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Original Article

Synthesis, Examination of Various Seven Rings, and Effects on Corrosion and Fungus

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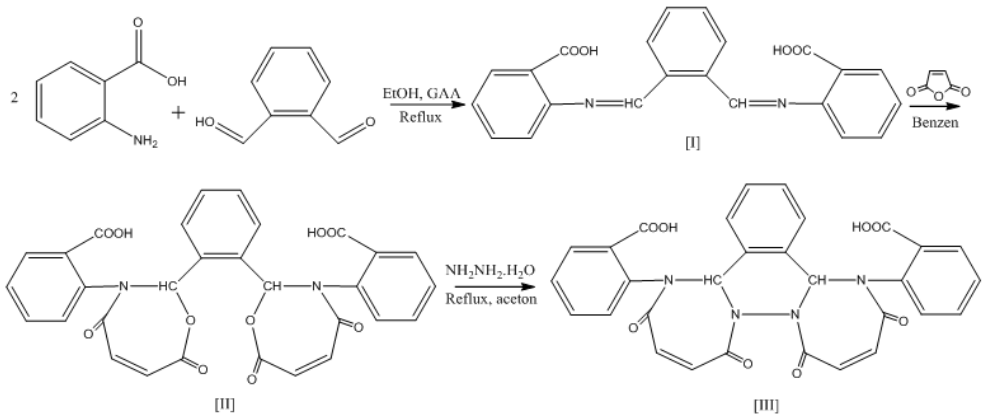
ABSTRACT

The majority of benzodiazepines is administered orally and has various beneficial effects, including psychotropic, anxiolytic, hypnotic, sedative, muscle relaxing, anticonvulsant, and amnesic ones. These include benefits for alcohol dependence, epileptic seizures, irritable disorders, scare, and insomnia. The goal of this study was to create bicycles from benzodiazepines through cyclization steps. All generated compounds were examined by using several analytical techniques, including: FT-IR, ^{1}H-NMR, Mass spectroscopy analysis, and other chemical characterization, with formatted compounds being assessed as antifungals and inhibitors. These compounds were utilized to explain biological activity against "*Aspergilla's and Candida*" albicans at various concentrations (5, 10, 15, and 20 mg/ml^{-1}). The findings demonstrated that all compounds were active against all varieties of fungi and that oxazepine, diazepine bicycles, and heteroatoms in the structure inhibited the corrosion of mild steel in 0.5M HCl.

GRAPHICAL ABSTRACT



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Introduction

Any important family of organic chemical compounds that have a part or all of their atoms connected in rings with at least one atom of an element other than carbon are known as heterocyclic compounds, sometimes known as heterocyclic (C) [1]. Heterocyclic compounds are needful for our life, like alkaloids, antibiotics, hemoglobin, hormones, and enormous numbers of designed drugs and pigments [2]. The majority of hallucinogens and many naturally occurring colors, vitamins, and antibiotics are heterocyclic substances. Because they are frequently utilized in forensic and clinical contexts, the benzodiazepine (oxazepine) and diazepine medication classes are used as relaxants, mild tranquilizers, hypnotics, and muscle relaxants [3]. In the pharmaceutical and medical fields, Schiff bases are well- known due to the broad range of biological efficacy that have been demonstrated for them. Schiff bases are the condensation products of the primary amines and energetic carbonyl groups [4]. According to their chemical makeup, mode of operation, etc., corrosion inhibitors can be categorized. Because they are simple to make, inexpensive to produce, and have a high level of protection, organic corrosion inhibitors are one of the popular kinds [5]. Adsorption on the steel superficies and preventing the active corrosion positions are causes of the prevention strategy. The forming of a pre-emptive barrier between "the attacker solution and the metal surface" prevents the mind from dissolving and minimizes corrosion damage. In both theory and practice, it has been demonstrated that derivative inhibitors with hetero-atoms, like N, O, and S effectively prevent corrosion in a diverse species of acidic solutions. Therefore, seven heterocyclic compounds were created in this study and chosen to operate as corrosion inhibitors for steel in HCl solution and antifungal activity [6].

Materials and Methods

Chemical study [7]

*Synthesis of 2,2'-((1,2-phenylenebis(methaneylylidene))bis(azaneylylidene))dibenzoic acid (**I**)*

Phthalaldehyde (0.01 mole) was dissolved in 25 mL absolute ethanol and condensed with (0.02 mole) of anthranilic acid, followed by the addition of 1-2 drops of glacial acetic acid, all while continuously shaking for 20-25 min on a magnetic stirrer at 65-70 °C in four hours to prepare the combination for recrystallization from 100% ethanol, the mixture was evaporated and dried to give compound (**I**).

