298 K), %
6	Conformer–6	–1110.29199733	32.10	0.00
	Conformer–5	–1110.29728690	18.22	0.04
7	Conformer–1	–1224.81524964	0.00	45.77
	Conformer–2	–1224.81502854	0.58	36.20
	Conformer–3	–1224.81319017	5.41	5.17
	Conformer–4	–1224.81292079	6.11	3.89
	Conformer–5	–1224.81263566	6.86	2.87
	Conformer–6	–1224.81257421	7.02	2.69
	Conformer–7	–1224.81241522	7.44	2.27
	Conformer–8	–1224.81077869	11.74	0.40
	Conformer–9	–1224.81072273	11.89	0.38
	Conformer–10	–1224.81009643	13.53	0.20
	Conformer–11	–1224.80974816	14.44	0.13
	Conformer–12	–1224.80812036	18.72	0.02

Antimicrobial activity

In the present study, the *in vitro* antimicrobial activities of several compounds were tested using agar well diffusion method and microdilution broth method. The *in vitro* antimicrobial activity of the compounds synthesized was assayed against nine bacterial strains and one yeast strain. These microorganisms were obtained from the Laboratory of Microbiology, Kırşehir Ahi Evran University, Kırşehir, Türkiye. The antimicrobial activities of **5**–**7** were determined according to the procedure described in the literature.[17] The antimicrobial results for the compounds and standard antibiotics and the *MIC* measurements of the new azine derivatives against the bacteria and yeast are presented.

RESULTS AND DISCUSSION

Chemistry

The compounds 1-(diphenylmethylene)-2-(4-methoxybenzylidene)hydrazine (**5**), 1-(3,5-dimethoxybenzylidene)-2-(diphenylmethylene)hydrazine (**6**) and 1-(diphenylmethylene)-2-(2,3,4-trimethoxybenzylidene)hydrazine (**7**) were prepared by the condensation of benzophenone hydrazone (**1**) with different aromatic aldehydes (**2**–**4**) at a ratio of (1:1) and exposure to microwave irradiation for 5 min.[12,16,17] The synthesized compounds' percentage yields were excellent (97, 96 and 97 %, respectively). In the experimental part, the physical properties of the compounds synthesized are described. The infrared spectra of the compounds confirm the presence of stretching of C=N bands at 1600–1660 cm^{-1} and the absence of carbonyl (C=O) at 1700 cm^{-1}, whereas NH has vanished or is hidden beneath the broad bands at 3450–3300 cm^{-1} in azines. In the ^{1}H-NMR spectrum of the compounds, the azomethine proton resonates as a singlet in the range of 8.30–8.76 ppm. All aromatic protons showed multiplet peaks in the range of 6.38–8.39 ppm. Additionally, the ^{13}C-NMR analysis of compounds **5**–**7** showed

that the carbon atoms in the H–C=N bond give signal at 159.30, 158.84 and 153.40 ppm, respectively.

Vibrational assignment

Compounds **5**–**7** have 42, 46 and 50 atoms, respectively. They have 120 (for **5**), 132 (for **6**), and 144 (for **7**) normal modes. Compounds **5**–**7** have C_1 symmetry. All basic vibrations are active in the FT-IR spectra. The frequencies calculated in the harmonic approximation were scaled to closely reproduce the experimental value. The frequencies calculated for the theory level B3LYP/6--311++G(d,p) were scaled to 0.960 in the high wavenumber region and 0.988 in the low wavenumber region (below 1800 cm^{-1}). The experimental and theoretical infrared spectra of compounds **5**–**7** are shown in Fig. 3. It is seen that both sets of spectral data almost completely overlap when the experimental FT-IR spectral data of compounds **5**–**7** are compared with those of the expected spectral data.[28,29]

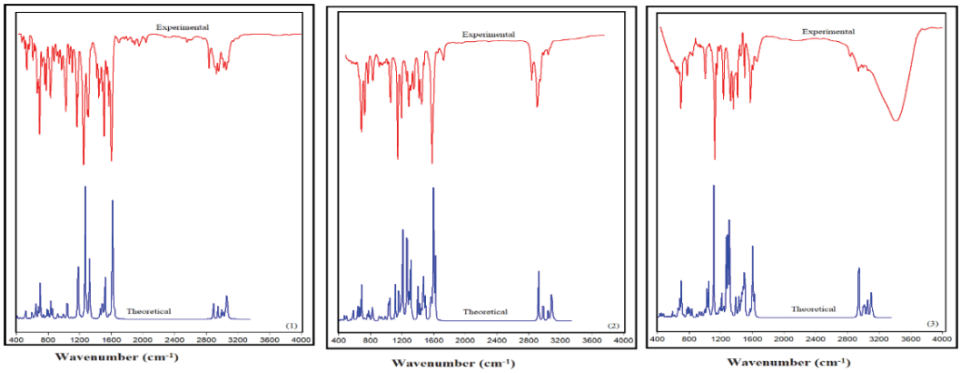


Fig. 3. The experimental and theoretical infrared spectra of **5**–**7**.

