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Abdulameer & Al-Lami
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ANTICORROSION ACTIVITY OF SOME NEW SYNTHESIZED ISOXAZOLE DERIVATIVES

***Zeena Ali Abdulameer*[1], *Naeemah Jabbar Al-Lami*[2]**
[1]Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq, zena.ali1205m@sc.uobaghdad.edu.iq
[2]Prof. Dr. Department of Chemistry, College of Sciences, University of Baghdad, Baghdad, Iraq. naeemah.owaid@sc.uobaghdad.edu.iq

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ABSTRACT

Together with a new series of imidazoles [2,1-b]benzthiazoles connected with various heterocyclic scaffolds, a novel Mannich base link with the drug Cefixime was also developed. In order to create the isoxazole ring, a Mannich base with a terminal methyl group was condensed with various substituted aromatic aldehydes, resulting in new chalcones. These chalcones were then brought closer together with hydroxylamine hydrochloride to produce new isoxazole derivatives. All compounds were identified by the spectra of carbon-13 (C13) nuclear magnetic resonance, proton nuclear magnetic resonance, and Fourier transform infrared spectroscopy. The effectiveness of certain novel compounds as anticorrosion agents was demonstrated by others.

Keywords: Fused rings, Imidazobenzthiazole, Isoxazole, Anticorrosion

الفعالية المضادة للتأكل لبعض مشتقات الايزوكسوزال المحضرة جديدا

***زينه علي عبد الامير*[1] *، نعيمة جبار اللامي*[2]**
[1] قسم الكيمياء، كلية العلوم، جامعة بغداد، بغداد، العراق. zena.ali1205m@sc.uobaghdad.edu.iq
[2] أستاذ دكتور، قسم الكيمياء، كلية العلوم، جامعة بغداد، بغداد، العراق. naeemah.owaid@sc.uobaghdad.edu.iq

الخلاصة

تم تحضير سلسلة جديدة من الاميدازو [b-1,2] بنزوثايازول المرتبطة مع الحلقات الغير متجانسة. وسلسلة جديدة من قواعد مانخ المرتبطة مع الدواء (Cefixime). حضرت حلقة الايزوكسوزال من تفاعل قواعد مانخ المحتوية على مجموعة المثيل مع مختلف الالديهايدات الاروماتية المعوضة لانتاج الجالكونات الجديدة، والذي تم غلقها بالهيدروكسيل امين هيدروكلورايد لتعطي مشتقات الايزوكسوزال الجديدة. شخصت هذه المركبات بـ FT-IR و ^{1}HNMR و^{13}CNMR . واظهرت بعض المركبات التي تم تحضيرها نشاطاً حيويا مضادا للتأكل.

الكلمات المفتاحية : الحلقات الملتحمة، اميدازو بنزوثايوزول، الايزوكسوزال، الفعالية المضادة للتأكل.

INTRODUCTION

One of the most important core structures in organic molecules is the imidazo- fused heterocyclic scaffolding, which is found in many naturally occurring products and physiologically active substances with antibacterial **(Katritzky, Xu, & Tu 2003),** anticancer **(A. Rehan, Lami, & Khudhair 2021)**, antimicrobial **(Revankar *et al.*, 1975)**, antifungal **(Rival *et al.*, 1991)** and anti-inflammatory **(Almirante *et al.*, 1966)** properties. They are structural motifs seen in many commercially available medications **(Enguehard-Gueiffier & Gueiffier, 2007),** such as divaplon and fasiplon **(Jismy *et al.*, 2019)**. Due to their wide range of intriguing pharmacological effects, imidazo-fused benzothiazoles are extremely relevant in the pharmaceutical industry **(Kumar *et al.*, 2014)**. Due to the possibility of a wide range of structures, mild reaction conditions, and further modification of the goods manufactured by Mannich based **(Tret'yakova *et al.*, 2018).** One of the key methods used in contemporary organic chemistry is the Mannich reaction. The biological and pharmacological properties of