*Synthesis of 2,2'-(1,2-phenylenebis(4,7-dioxo-4,7-dihydro-1,3-oxazepine-2,3(2H)-diyl)) dibenzoic acid (**II**)*

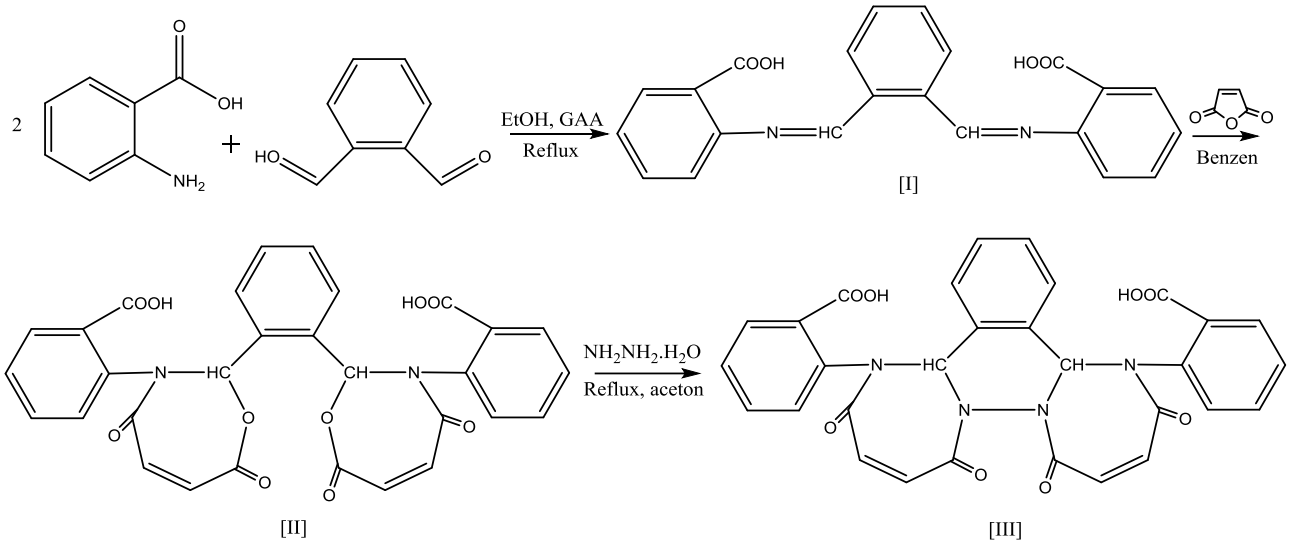
As a solvent, (0.01 mole) of compound (**I**) was dissolved in 20 mL of dry benzene, and then (0.02 mole) maleic anhydride was added gradually to finish the reaction at 60-65 °C in 12 hours. To prepare the combination for recrystallization from absolute ethanol, the mixture was evaporated and dried to give compound (**II**).

Synthesis of 2,2'-(2,5,8,11-tetraoxo-2,5,8,11,12a,16b-hexahydrobis([1,3]diazepino)[2,1-a:1',2'-c]phthalazine-1,12-diyl)dibenzoic acid [III]

Hydrazine hydrate (80%) (0.02 mole) was condensed (0.01) mole from compound (**II**) in the presence of acetone as a solvent while refluxing in (10 hours). To prepare the combination for recrystallization from absolute ethanol, the mixture was evaporated and dried to give compound (**III**). TLC was applied to the final product, as displayed in Scheme 1. All the physical properties of compounds (**I-III**) are listed in Table 1.

Table 1: All chemical and physical parameters as well as additional characterization

Compound No.	Yield (%)	Color	mp (°C)	Rf.	Solvents (TLC)
(I)	70	Deep Yellow	188	0.68	Ethanol:Hexane
(II)	76	Yellowish Orange	196	0.60	Ethanol:Hexane
(III)	82	Orange	223	0.64	Ethanol:Hexane



Scheme 1: Synthesis of compounds (**I-III**)

Corrosion study

Carbon steel used in the trial sample has the chemical elements (in %wt.): (0.1 C), (0.335 Mn), (0.033 Si), (0.0067 S), (0.0056 P), (0.057 Al), (0.0476 Cu), (0.0201 Cr), (0.001 Co), (0.0007 Ti), and the remaining amount is F. The steel electrode was prepared for each measurement by being scrabbled with emery papers with a grade of (800-1500), laundered ultrasonically with distilled H_2O, and finally dehydrated under the dry air. Acetone was then made by mixing Angler Grade 37% HCl with alcohol. The corrosion inhibition of mild steel in 0.5 M HCl by synthesized compounds was studied by using weight loss measurements. To ensure a reasonable level of repeatability, each measurement was carried out three times at a temperature range of 20–50 °C [8].

