Design, Synthesis, And Characterization Of New Schiff Bases For 3-Amino-1,2,4-Triazole-5-Thiolate Salt, Bearing Morpholine Ring And Biological Evaluation As Antibacterial Agents



Abeer Hussein Alia, and Mukhlif Mohsin Slaihimb*.

Abstract

Schiff bases (T1-T10) were prepared from the reaction of various benzaldehyde derivatives with 3-amino-1,2,4triazole-5-thiol in the presence of Morpholine, and all the prepared compounds were characterized using UV, FIR spectroscopy, in addition to GC-Mass, 1H-NMR for some combinations and measuring their melting points. The obtained results confirmed the validity of the proposed structures of the prepared compounds. The biological activity of all prepared compounds (T1-T10) was tested against four types of Gram-positive and Gram-negative bacteria. The study showed that the compound T8 inhibited Staphylococcus aureus with an IC50 of 22 μg/mL, followed by T1, T10, T2, and T3 with IC50 values of 25, 26, 33, and 33 μg/mL, respectively. In addition, T3, T10, T2, T1, and T4 had an inhibitory effect on Pseudomonas aeruginosa with IC50 values of 22, 28, 39, 44, and 50 µg/mL, respectively. T4, T2, and T5 inhibited Streptococcus mutans with IC50 values of 28, 32, and 38 μg/mL, respectively. Interestingly, T6 had the strongest inhibitory effect on Klebsiella pneumoniae with an IC50

Significance | Antibacterial efficacy of new chemical compounds named benzaldehyde derivatives.

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of 15 µg/mL. The results of this study suggest that T8, T3, T4, and T6 may be potential new antibiotics for the treatment of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus mutans*, and *Klebsiella pneumoniae*. However, further studies are needed to confirm these findings and evaluate these compounds' safety and efficacy in humans.

Keywords: 3-amino-1,2,4-triazole-5-thiol, morpholinium salt, Schiff base, antibacterial activity.

1. Introduction

A five-membered ring molecule called triazole when has two carbon and three nitrogen atoms. Depending on the location of three nitrogen atoms can be divided the triazole ring into two isomers: 1,2,3-triazole, and 1,2,4-triazole (Singh and Chauhan, 2014; Shneine and Alaraji, 2016). Some sources of nitrogen substrates are also flexible to prepare new triazole derivatives (Slaihim, et al., 2019; Neto and Zeni, 2020). The triazole ring's six (π) electrons are present in both two isomers of the triazole ring, with type sp² hybridization, and have an aromatic property (Li and Zhang, 2020). After the discovery of the triazole ring and the development of triazole chemistry, many reactions for the synthesis of novel triazoles and their various biological systems were developed.

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Figure 1. Clinically used drugs having 1,2,4-triazole scaffold.

Figure 3. Morphline-4-ium-5-(4-hydroxy-3-methoxybenzylidene) amino)-4 H1,2,4-triazole-3-thiolate (T2)

$$N^{-N} \xrightarrow{\Theta} \oplus$$

$$N-N$$
 Θ Θ Θ SH_2N O

Figure 6. Morpholine-4-ium(E)-5-(4-methoxybenzylidene)amino)-4H1,2,4triazole-3-thiolate (T5)

$$H_{3}C$$
 $N-N$
 O
 $SH_{2}N$
 O
 O
 O

Figure 7. Morpholine-4-ium(E)-5-(4-methylbenzylidene)amino)-4H1,2,4-triazole-3-thiolate (T6)

$$(H_3C)_2N \xrightarrow{N-N} SH_2N \xrightarrow{\bigcirc} O$$

Figure 8. Morpholine-4-ium(E)-5-(4-dimethylaminobenzylidene) amino)-4 H1,2,4-triazole-3-thiolate (T7)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

Figure~9.~Morpholine-4-ium(E)-5-(4-dihydroxybenzylidene)amino)-4H1,2,4-triazole-3-thiolate(T8)

Figure 10. Morpholine-4-ium(E)-5-(2,4-dihydroxybenzylidene)amino)H1,2,4-triazole-3-thiolate (T9)

$$\begin{array}{c|c} N-N & \bigoplus & \bigoplus \\ N-N & SH_2N & O \\ \end{array}$$