Mannich bases are quite diverse, such as anti-inflammatory **(Liu *et al.*, 2019)**, antibacterial **(Pishawikar & More, 2017)**, anti-oxidant **(Sharma *et al.*, 2018),** and antifungal **(Vereshchagin *et al.*, 2018)**. Mannich bases also serve as significant pharmacophores or bioactive leads that are employed to synthesize a variety of possible high-value drugs with aminoalkyl chains. Cocaine, fluoxetine, atropine, ethacrynic acid, trihexyphenidyl, procyclidine, ranitidine, biperiden, and other substances are examples of clinically effective Mannich bases that contain an aminoalkyl chain. Chalcone chemistry has been the subject of a number of specialized scientific investigations; their applications in biology, business, and medicine stand out in particular **(Huo *et al.*, 2021)**. Chalcones are pigmented substances due to the presence of auxochrome and chromophore groups in their structures **(Aljamali, Hamzah Daylee, & Jaber Kadhium 2020)**. These are acknowledged as benzal acetophenone derivatives. Chalcone has an excellent synthon, allowing for the construction of numerous novel heterocycles with favorable medicinal properties. Chalcones are unsaturated ketones with the reactive ketoethylenic group -CO-CH=CH-. Because the chromophore CO-CH=CH, which is dependent on the presence of other auxochromes, is present, these molecules are colored. Isoxazole are heterocyclic compounds with five members including three carbon atoms and two heteroatoms: oxygen and nitrogen **(Walunj *et al.*, 2021)**. In medical chemistry, industry, and biological materials heterocyclic compounds that containing oxygen and nitrogen are essential molecules that aid in the understanding of life processes **(Agrawal & Mishra, 2018; Sysak & Obmińska-Mrukowicz, 2017; Zhu *et al.*, 2018)**.

MATERIALS AND METHODS

The solvents and chemicals were all purchased from Sigma/Aldrich, B.D.H., and C.D.H. through Reagent World and C.D.H., respectively. Thin-layer chromatography (T.L.C.) was performed on aluminum sheets provided by the Merck Corporation that had been pre-coated with silica gel 60, and spots were located using iodine vapours.

Instrumentation

1) Melting points were measured in an uncorrected manner using the Gallenkamp capillary melting point device.
2) To record infrared spectra, the University of Baghdad College of Science used a Shimadzu Fourier Transform Infrared (FT-IR-8400S) Spectrophotometer.
3) Proton nuclear magnetic resonance and carbon-13 (C13) nuclear magnetic resonance spectra were obtained using the Varian model ultra-shield nuclear magnetic resonance spectrometer at 400 and 499.67 MHz and 125 MHz, respectively (DMSO-d6).

Tetra-methyl silane (T.M.S.) was used as the internal reference, and chemical changes associated to it were measured in parts per million at the University of Mashhad in Iran (ppm).

Synthesis 6-(4-bromophenyl) imidazo [2, 1-b] benzathiazole (1A) (Al-Jamal *et al*., 2020).

In EtOH absolute (100 mL), a solution of 2-aminobenzothiazole (3 mmol) (0.5 g) and 4-Bromo phenacyl bromide (3 mmol) (0.9 g) was dissolved before being heated at reflux for 15 hours. The reaction was monitored by TLC (ethyl acetate: petroleum ether, 2:1). The reaction mixture was then basified with NaOH (5%) till the pH reached 10-11. To produce yellowish-orange crystals with an 80% yield, the precipitate was removed, cleaned with hot distilled water, dried, and recrystallized using absolute ethanol. The physical features of this chemical are shown in Table 1. (1A).

Synthesis of Mannich bases derivatives compounds (2A,3A) (Rostoll-Berenguer *et al.*, 2021).

A mixture of compound 1 (2 mmol) in EtOH (25 mL) was added to (37%) formaldehyde (2 mmol) and some drops of conc. HCl was added until the pH of the reaction medium became around (4-5), and then the mixture was stirred for 30 minutes. After that, p-aminoacetophenone and Cefixime (2 mmol) was added and heated for (3,10) hours. The reaction was monitored by TLC (ethyl acetate: petroleum ether, 2:1). After the reflux stopped, allowing the reaction mixture cool to room temperature, the solid mass was filtered, washed, dried, and recrystallized from EtOH. The physicochemical properties of these compounds are listed in Table 1.