*Isolation of the studied fungi **1-3***

Aspergilla's species are significant both medically and commercially. A few species can infect both people and other animals. Opportunistic pathogenic yeast *Candida albicans* is a frequent constituent of the flora of the human gut. It can even persist without a human body. "*Candidaalbicans and Aspergilla*" were two fungi studied in this paper. While the samples were immediately put on (PDA) Potato dextrose agar media, and then chloramphenicol was added to inhibit bacterial development, and they were incubated at 25 °C for 48 hours. Thereafter, by using a conventional taxonomic key, these fungi were identified based on their micro- and macro-morphological properties [9].

Results and Discussion

Spectral investigation

Typically, Schiff base (**I**) was investigated by melting points and FT-IR spectroscopy. The FT-IR spectrum revealed the disappearance of absorption peaks caused by NH_2 and C=O groups with the emergence of a new stretching vibration at 1661 cm^{-1} in which is assigned to azomethine group (CH=N), peak at 1702 cm^{-1} due to the C=O group, and at 3341-2831 cm^{-1} because of the hydroxyl of the carboxyl group. The 1,3-oxazepine (**II**) was synthesized by addition reaction (2+5) of azomethine C=N with maleic anhydrides in dry benzene, due to the cyclic amid group (CO-N) in lactam new bands formed at 1641 cm^{-1}. A band at 1755 cm^{-1} was caused by a lactone, band at 3330-2700 cm^{-1} owing to OH hydroxyl of carboxyl group, band at 3044 cm^{-1} due to alkene (CH=CH), and another band at 1711 cm^{-1} due to carbonyl of carboxyl group in carboxylic acid [10]. The most characteristic evidence of the FT-IR absorption bands of compound (**III**) showed that other bands at 1710 owing to carbonyl of carboxylic acid, band at 3290-2775 cm^{-1} due to hydroxyl of carboxyl group, band at 3031 due to alkene (-CH=CH), and

new bands at 1648 and 1620 cm^{-1} due to two groups of cyclic amid group in lactam ring. The collective FT-IR spectral data obtained for target compounds are listed in Table 2.

^{1}H-NMR spectral identification

Compound (**II**), ^{1}H-NMR spectrum (DMSO-d_6), revealed a singlet signal for one proton of carboxyl group at δ 12.17 ppm. Many signals indications at δ 7.83-7.77 ppm are the result of twelve aromatic protons. Finally, the ^{1}H-NMR spectrum reveals two peaks at δ 6.06 and 6.04 and δ 7.05 ppm that could be identical to CH=CH ring of oxazepine ring and one proton of CH-N group [11, 12].

The ^{1}H-NMR spectrum (DMSO-d_6), of compounds (**III**) showed a sharp signal at δ 3.34 ppm for one proton of diazepine group (N-CH-N), doublet signal at δ 6.29 and 6.11 ppm for two protons of CH=CH and twelve aromatic protons appear at the range δ 7.83-7.54 ppm. Furthermore, a singlet signal of proton of carboxyl group absorbed at δ 12.22 ppm. All the ^{1}H-NMR spectra data are given in Tables 3.

Table 2: Characteristic FT-IR absorption band spectra (cm^{-1}) of compounds (**I-III**)

Compound No.	υ (O-H) carboxylic	υ (C-H) aromatic	υ (C=O) carboxylic acid	υ (C=O) Lactone	υ(C=O) lactam	υ(C=N)	υ (C=C) aromatic
(I)	3341-2831	3095	1702	-	-	1661	1575,1489
(II)	3330-2700	3044	1711	1755	1641	-	1588, 1528
(III)	3290-2775	3031	1710	-	1648, 1620	-	1574, 1470

Table 3: ^{1}H-NMR spectral data for compounds (**II** and **III**)

Compound No.	Signals in ^{1}H-NMR spectra in DMSO-d_6
[II]	12.17 (s,1H, COOH), 7.83-7.77 (m, 12H, Ar-H), 7.05 (s, 1H, CH-N), 6.06-6.04 (d, 2H, CH=CH)
[III]	12.22 (s, 1H, COOH), 7.54-7.83 (m, 12H, Ar-H), 6.11-6.29 (d, 2H, CH=CH), 3.34 (s, 1H, N-CH-N),