NMR spectra

Theoretical ^{1}H- and ^{13}C-NMR chemical shifts were estimated *via* the GIAO method using the B3LYP/6-311G++(d,p) level employing the optimized geometry of compounds **5**–**7**. Table II shows the experimental and computed chemical shifts for ^{1}H and ^{13}C nuclei. The experimental and theoretical ^{1}H- and ^{13}C--NMR spectra were observed in $CDCl_3$. The detected and expected NMR data for ^{1}H and ^{13}C nuclei are compared in Table II, which shows excellent agreement between the experimental ^{1}H- and ^{13}C-NMR data.

The GIAO approach was used to determine the theoretical ^{1}H- and ^{13}C--NMR chemical shifts of the **5**–**7**. In Table II, the detected and predicted NMR data for ^{1}H and ^{13}C nuclei are compared. The experimental ^{1}H- and ^{13}C-NMR spectra of **5**–**7** are given in Supplementary material to this paper.

TABLE II. Experimental and theoretical ^{1}H- and ^{13}C-NMR spectra of **5**–**7**

Compound **5**			Compound **6**			Compound **7**		
Atoms	Theo.	Exp.	Atoms	Theo.	Exp.	Atoms	Theo.	Exp.
C_{29}	168.5	166.02	C_{29}	170.1	166.27	C_{12}	164.6	166.18
C_{12}	165.1	161.86	C_{30}	167.4	160.86	C_{29}	163.7	158.56
C_{26}	155.1	159.30	C_{12}	163.7	158.84	C_{30}	162.3	
C_{3}	146.1		C_{26}	148.1		C_{26}	149.4	153.40
C_{13}	142.2		C_{3}	146.3		C_{33}	149.4	
C_{31}	139.3		C_{13}	142.2		C_{3}	146.2	
C_{30}	138.5	138.51	C_{31}	139.9	138.23	C_{13}	142.1	140.48
C_{16}	138.1		C_{16}	138.0	136.58	C_{15}	138.1	138.24
C_{6}	135.7	135.58	C_{6}	135.7	135.29	C_{6}	135.9	135.46
C_{2}	134.3		C_{2}	134.1		C_{2}	134.3	130.61
C_{14}	134.2	130.49	C_{14}	134.1		C_{14}	134.2	130.31
C_{15}	134.0	130.21	C_{15}	134.0	130.57	C_{16}	134.0	130.17
C_{7}	133.6	130.13	C_{7}	133.6	130.32	C_{31}	133.9	129.18
C_{4}	132.8	129.12	C_{4}	132.7	129.20	C_{7}	133.8	129.01
C_{5}	132.3	128.88	C_{18}	132.2	129.06	C_{4}	132.7	128.68
C_{18}	132.2	128.23	C_{5}	132.1	128.27	C_{17}	132.2	128.29
C_{17}	131.8	127.53	C_{17}	131.8	127.47	C_{5}	132.1	127.90
C_{28}	130.5	127.46	C_{28}	119.4		C_{18}	131.8	127.44
C_{32}	121.8		C_{32}	103.9	106.12	C_{28}	124.7	
C_{33}	112.8	114.16	C_{33}	101.6	103.42	C_{32}	109.1	105.44
C_{39}	55.06	55.37	C_{37}	55.22	55.41	C_{43}	61.72	60.94
H_{11}	8.66	8.59	C_{42}	55.15		C_{47}	60.10	56.07
H_{34}	8.59	7.84-7.72	H_{11}	8.60	8.51	C_{37}	55.21	
H_{27}	7.77		H_{34}	8.54	7.75	H_{11}	8.59	8.51
H_{8}	7.72	7.65	H_{27}	8.43		H_{27}	8.38	7.82-7.71
H_{1}	7.67		H_{8}	7.71	7.53-7.33	H_{34}	8.30	
H_{23}	7.64	7.56-7.35	H_{1}	7.68		H_{8}	7.70	7.49-7.35
H_{22}	7.62		H_{23}	7.66		H_{1}	7.69	
H_{21}	7.59		H_{22}	7.62		H_{23}	7.65	
H_{35}	7.59		H_{21}	7.54		H_{21}	7.62	
H_{9}	7.53		H_{9}	7.50		H_{22}	7.56	
H_{20}	7.46		H_{20}	7.43		H_{9}	7.51	
H_{19}	7.39		H_{19}	7.38		H_{19}	7.46	
H_{10}	7.30		H_{10}	7.27	6.85	H_{20}	7.39	
H_{36}	7.24	6.93	H_{46}	6.53		H_{10}	7.30	6.94
H_{37}	6.83		H_{35}	6.30	6.54	H_{35}	6.57	
H_{41}	4.04	3.86	H_{45}	4.18	3.79	H_{44}	4.61	3.91
H_{40}	3.68		H_{39}	4.00		H_{50}	4.21	
H_{42}	3.66		H_{43}	3.73		H_{39}	4.15	
			H_{44}	3.70		H_{46}	3.97	3.84
			H_{38}	3.66		H_{48}	3.94	
			H_{40}	3.64		H_{40}	3.70	
						H_{38}	3.64	
						H_{45}	3.47	
						H_{49}	3.47	