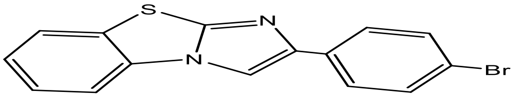
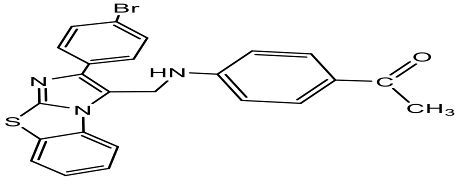
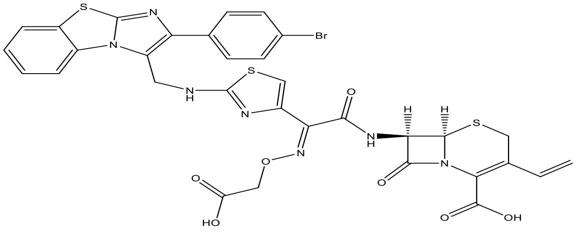
Synthesis of chalcones compounds (4A-10A)

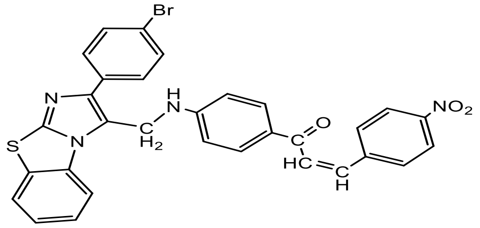
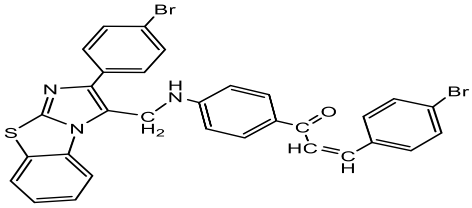
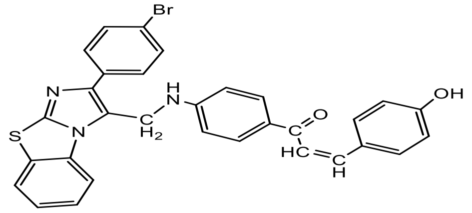
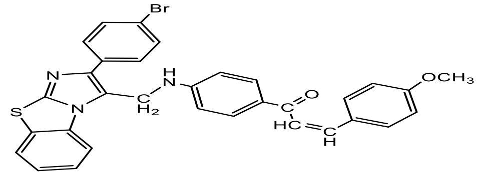
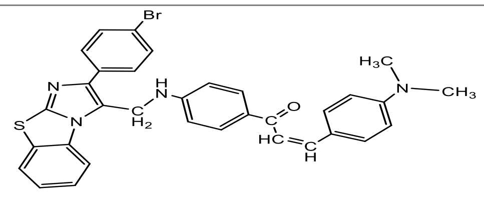
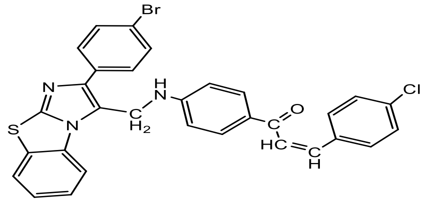
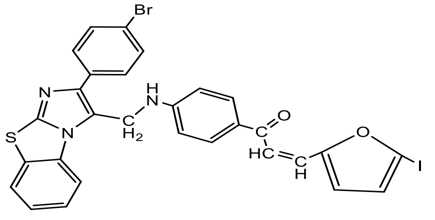
A solution of 40% NaOH was added to a solution of compound (2A) (1 mmol) (0.8 g) in ethanol (15 ml) and agitated for 25 to 30 minutes. Following that, 0.3 g of substituted benzaldehydes (1 mmol) were added. The resulting mixture was swirled continuously for 24 hours. The items underwent cooling, filtering, drying, and recrystallization from ethanol. Table 1 displays the physicochemical properties of these compounds.