Figure 11. Morpholine-4-ium(E)-5-(2-bromobenzylidene)amino)H1,2,4-triazole-3-thiolate (T10)

Scheme (1): General reaction to prepare new Schiff bases series (T1-T10)

Ar = P-NO₂; P-OH, 3-OCH₃; P-Br; P-Cl; P-OCH₃; P-CH₃; P- N(CH₃)₂; 2,4-DiOH; 2,4-DiCl; 2-Br.

medicinal chemists during the past ten years due to their fascinating pharmacophoric characteristics (Gupta, et al., 2023). 1,2,4-Triazoles act as significant pharmacophores by interacting with the biological receptors with high selectivity owing to their hydrogen bonding capacity, dipole character, solidity, and

1,2,4-triazole-based derivatives have driven the attention of

with the biological receptors with high selectivity owing to their hydrogen bonding capacity, dipole character, solidity, and solubility. 1,2,4-Triazoles motif is an integral part of a variety of drugs available in clinical therapy including antiviral (ribavirin), anticancer (anastrozole) ,antifungal (fluconazole), anticonvulsant (loreclezole), skeletal muscle relaxant (etizolam), anxiolytic (alprazolam), antimigraine (rizatriptan), Antidepressant (trazodone), antiplatelet (trapidil), and an aromatase inhibitor (letrozole) (Fig. 1) (Aggarwal, et al., 2020).

On the other hand, Schiff bases of 1,2,4-triazoles have a wide range of biological activities, including those that are antibacterial (Amin, et al., 2021), antifungal (Qi, et al., 2021), antitumor (Li, et al., 2012), anti-inflammatory (Sachdeva, et al., 2013), antitubercular (Venugopala, et al., 2020), antidepressant (Radhika, et al., 2012), anticonvulsant (Küçükgüzel, et al., 2004), analgesic (Karrouchi, et al., 2016), antiviral (Chen, et al., 2019), anticancer (Slaihim, et al., 2023), antimalarial (Thakkar, et al., 2017), and antioxidant (Saadaoui, et al., 2019). Triazole ring derivatives also have some industrial applications, such as ecological corrosion inhibitors for mild steel (Nahlé, et al., 2021), and Gas Generating Agent (Xue, et al., 2021).

In this study; 1, 2, 4-triazole ring substitutes with amino and thiol groups were focused. Our field research aims to design new types of Schiff bases utilizing 3-amino-1,4,2-triazole-5-thiol that have specificity in the thiol and amino groups.

The condensation reaction of the amino group with a series of aromatic aldehyde or ketone derivatives can prepare novel types of Schiff bases (Arafath et al., 2017; Slaihimet al., 2019). According to prior research, various kinds of novel Schiff bases are produced from organic piperidinium triazole salts. Up to our knowledge, and for the first time, new Schiff bases were prepared via morpholinium triazole salts.

2. Materials and Methods

2.1. Chemicals

4-Chlorobenzaldehyde, 4-Bromobenzaldehyde, 4-Methoxybenzaldehyde, 4-Hydroxy-3-methoxy benzaldehyde, and Piperidine were purchased from (BDH, England). 4-Dimethylaminobenzaldehyde and Dimethyl sulfoxide from (MERCK, Germany). 2,4-Dihydroxybenzaldehyde and 3-Amino-1,2,4-triazole-5-thiole from (Sigma). 4-Methylbenzaldehyde (Fluka); 2,4-Dichlorobenzaldehyde (CDH, India); 4-Nitrobenzaldehyde and 2-Bromobenzaldehyde (Alfa Aesar, USA). Absolute ethanol (QRëC).TLC silica gel 60 F254, aluminium sheet, 20cm x 20cm (Merck, Germany).

to determine the structure of produced chemicals are located at the College of Applied Sciences, Samarra University. Infrared spectra were recorded using a Shimadzu Japanese Company-supplied Fourier Transform Infrared Spectrophotometer/FTIR-8400S device: samples were created as (KBr) discs. The nuclear magnetic resonance (1 H-NMR) spectra were measured using a Bruker Advance (4 00 MHz) at Basra University's College of Education, Department of Chemistry. Using DMSO- d_6 as an internal reference [1 H (DMSO- d_6) = 2.51 ppm and 13 C (DMSO- d_6) = 39.9 ppm]. Shimadzu GC-MS-QP 2010 Ultra mass spectrometer recorded mass spectra: solvent, MeOH.