The C_{26} NMR chemical shift of each compound was calculated at 155.1 (**5**), 163.7 (**6**) and 149.4 ppm (**7**) by DFT method. Peaks experimentally measured as 3.86 (**5**), 3.79 (**6**) and 3.91 and 3.84 (**7**) ppm belonged to the proton of the methoxy groups. The proton peaks in the H–C=N group were reported in the ^{1}H-NMR spectra at 8.59 for **5** and 8.51 ppm for **6** and **7**. The chemical shift of H_{11} atoms was estimated by DFT calculations as 8.66 (**5**), 8.60 (**6**) and 8.59 ppm (**7**). The C_{26} peaks of each compound were measured experimentally in ^{13}C-NMR spectra at 159.3 (**5**), 158.84 (**6**) and 153.40 ppm (**7**). The C_{26} NMR chemical shift of each compound was calculated by DFT calculations at 155.1 (**5**), 163.7 (**6**) and 149.4 ppm (**7**). The peaks measured as 3.86 (**5**), 3.79 (**6**) 3.91 and 3.84 (**7**) ppm experimentally belong to the protons of the methoxy groups. The predicted ^{1}H-NMR chemical shift of each compound appeared in the 4.61–3.47 ppm region by DFT. The ^{13}C-NMR peaks were detected at 55.37 (**5**), 55.41 (**6**) and 60.94 and 56.07 ppm (**7**). The smallest ^{13}C-NMR chemical shift values were theoretically calculated for the metoxy group. For both ^{1}H- and ^{13}C-NMR, the theoretical and experimental values were apparently in good agreement. Except for the methoxy group, the predicted and experimental ^{13}C-NMR values all appeared to be over 100 ppm. The nitrogen atom, which displayed greater electronegative characteristics, was bound to carbon atoms that were more de-shielded.[30–33] Therefore, these atoms showed increased ^{13}C-NMR peaks than the others.

Frontier molecular orbital (FMO) analysis

Fig. 4 shows the plots for the **5**–**7**'s HOMO and LUMO. Red and green are used to represent the positive and negative phases, respectively. The HOMO and LUMO are distributed in all compounds. However, this distribution is not uniform. The HOMO is more concentrated on the pyridine group, whereas the LUMO is more concentrated on the phenyl and N–CH_3 groups.

B3LYP/6-311++G(d,p) theory was used to calculate the HOMO, LUMO, band gap energies and other molecular characteristics. Molecular characteristics such as ionization potential (I), electron affinity (A), electronegativity (A'), chemical potential (B), spherical hardness (S), spherical softness (S') and electrophilicity (B') were calculated using the formulae provided at the end of Table S-I of the Supplementary material.[34–36] Table S-I contains a list of these properties.

The literature indicates that a compound with lower reactivity and higher stability has a larger HOMO–LUMO gap. The values of the HOMO–LUMO gap calculated for compounds **5**–**7** were 4.083, 4.058 and 3.993 eV, respectively. The predicted η value of **5**–**7** was at 2.042, 2.029 and 1.997 eV, respectively. The σ value of the **5**–**7** compounds were determined at 0.245, 0.246 and 0.250 eV, respectively. As seen in Table S-I, the global hardness (η) of the compounds is greater than the global softness (σ). According to these results, the compounds are hard. A compound's characteristics vary according to its hardness or softness.