Mass spectra of new compounds

Figure 1 displays the mass spectrum of compound (**II**): $C_{30}H_{20}N_2O_{10}$ (M.Wt.=568.11) showed the base peak at ($m\backslash z$ = 119), further it revealed several fragments at ($m\backslash z$ = 308,221, 187, 147, and 92) which was in agreement with the molecular weight of structure proposed for this compound (**II**). Figure 2 depicts the mass spectrum of compound (**III**): $C_{30}H_{20}N_4O_8$ (M.Wt. = 564.12) indicated the interesting base peak at ($m\backslash z$ = 119), and also it showed several fragments at ($m\backslash z$ = 321, 287, 256, 162, 147, and 92). The same structure was discovered by comparing the predicted structure of the synthesized compound to their spectral fragments. Several spectra are depicted in illustrations [13-15].

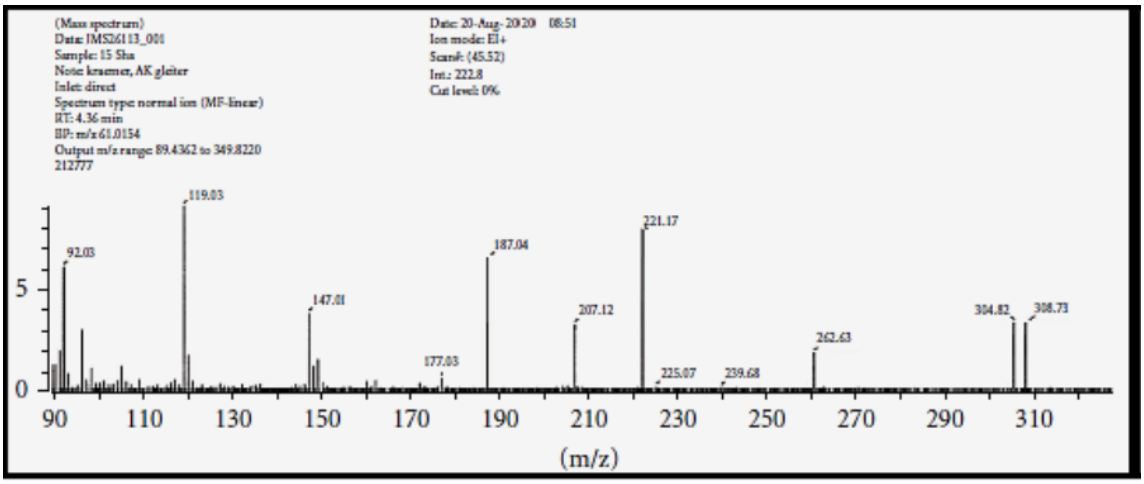


Figure 1: Mass–spectrum of compound (**II**)

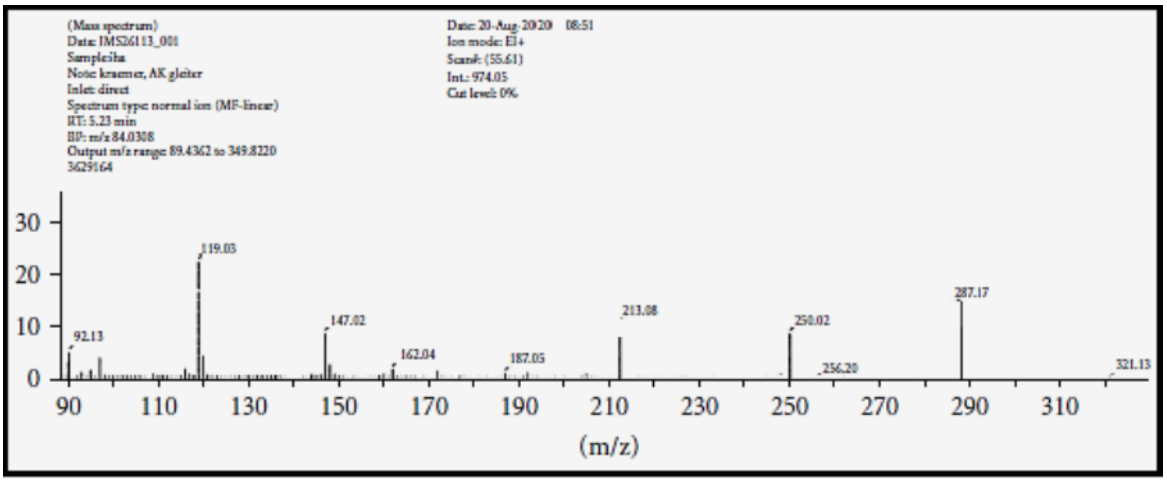


Figure 2: Mass-spectrum of compound (**III**)

Corrosion investigation

According to Table 1, the concentration of derivatives causes a reduction in the rate of steel corrosion at a given testing temperature. As concentrations of **1**, **2**, and **3** compounds are increased, values of inhibitor efficiency are increased, reaching an ultimate value of the inhibition efficiency 95.8% at higher temperatures and inhibitor levels, Table 4, and Figure 3 displays the Langmuir adsorption isotherms of derivatives [16, 17].