Except for a Bruker Avance, all of the devices or instruments used

2.3. Biological assay

2.3.1. Compounds and cells

Before being serially diluted for utilization in a culture medium, all test compounds were dissolved in DMSO at an initial concentration of 0.032 mg/mL. Pathogenic microorganisms of four types were utilized, including klebsiella Pneumoniae and Pseudomonas aeruginosa (Gr-ve), examples of Gram-negative bacteria. Gram-positive (Gr+ve) microorganisms include *Staphylococcus aureus* and *Streptococcus mutans*. The four bacterial species were examined at Samarra University's Microbiology Laboratory, Pathological Analysis Department, and College of Applied Sciences.

2.3.2. Antibacterial assay

The organic solvent DMSO was used to create test solutions for the substances (T1-T10) at varying concentrations (0.032, 0.016, 0.008, 0.004, 0.002, 0.001, and 0.0005 mg/ml, respectively). Then, the modified agar diffusion method (Dahham et al., 2014 Nalawade et al., 2016), also known as the Kerby-Bauer method, was used to produce and sterilise the nutritional medium, after which the dishes were infected with bacterial isolates using the diffusion method. The seven concentrations were distributed across two plates dug at a rate of 3-4 holes with a diameter of 5 mm in the vicinity of each dish. Finally, 50-70 µL of each of the seven concentrations prepared were added to each pit. The dishes were then incubated at 37 °C for 24 hours. All the results were read the next day to determine the sensitivity of the used derivatives, which depend on the diameter of inhibition. An increase in the diameter of inhibition means an increase in the biological activity of the prepared compounds.

2.4. Synthesis method

2.4.1 General procedure for properties of the new Schiff bases series (T1-T10)

Table 2. Spectral data of Synthesized Compounds (T1-T10)

IR µmax cm	IR μmax cm-¹						
Comp. No	UVλmax(nm)	A	ν(N-H) Ring	ν(C-H) Ar	ν(C-H) Al	ν(C=N)	ν(C=C) Ar
T1	324	3.62899	3263	3040	2966	1604	1560
T2	318	3.45661	3267	3035	2933	1662	1604
T3	308	3.29534	3448	3150	2966	1643	1595
T4	302	1.257114	3250	3080	2962	1640	1597
T5	304	1.96702	3394	3040	2970	1645	1604
T6	302	1.28525	3253	3120	2966	1651	1598
T7	348	3.74334	3421	3025	2958	1633	1604
T8	328	2.07894	3442	3038	2970	1647	1587
T9	312	3.93288	3259	3044	2962	1591	1564
T10	314	2.11143	3251	3078	2962	1597	1560

Table 3. ¹H-NMR Characteristic data of Synthesized Compounds

Structure	Chemical Shift (δ)	Signal Features	No. of Protons	Type of Protons	
	ppm				
T1	8.48	s	Н	(CH=N-)imine	
	8.28	d, J = 8.0 Hz	2H	aromatic	
	8.03	d, J = 8.2 Hz	2H	aromatic	
	3.81	t, J = 4.0 Hz	4H	morpholinium	
	3.11	t, J = 4.0 Hz	4H	morpholinium	
Т3	8.35	s	Н	(CH=N-)imine	
	7.79	d, J = 8.0 Hz	2H	aromatic	
	7.48	d, J = 8.2 Hz	2H	aromatic	
	3.82	t, J = 4.0 Hz	4H	morpholinium	
	3.13	t, J = 4.0 Hz	4H	morpholinium	
Т6	8.29	s	Н	(CH=N-)imine	
	7.70	d, J = 8.0 Hz	2H	aromatic	
	6.97	d, J = 8.0 Hz	2H	aromatic	
	3.79	t, J = 4.0 Hz	4H	morpholinium	
	3.08	t, J = 4.0 Hz	4H	morpholinium	
Т9	8.63	s	Н	(CH=N-)imine	
	8.02	d, J = 8.0 Hz	1H	aromatic	
	7.60	s	1H	aromatic	
	7.57	dd, J = 8.0 Hz	1H	aromatic	
	3.82	t, J = 4.0 Hz	4H	morpholinium	
	3.13	t, J = 4.0 Hz	4H	morpholinium	