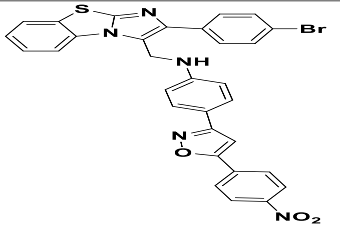
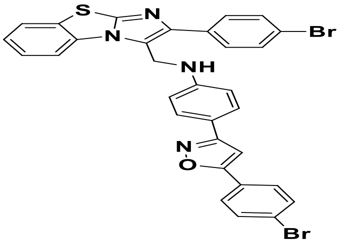
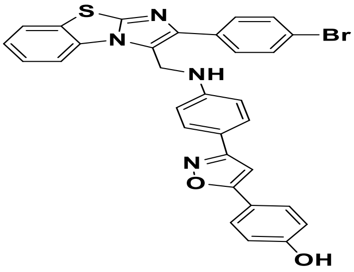
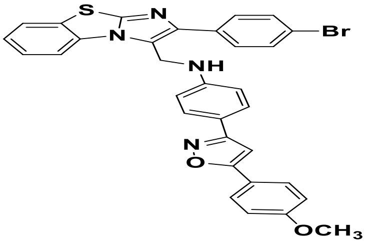
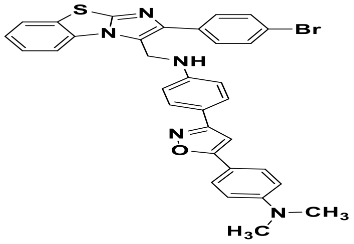
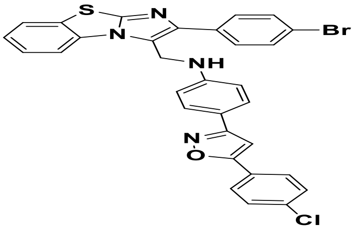
Synthesis of Isoxazole compounds (11A-17A)

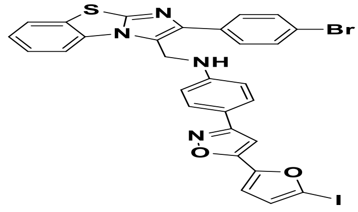
Anhydrous sodium acetate (3mmol), hydroxylamine hydrochloride (3mmol) in water, and a solution of compounds (4-10A) (3mmol) in ethanol (10 ml) were added. Refluxing the reaction mixture took 6 to 9 hours. From ethanol, the substance was separated and crystallized. (Table, 1) lists the chemical compound's physical characteristics.

Table (1): physical characteristics of Compounds (1A-17A)

Comp. No.	Structure	Molecular formula	Molecular Weight (g /mole)	Colour	m.p. (°C)	Time (h)	Yield (%)
1A		$C_{15}H_9BrN_2S$	329.22	yellowish-orange	123-125	15	80%
2A		$C_{24}H_{18}BrN_3OS$	476.39	Pale yellow	205-208	3	58%
3A		$C_{32}H_{24}BrN_7O_7S_3$	794.67	Off white	155-160	10	51%