For instance, soft materials have a small energy gap compared to that of hard materials. Soft compounds are more easily polarized than hard ones. As a result, soft molecules are more biologically reactive than hard compounds.[34–36]

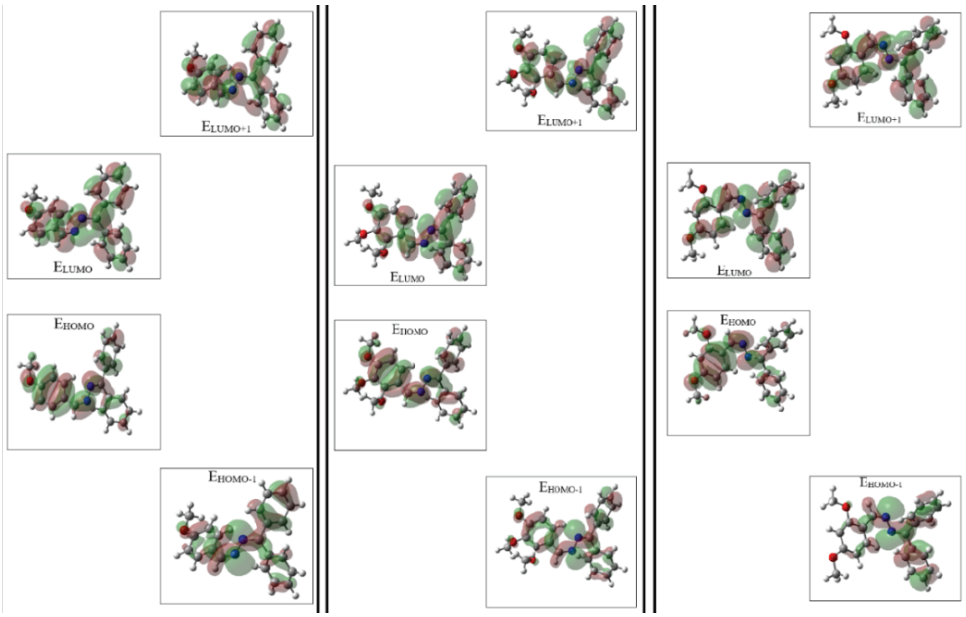


Fig. 4. HOMO and LUMO plots of the **5**–**7**.

Molecular electrostatic potential maps

A 3D plot of the molecular electrostatic potential (*MEP*) of compounds **5**–**7** is given in Fig. 5. Using the *MEP* diagram, it is simple to determine the compounds' reactive sites. Electron-deficient regions are depicted in blue, whereas electron-rich regions are depicted in red. The region around the nitrogen atom of the azine group and oxygen atom of the O–CH_3 groups was electron-rich (red) regions.[37–39]

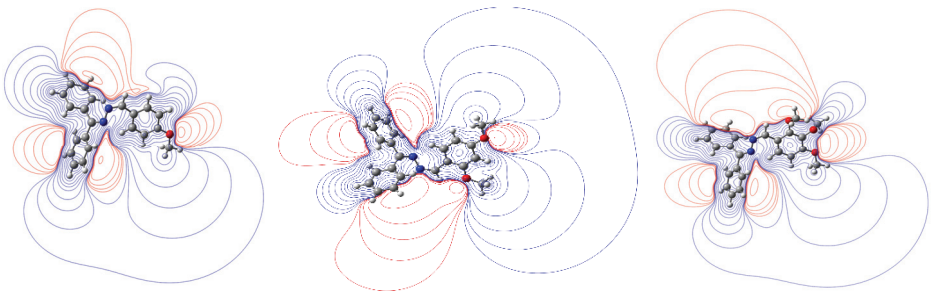


Fig. 5. Molecular electrostatic potential maps of compounds **5**–**7**.

Antimicrobial evaluation of the synthesized compounds

Using the micro-dilution and agar well diffusion methods, the compounds were examined for their antibacterial effects on nine bacteria and one yeast. Table III lists the antibacterial activity results for the compounds with minimal inhibitory concentrations (*MIC*) values and inhibition zone diameters (mm).