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Table 4. Mass spectral data of Synthesized Compounds

Product	Chemical	Exact	Mass spectrum m\z (relative intensity) of fragments				
NO.	formula	Mass					
T4	C ₁₃ H ₁₆ ClN ₅ OS	325.8	326(M+,15%)	102(M+,85%)	74(M+,60%)	43(M+,100%)	
T5	$C_{14}H_{19}N_5O_2S$	321.4	322(M+,10%)	158(M+,48%)	113(M+,43%)	71(M+,100%)	
Т6	C ₁₄ H ₁₉ N ₅ OS	305.4	306(M ⁺ ,25%)	117(M ⁺ ,65%)	56(M ⁺ ,65%)	44(M ⁺ ,100%)	
T7	C ₁₅ H ₂₂ N ₆ OS	334.4	335(M+,7%)	122(M+,14%)	106(M ⁺ ,35%)	91(M ⁺ ,100)	
T8	$C_{13}H_{17}N_5O_3S$	323.3	324(M+,11%)	247(M+,10%)	168(M+,13%)	108(M+,100%)	

Table 5. IC₅₀ of Synthesized Compounds (T1-T10)

Inhibition concer	Comps. Codes			
Pseudomonas aeruginosa	Klebsiella Pneumoniae	Streptococcus mutans	Staphylococcus aureus	
44	55	-	25	T1
39	32	32	33	T2
22	-	-	33	T3
50	-	28	-	T4
-	40	38	-	T5
	15	-	-	Т6
-	50	-	-	T7
-	41	-	22	Т8
-	46	-	-	Т9
28	-	-	26	T10

The compounds (T1-T10) were synthesized by combining 70 μ L of morpholine with 2-amino-4,2,1-triazole-5-thiol (0.5 g, 0.004 mol) and stirring at 15 minutes before adding equivalent moles of the respective aldehydes (0.004 mol) in 100mL of absolute ethanol and refluxing while stirring for 6 hours.

Yield: (1.33g, 74.2%), Light Orange crystals; mp: (159-162) °C. **UV** $λ_{max}$ (MeOH):324 nm. **IR** (KBr, cm⁻¹):3263 (N-H); 3040 (C-H aromatic); 2966 (C-H aliphatic); 1604 (C=N); 1560 and 1456 (C=C aromatic); 1355 (-NO₂ asymmetrical stretching); 702 (C-S). ¹**H-NMR (400 MHz, DMSO-d6) δ, ppm**: 8.48 (1H, s, -CH=N-)imine; 8.03 (2H, d, J=8.2 Hz, H-3, H-5)ph; 8.28 (2H, d, J=8.0 Hz, H-2, H-6)ph; 3.11 (4H, t, J=4.0 Hz, H-2', H-6')mor; 3.81 (4H, t, J=4.0 Hz, H-3', H-5')mor (Fig.2).

Yield: (1.34g, 53.8%), Red; mp: sticky $^{\circ}$ C. **UV** $^{\circ}$ M_{max} (MeOH):318 nm. **IR** (KBr, cm $^{-1}$):3329(O-H); 3267 (N-H); 3035 (C-H aromatic); 2933 (C-H aliphatic); 1662 (C=N); 1604 and 1529 (C=C aromatic); 1168 (C-O)(Fig.3).

Yield: (1.47g, 75.7%), Light Yellow crystals; mp:(173-175) C°. UV $λ_{max}$ (MeOH):308 nm. IR (KBr, cm⁻¹): 3448 (N-H); 3150(C-H aromatic); 2966 (C-H aliphatic); 1643 (C=N); 1595 and 1544 (C=C aromatic); 657 (C-Br). ¹H-NMR (400 MHz, DMSO-d6) δ, ppm: 8.35 (1H, s, -CH=N-)imine; 7.79 (2H, d, J=8.0 Hz, H-3, H-5)ph; 7.48 (2H, d, J=8.2 Hz, H-2, H-6)ph; 3.13 (4H, t, J=4.0 Hz, H-2', H-6')mor; 3.82 (4H, t, J=4.0 Hz, H-3', H-5')mor (Fig.4).