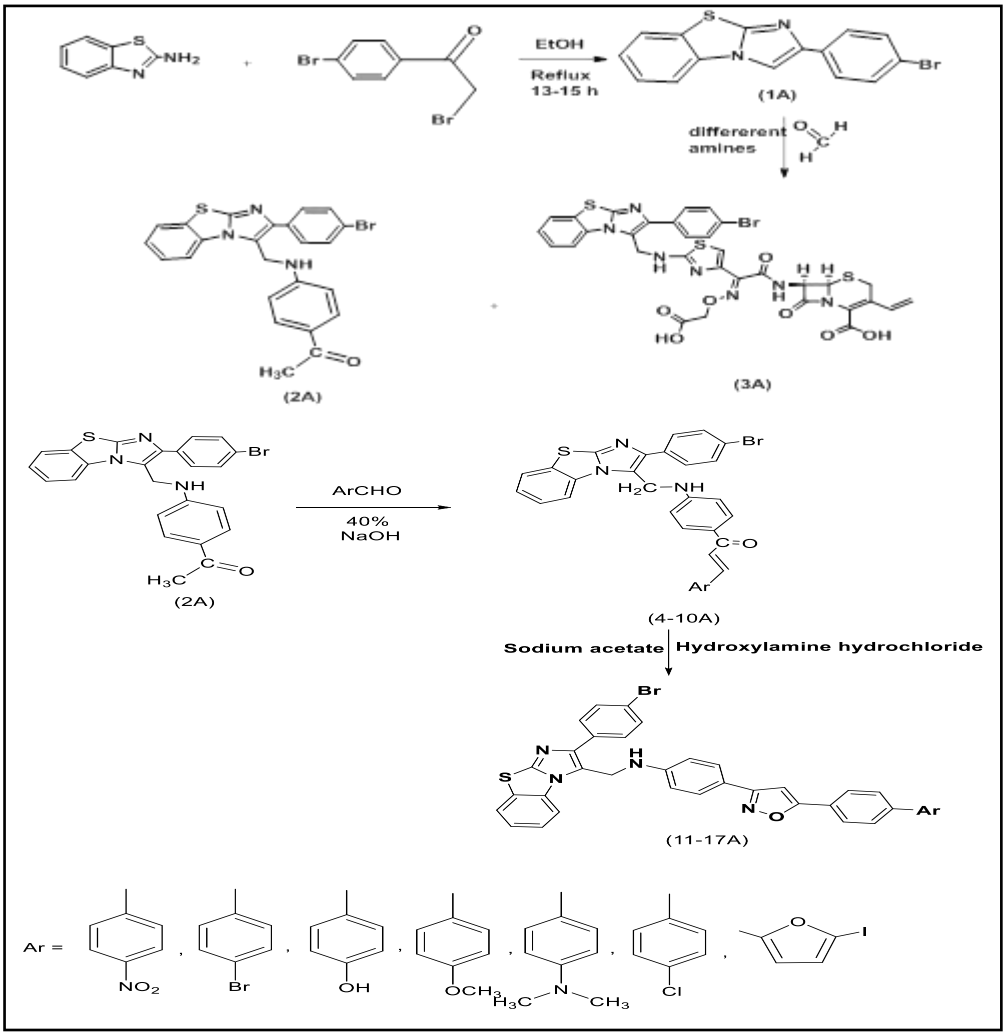
4A		$C_{31}H_{21}BrN_4O_3S$	609.5	Orange	110-115	24	60%
5A		$C_{31}H_{21}Br_2N_3OS$	643.4	Pale yellow	111-118	24	55%
6A		$C_{31}H_{22}BrN_3O_2S$	580.5	Pale yellow	153-156	24	50%
7A		$C_{32}H_{24}BrN_3O_2S$	594.53	Light orange	147-150	24	52%
8A		$C_{33}H_{27}BrN_4OS$	607.57	Orange	147-150	24	55%
9A		$C_{31}H_{21}BrClN_3OS$	598.94	yellow	172-176	24	75%
10A		$C_{29}H_{23}BrIN_3O_2S$	684.39	black	274-277	24	88%

11A		$C_{31}H_{20}BrN_5O_3S$	622.50	Pale Yelow	123-125	6	80%
12A		$C_{31}H_{20}Br_2N_4OS$	656.4	Pale Yelow	138-140	6	87%
13A		$C_{31}H_{21}BrN_4O_2S$	593.5	Off White	236-240	6	73%
14A		$C_{32}H_{23}BrN_4O_2S$	607.53	Pale Yelow	186-190	8	50%
15A		$C_{33}H_{26}BrN_5OS$	620.57	Pale Orange	105-110	9	97%
16A		$C_{31}H_{20}BrClN_4OS$	611.94	Pale Yellow	118-120	9	96%