TABLE III. Antimicrobial evaluations of the synthesized compounds *MIC* (μg/mL) values and inhibition zone diameter (mm); concentration of compounds: 1000 μg/mL; –: *MIC* > 250 μg/mL; AMP: ampicilin; Cyclohex.: cycloheximide

Microorganism	*MIC*			Diameter of inhibition zone				
	5	**6**	**7**	**5**	**6**	**7**	AMP (10 μg)	Cyclohex.
L. monocytogenes ATCC 7644	–	–	–	–	–	–	10	–
S. aureus ATCC 25923	–	–	–	–	–	–	18	–
B. subtilis ATCC 6633	–	–	–	–	–	–	24	–
E. faecalis ATCC 29212	–	–	–	–	–	–	–	–
*K. pneumoni*ae ATCC 21541	–	–	7.81	–	–	15	18	–
P. aeruginosa ATCC 27853	–	–	7.81	–	–	15	18	–
S. dysenteriae ATCC 11835	–	–	–	–	–	–	20	–
S.typhimurium ATCC 14028	–	–	250	–	–	10	18	–
E. coli ATCC 25922	–	–	–	–	–	–	–	–
C. albicans ATCC 10231	–	–	–	–	–	–	–	18

According to this study, compound **7** showed good activity in the range of 7.81–250 μg/mL MIC values against *Klebsiella pneumoni*ae, *Pseudomonas aeruginosa* and *Salmonella typhimurium*. Compound **7** showed the zone of inhibition values in the range of 10–15 mm against *K. pneumoniae*, *P. aeruginosa* and *S. typhimurium.* Compound **7** showed activity of 250 μg/mL *MIC* against *S. typhimurium*. Compounds **5** and **6** did not show antimicrobial activity against the investigated bacteria and yeast (Table III). In 2011, Shams *et al.* reported that the *MIC* values of dyes and dye precursors against all microbial strains tested were generally in the range of 0.04–30.00 μg/mL, resulting in significant and potent antimicrobial activity.[40] The results obtained are similar to those published by Shams *et al.*

CONCLUSION

In the present study, a series of azine derivatives were synthesized in a short time with high yield by microwave method. NMR and FT-IR spectroscopy were used to verify the structures of the compounds prepared. Two conformers of **5**, six conformers of **6** and twelve conformers of **7** were determined using the PES scan result. The most stable conformers of the compounds were identified and then re-optimized for further calculations using the 6-311++G(d,p) basis set. There was perfect agreement between the experimental FT-IR, ^{1}H- and ^{13}C--NMR data and the theoretical data of the most stable isomer. Examination of the

antimicrobial screening data revealed that compounds **5** and **6** did not show antimicrobial activity against any of the bacterial strains and yeast. Compound 1-(diphenylmethylene)-2-(2,3,4-trimethoxybenzylidene)hydrazine (**7**) showed good activity in the range of 7.81–250 μg/mL *MIC* values against *K. pneumonia* ATCC 21541, *P. aeruginosa* ATCC 27853 and *S. typhimurium* ATCC 14028.

SUPPLEMENTARY MATERIAL

Additional data and information are available electronically at the pages of journal website: https://www.shd-pub.org.rs/index.php/JSCS/article/view/12551, or from the corresponding author on request.

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ИЗВОД

СИНТЕЗА И ТЕОРИЈСКО ПРОУЧАВАЊЕ НЕКИХ АЗИНСКИХ ДЕРИВАТА И ИСТРАЖИВАЊЕ ЊИХОВИХ АНТИМИКРОБНИХ ДЕЈСТАВА

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Ова студија укључује експериментална, теоријска, и антимикробна истраживања 1-(дифенилметилен)-2-(4-метоксибензилиден)хидразина (**5**), 1-(3,5-диметоксибензилиден)-2-(дифенилметилен)хидразина (**6**) и 1-(дифенилметилен)-2-(2,3,4-триметоксибензилиден)хидразина (**7**). Структуре једињења синтетисаних микроталасном методом, одређене су спектроскопским методама и елементалном анализом. Конформациона анализа, структура основног стања, FT-IR и NMR спектри једињења су израчунати користећи теорију функционала густине (DFT) у теоријском истраживању. На нивоу B3LYP/6-31G(d,p), оптимизовани су конформери, због торзионе баријере. B3LYP/6-311++G (d,p) је коришћен за одређивање хармонијских вибрационих фреквенци, расподеле потенцијалне енергије (PED), IR интензитета и NMR хемијских помака најстабилнијих конформера. Експериментални налази упоређени су са теоријски очекиваним спектралним подацима. Антибактеријска активност припремљених једињења тестирана је *in vitro* на девет бактерија и једној врсти квасца. Антимикробна активност једињења тестирана је преко минималне инхибирајуће концентрације (*MIC*) методом дифузије у бунарићима агара. Једињење **7** је показало добру активност против бактерија и квасца, док **5** и **6** нису показали антимикробну активност. Једињење **7** показало је вредности зоне инхибирања у распону од 10–15 mm према *Klebsiella pneumonia, Pseudomonas aeruginosa* и *Salmonella typhimurium*. Према резултатима, једињење **7** је од испитаних најефикасније против бактерија.

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