Yield: (1.29g, 63.5%), Off White crystals; mp: (225-227) C° . **UV** λ_{max} (MeOH):302 nm. **IR** (KBr, cm⁻¹):3250 (N-H); 3080(C-H aromatic); 2962 (C-H aliphatic); 1640 (C=N); 1597 and 1473 (C=C aromatic); 700(C-Cl). **GC-MS:** [m/z, (%)]: 326 ([M]⁺,15%), 102 (85%), 74 (60%), 43 (100%)(Fig.5).

Yield: (1.27g, 61.4%), Light Yellow crystals; mp: (164-166) C°. **UV** λ_{max} (MeOH):304 nm. **IR** (KBr, cm⁻¹):3394 (N-H); 3040(C-H aromatic); 2970 (C-H aliphatic); 1645 (C=N); 1604 and 1516 (C=C aromatic); 2854 and 1456(O-CH₃).**GC-MS:** [m/z, (%)]: 322([M]⁺, 10%), 158 (48%), 113 (43%), 71(100%) (Fig.6).

Yield: (1.21g, 42.5%), Off White crystals; mp: (190-192) C°. UV λ_{max} (MeOH):302 nm. IR (KBr, cm⁻¹):3253 (N-H); 3120(C-H aromatic); 2966 (C-H aliphatic); 1651(C=N); 1598 and 1550 (C=C aromatic); 2912 and 1463(-CH₃). ¹H-NMR (400 MHz, DMSO-d6) δ, ppm: 8.29 (1H, s, -CH=N-)imine; 7.70 (2H, d, J=8.0 Hz, H-3, H-5)ph; 6.97 (2H, d, J=8.0 Hz, H-2, H-6)ph; 3.08 (4H, t, J=4.0 Hz, H-2', H-6')mor; 3.79 (4H, t, J=4.0 Hz, H-3', H-5')mor. GC-MS: [m/z, (%)]: 306 ([M]⁺,25%), 117 (65%), 56 (65%), 44 (100%)(Fig.7).

Yield: (1.34g, 81.5%), Light Orange crystals; mp: (175-177) C°. **UV** λ_{max} (MeOH):348 nm. **IR** (KBr, cm⁻¹):3421 (N-H); 3025(C-H aromatic); 2958(C-H aliphatic); 1633(C=N); 1604 and 1527 (C=C aromatic); 1357(C-N); 2856(CH3-N). **GC-MS:** [m/z, (%)]: 335 ([M]⁺,7%), 122 (14%), 106 (35%), 91 (100%)(Fig.8).

Yield: (1.28g, 75.0%), Dark Brown; mp: sticky C°. **UV** λ_{max} (MeOH):328 nm. **IR** (KBr, cm⁻¹):3442 (N-H); 3038(C-H

aromatic); 2970 (C-H aliphatic); 1647 (C=N); 1587 and 1506 (C=C aromatic); 1336(C-O). **GC-MS:** [**m/z**, (%)]: 324 ([M]⁺,11%), 247 (10%), 168 (13%), 108 (100%) (Fig.9).

Yield: (1.43g, 72.0%), Light Brown crystals; mp: (251-253) C°. **UV** $λ_{max}$ (MeOH):312 nm. **IR** (KBr, cm⁻¹):3259 (N-H); 3044(C-H aromatic); 2962 (C-H aliphatic); 1591(C=N); 1564 and 1463 (C=C aromatic); 773(C-Cl). ¹**H-NMR (400 MHz, DMSO-d6) δ, ppm**: 8.63 (1H, s, -CH=N-)imine; 8.02 (1H, d, J=8.0 Hz, H-6)ph; 7.57 (1H, dd, J=8.0 Hz, H-5)ph; 7.60 (1H, s, Hz, H-3)ph; 3.13 (4H, t, J=4.0 Hz, H-2', H-6')mor; 3.82 (4H, t, J=4.0 Hz, H-3', H-5')mor(Fig.10).

Yield: (1.47g, 63.9%), Yellow crystals; mp: (277-279) C°. **UV** λ_{max} (MeOH):314 nm. **IR** (KBr, cm⁻¹):3251 (N-H); 3078(C-H aromatic); 2962 (C-H aliphatic); 1597 (C=N); 1560 and 1473 (C=C aromatic); 600(C-Br)(Fig.11).