17A		$C_{29}H_{18}BrIN_4O_2S$	693.36	Orange	125-130	9	92%

RESULTS AND DISCUSSION

The calculation of FT-IR spectra in the range 400-4000 cm^{-1}. Moreover, the chemical displacement of the 1H and 13C NMR of the compound in the ground state was studied.**(Kadhum, 2021)** The process of creating compound (1A) is described in the written word (**Al-Sultani, 2016**) and supported by FT-IR spectrum data, which includes additional bands of (C=N) imidazo at (1679-1662 cm^{-1}) linked with the creation of the imidazole ring, as well as the elimination of the (NH_2) band at (3400 cm^{-1}) and the (C=O) band at (1700 cm^{-1}). The second phase involves reacting novel Mannich bases, such as compound (1A), with formaldehyde (37%) and various primary aromatic amines to create compounds (2-3A). As indicated in Table 2, the FT-IR of Mannich bases derivatives revealed novel stretching bands (N-H) at 3290 to 3396 cm-1, as well as (C-H) aromatic bands at 3066 to 3095 cm^{-1} , (C-H) aliphatic bands at (2968 to 2977 cm-1) and new bands to the carbonyl group in the region 1720 cm^{-1} (C=O) **(Aldujaili & Zimam, 2021)**. As indicated in Table 3, the singlet signal of ($-CH_2$) protons appears at about 4.7 ppm, multiple aromatic ring protons emerge at about 6.7-8 ppm, and (N-H) protons appear at about 4.8 ppm in the ^{1}H NMR spectrum data of Mannich derivatives. As demonstrated in Table 3, 19.2 of (CH_2) aliphatic are visible in the ^{13}C-NMR data. The third step, α,β-Unsaturated compounds (4-10A) were created in accordance with the crossed Aldol condensation reaction (Claisen-Schmidt reaction) (Gudmundsson & Johns, 2007), FT-IR spectrum of compounds [4-10A] showed the appearance of stretching bands of (C-H) olefin at (2979-2972) cm^{-1},(C=O) α,β-unsaturated ketone (1687-1656) cm^{-1} and (C=C) olefin bands at (1569-1556) cm^{-1}. according to Table 2. These bands collectively demonstrate the formation of the desired chalcone derivatives. The nuclear magnetic resonance spectrum data for the compound [4Aproton] showed appearance signals of (CH=CH) protons at = (6.7-6.9) ppm and multiple signals of protons from aromatic rings at = as shown in Table 3. (7.2-8.8). ^{13}C-NMR data are found in the ranges 121–147 (m, C aromatic), 185 (C=O), and 119–120 (C=C), as shown in Table 3. When chalcones derivatives (4–10A) are cyclized in the presence of hydroxylamine hydrochloride and sodium acetate in water, the resulting isoxazole is produced. The FTIR spectrum of the isoxazole derivative (11–17A) revealed characteristic peaks at 1620 cm^{-1}belonging to (C=N Isoxazole) in fused imidazopyridine derivative. This peak appeared at 1643 cm-1in the FT-IR (Bingham et al., 2004)(Barbachyn et al., 2003)(Matsuoka et al., 1999)(Reddy et al., 2015). Table 2 contains a complete listing of all the information regarding the FT-IR spectrum data of the compounds (11-17A). Whereas ^{1}H NMR revealed a signal band at 6.78 (s, 1H, CH-isoxazole ring) and Carbon-13 (C13) NMR spectra revealed additional bands at 152 that correspond to C=N cyclic, both of these findings are reported in (Table, 3).



Scheme (1): Synthesis of new Mannich bases (2A,3 A) and Isoxazole derivatives (11A-17A).

Table (2): The FT-IR spectral data (Cm^{-1}) Of all prepared compounds (1-17A).

Comp. NO.	***υ* (C-H) Aromatic**	***υ* (C-H) aliphatic**	***υ* (C=C) Aromatic**	***υ* (C=N)**	***υ* (C=O)**	**Others**
1A	3055	-	1596, 1492	1639	_	*υ* (C-N) 1147 *υ* (C-Br) 642 *υ* (C-S-C) 746
2A	3066	2968	1595, 1492	1639	1720	*υ* (N-H) 3290 υ (C-N) 1338 υ (C-Br) 642 υ (C-S-C) 748

3A	3095	2977	1575, 1494	1650	1751	υ (N-H) 3396 υ (C-N) 1373 υ (C-Br) 649 υ (C-S-C) 748
4A	3070	2974	1595, 1492	1658	1683	υ (C=C) aliph. 1556 υ(NO2) asym 1523, Sym. 1357 υ(C-Br) 648 υ (C-S-C) 748
5A	3060	2972	1595, 1492	1641	1683	υ(C=C) aliph. 1558 υ(C-Br) 642 υ (C-S-C) 748
6A	3056	2979	1595, 1494	1639	1683	υ(C=C) aliph. 1560 υ (C-OH) 3431 υ (C-Br) 642 υ (C-S-C) 746
7A	3076	2979	1595, 1492	1639	1687	υ(C=C) aliph. 1562 υ (C-O) 1255 υ (C-Br) 642 υ (C-S-C) 748
8A	3070	2974	1595, 1494	1641	1658	υ(C=C) aliph. 1556 υ (C-N) 1359 υ (C-Br) 640 υ (C-S-C) 748
9A	3180	2972	1595, 1494	1639	1683	υ(C=C) aliph. 1562 υ (C-Cl) 1083 υ (C-Br) 644 υ (C-S-C) 748
10A	3058	2972	1596, 1492	1639	1656	υ(C=C) aliph.