Table 4: The rate of low carbon steel alloy corrosion and the effectiveness of synthetic (oxazepine, diazepine) corrosion inhibitors under various circumstances in 0.5 M HCl solution

Test No.	Inhibitor conce. (M)	Temperature (°C)	Corrosionrate (g/m,48 hours)	Inhibitor efficiency (%)
1	Zero	20	33.99	-
2	Zero	30	80.52	-
3	Zero	40	142.96	-
4	Zero	50	419.21	-
5	0.001	20	9.57	71.8
6	0.002	-	8.36	75.4
7	0.003	-	6.21	81.7
8	0.004	-	5.06	85.1
9	0.001	30	15.17	81.2
10	0.002	-	15.05	81.3
11	0.003	-	11.23	86.1
12	0.004	-	10.75	86.6
13	0.001	40	21.27	85.1
14	0.002	-	18.47	87.1
15	0.003	-	17.66	87.7
16	0.004	-	16.83	88.3
17	0.001	50	22.57	94.6
18	0.002	-	20.52	95.1
19	0.003	-	18.91	95.5
20	0.004	-	17.66	95.8

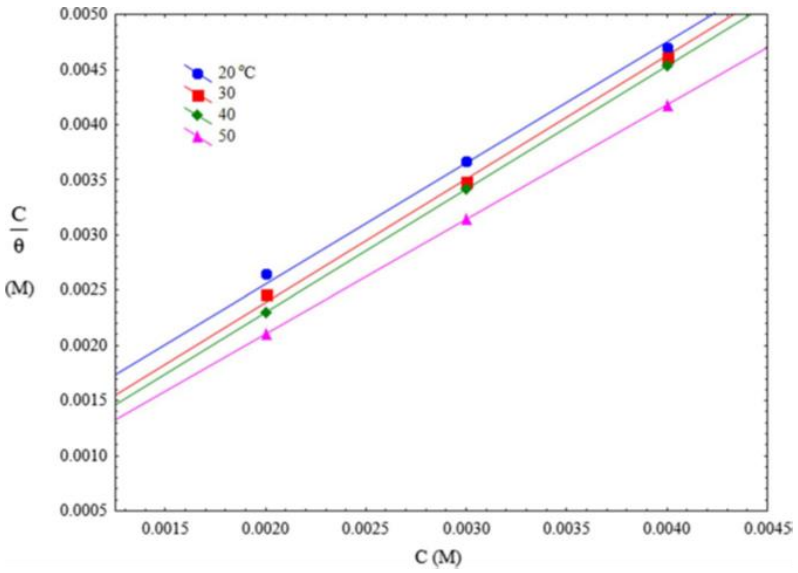


Figure 3: The Langmuir adsorption isotherms of derivatives in (0.5 M HCl) solution on the surface of steel at diverse temperatures

Biological investigation

The seven generated rings derivatives were examined by using a live fungal study on various types of fungi to gauge how well the synthesized derivatives affected the growth of the study's chosen fungi. Evaluation of derivatives was done against two different fungi, *aspergillus* and *candida albicans*, at four different concentrations (5, 10, 15, and 20 g) for all derivatives [18-21]. The antifungal activity of the synthesized compounds was assessed by comparing the widely used antifungal Fluconazole as a common antifungal drug are listed in Table 5.

Table 5: Antifungal Assay of derivatives in different Concentration

Compounds	*Aspergillus*	Candida albicans
(I)	++	+
(II)	++	++
(III)	+++	+++
Fluconazole	+++	+++

+ Inhibition (4-8) mm
++ Inhibition (9-12) mm
+++ Inhibition (13-16) mm

Conclusion

Through the analysis of spectrum data by using FT-IR, ^{1}H-NMR, and mass spectroscopy, these derivatives were confirmed. A lot of the chemicals have similar effects to those of popular drugs. It was also determined how well the drugs reduced inflammation *in vitro*, because the structure of these compounds contains lactone and lactam groups. Given their (oxazepine and diazepine) group and other cycle-based structures, the produced compounds demonstrated a good antifungal activity. These compounds as corrosion inhibitors for steel in acidic solution have undergone the successful testing.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

There are no conflicts of interest in this study.

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