3. Results and discussion

3.1. Spectra of Schiff bases of Morpholinium Triazole salts (T1-T10)

The series derivatives were created by the following scheme (1) depicts the neutralisation reaction to generate Schiff organic salts, which results from the final step of the instantaneous neutralization reaction in the reaction medium to form the appropriate salts (T1-T10):

A brand-new Schiff base series (T1–T10) was successfully synthesised and structurally described. The physical properties, IR, 1 H-NMR, GC-MS, and IC $_{50}$ of the new series (T1-T10) data are presented in five tables, 1, 2, 3, 4, and 5 respectively. Some organic identification methods, including IR, 1H-NMR, and GC-MAS spectroscopy support the Schiff base scaffold.

The IR spectra did not contain the -NH2 or carbonyl groups, but the N=CH absorption band of the imine group was visible at a wave number of 1591-1662 cm⁻¹with the appearance of a stretching band at Range 1560-1604 cm⁻¹ in related to the stretching of the double aromatic (C=C) bond. As well as absorption bands in the range 3025-3150 cm⁻¹ due to the stretching of the aromatic (C-H) bond. The aliphatic (C-H) stretch bands appeared in the range 2933-2970 cm⁻¹, and the red spectra of all the produced compounds demonstrated the removal of the bands associated with the stretching frequencies of the carbonyl group that was present in the blue spectra 1660-1712 cm⁻¹ ¹. In the ¹H-NMR spectrum, the Schiff base, or imine (-N=CH-), appears as a singlet between 8.29 and 8.63 ppm. In the IR and ¹H-NMR spectra, all the additional significant peaks and signals were seen. As for the ultraviolet (U.V) spectrum, it was maxed λ for the new Schiff base series (T1–T10) at max λ between (302) and (348) nm. These absorptions are attributed to electronic transitions of the type (n π^* , π π^*) and the reason for the appearance of these bands is that the compounds contain (C = N) bonds as well as other groups and electron pairs that do not share on the oxygen

and nitrogen atoms (Saito et al.,2012). Finally, the characteristics of molecular weight ions with a base peak in the mass spectrum are shown in Table 4.

3.2. Evaluation of the biological activity of the new Schiff bases series (T1-T10)

All generated Schiff base derivatives were tested against four grampositive and gram-negative bacterial species to determine their biological effects. The four bacterial species included in the present investigation are *Streptococcus mutans*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.

Most tested substances had inhibitory effects on at least one of the four bacterial species chosen for this study. According to the findings, the MIC values for this activity, which varies from mild to strong, were as follows:

At the lowest inhibitory concentration (MIC) used in the investigation (0.005 g/ml), T1 inhibited the Staphylococcus aureus, Pseudomonas aeruginosa and klebsiella Pneumoniae with IC50 25, 44, 55 µg/mL, respectively, where as T2, inhibited klebsiella Pneumoniae, Streptococcus mutans, Staphylococcus aureus and Pseudomonas aeruginosa with IC50 32, 32, 33, and 39 µg/mL, respectively.T3 and T10 inhibited the Pseudomonas aeruginosa and Staphylococcus aureus, with IC50 22, 33 and 28,26 µg/mL, respectively. T4 compound inhibited Streptococcus mutans and Pseudomonas aeruginosa with IC₅₀ 28, and 50 μg/m, respectively. In other hand, T5 compound inhibited Streptococcus mutans and klebsiella Pneumoniae with IC50 38 and 40 µg/mL, respectively. The compound T6,T7 and T9 inhibited the klebsiella Pneumoniae with IC50 15,50 and 46 µg/mL, respectively, While T8 inhibited the Streptococcus mutans and klebsiella Pneumoniae with IC50 22 and 41, respectively (Table 5).

4. Conclusion

This work described all new Schiff bases (T1–T10) and investigated the biological activities of these compounds. It also included the creation of novel amine salts with aliphatic ring structures, such as 4-morpholinium-5-amino-1,2,4-triazole-3-thiolate.

On the other hand, all of the current work's findings could be viewed as a key to future studies that reveal the significance of morpholinium triazole salts for various Schiff bases when compared to the findings of peer studies in the piperidinium triazole salts field.

Author Contributions

A.H.A synthesized the chemical and conducted the study and M.M.S. supervised the study.

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Competing financial interests

The authors have no conflict of interest.

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