						1569 υ (C-O) 1280 υ (C-I) 680 υ (C-Br) 748 υ (C-S-C) 748
11A	3261	3060	1575,1494	1596	-	υ (C=N) Isoxazole 1662 υ(C-S-C) 744 υ (C-Br) 649
12A	3149	3062	1577,1494	1598	-	υ (C=N) Isoxazole 1662 υ(C-S-C) 744 υ (C-Br) 696
13A	3149	3062	1577, 1492	1598	-	υ (C=N) Isoxazole 1664 υ(C-S-C) 742 υ (C-Br) 682
14A	3147	3062	1577, 1492	1600	-	υ (C=N) Isoxazole 1664 υ(C-S-C) 742 υ (C-Br) 638
15A	3226	3066	1577,1492	1598	-	υ (C=N) Isoxazole 1660 υ(C-S-C) 748 υ (C-Br) 649
16A	3095	3055	1577, 1488	1595	-	υ (C=N) Isoxazole 1685 υ(C-S-C) 757 υ (C-Br) 630
17A	3137	2974	1579, 1492	1649	-	υ (C=N) Isoxazole 1699 υ(C-S-C) 757 υ (C-Br) 630

Table (3): The ^{1}HNMR and ^{13}CNMR spectral data (δ ppm) of compounds (2,3,10,17A).

Comp. No.	Chemical shift
2A	^{1}HNMR: 4.8 (s,2H,CH_2NH), 4.8 (s, 1H, NH) 6.7-8 (m,12H,Ar-H), 2.6 (s,3H,CH_3).
3A	^{1}HNMR 4.7 (s,2H, CH_2NH), 4.8 (s, 1H, NH) 7.4-8 (m,12H, Ar-H) ^{13}CNMR: 19.2 (CH2NH), 120-133.5 (m, 23 C aromatic),145-147 (C=N), 170.8 (C=O).
10A	^{1}HNMR: 4.7 (s, 2H, CH_2NH), 6.7-6.9 (CH=CH), 7.2-8.8 (m, 12H, Ar-H) ^{13}CNMR: 26.5 (CH2NH),119-120(CH=CH), 121-147 (m, 23 C aromatic), 152-156 (2C=N), 185 (C=O).
17A	^{1}HNMR: 4.75 (S, 2H, CH_2NH), 6.78 (S, 1H, CH), 7.2--8.8 (m, 12H, Ar-H), 10.7 (s, 1H, NH) ^{13}CNMR: 26.4 (CH_2NH), 65.3 (CH isoxazole ring), 111-133.4 (23 C aromatic), 144-152 (3 C=N)

Anti corrosion

Derivatives of chalcone (4-10A) cyclization when there is The information gathered was used to evaluate the corrosion criterion and was presented in tables and figures. Determine the corrosion potential (Ecorrosion) and current density by extrapolating the cathodic and anodic Tafel in the absence and presence of the inhibitor molecules in NaCl (3.5%) solution (icorrosion). The values of the potential corrosion Ecorr (mV), corrosion current density icorr (A/cm2), cathodic and anodic Tafel slopes (mV/Dec), and protection efficiency PE% were also determined from Figures 1 and 4, and are shown in Table 4. Tafel plots show that, in comparison to a blank solution, the presence of C.S. inhibitors cause a shift to a higher (noble) position, establishing the protective laws as anodic protection. The following equation **(Heitz & Schwenk, 1976; Hoar, 1961)** was used to compute the inhibitory efficiency (% I.E.):

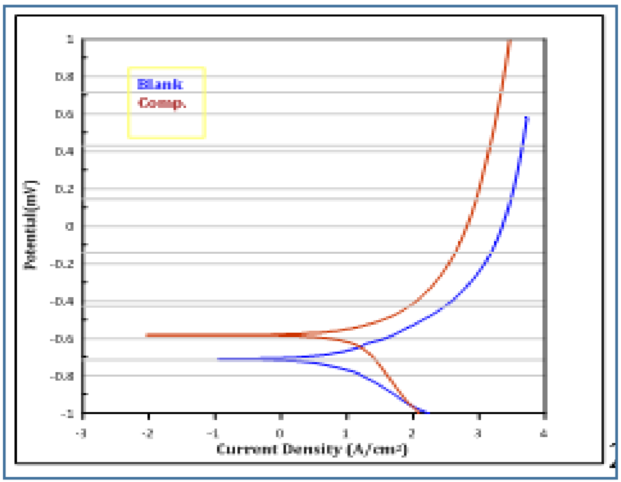
$$\%\mathbf{IE} = \frac{(\mathbf{icorr})\mathbf{o} - (\mathbf{icorr})}{(\mathbf{icorr})\mathbf{o}} * \mathbf{100} \qquad (1)$$

Where (icorrosion) refers to the corrosion current density with inhibitors and (icorrosion) refers to the corrosion current density without inhibitors **(Hoar, 1961; Khudhair & Al-Sammarraie, 2020)**.

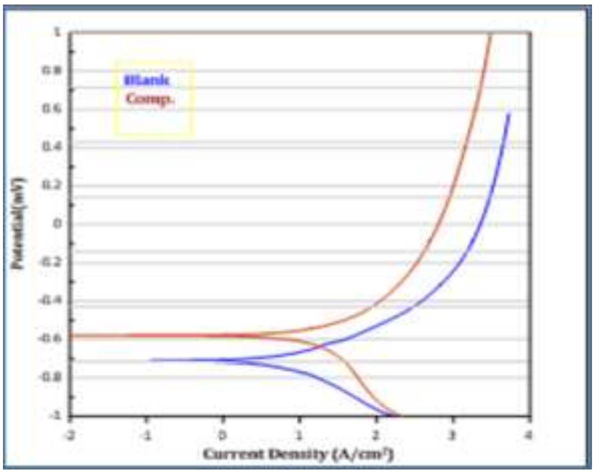
The compounds (2A, 3A, and 10A) demonstrated a good rate of inhibition when they were adsorbed with C-steel in 3.5% NaCl, demonstrating that the carbon surface atoms are bound by these atoms to inhibit corrosion. In this instance, the compound atoms are arranged to join up with the carbon surface atoms and stop surface corrosion.

Table (4): Information on the chemicals electrochemically corroding C-steel in seawater (3.5% NaCl) (2A,3A and 10A).

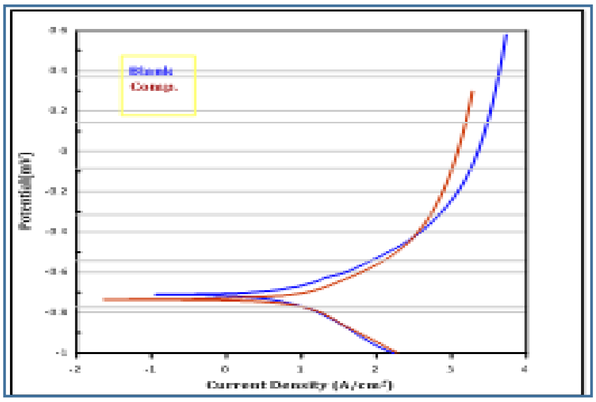
Comp. No.	E corr.	I corr.	I corr./r	Resis.	Anodic β	Cathodic β	Corr. Rate,	I.E. %
Blank	-0.998	146.4	1.464E-4	523.8	0.950	0.217	0.718	-
2A(0.278)	-0.585	13.30	1.330E-5	4280	0.189	0.428	0.065	91
3A(0.4061	-0.572	16.46	1.646E-5	3484	0.195	0.411	0.081	89
10A	-0.737	8.608	8.608E-6	4472	0.160	0.199	0.042	94



Figure(1): C-polarization steel's curve in saltwater with 3.5% NaCl (2A)



Figure(2): C-polarization steel's curve in saltwater with 3.5% NaCl (3A)



Figure(3): C-polarization steel's curve in saltwater with 3.5% NaCl (10A)

CONCLUSION

This work uses a compound derived from 2-aminobenzothiazole and 4-Bromo phenacyl bromide to make several forms of imidazo [2,1-b] benzothiazole (1A). Similar results were obtained when different primary aromatic amines interacted with 6-(4-bromophenyl) imidazo [2, 1-b] benzothiazole (1A), as shown in Scheme 1. (2A,3A).

By using Chalcones (4-10A) in a specific order, new five-membered isoxazole rings with fused imidazo benzothiazole rings have been created. FT-IR, ^{1}H NMR, and ^{13}CNMR spectra were used to identify these new derivatives. Finally, the anticorrosion ability of compounds (2A, 3A, and 10A) Saltwater containing 3.5% NaCl was tested on the surface of carbon steel. By creating an adsorbed layer on the surface of the carbon steel, these chemicals demonstrated effective anticorrosion action. As a result, corrosion was prevented on the metal surface.

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