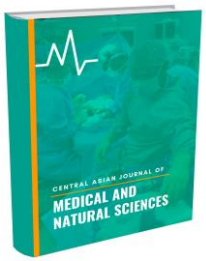

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Article

The Use of the Products of the Bijnelli Reaction as Nucleophiles for the Preparation of New Derivatives of Azetidine and the Evaluation of the Bacterial Effectiveness of the Resulting Compounds

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Abstract: This study produced new azetidine derivatives by reacting derivatives of hydrazones (Benelli reaction products were used for this preparation) with chloroacetyl chloride. The produced compounds were then identified using spectroscopic techniques like infrared spectra (FT-IR) and resonance spectra (H1-NMR & C13-NMR). Among the four bacterial isolates used to evaluate the biological efficacy of some of the prepared compounds on their growth were Escherichia coli and Staphylococcus aureus. Thin layer chromatography (TLC) was employed in addition to these analyses to monitor the reactions' progress and ascertain the purity and melting points of the produced compounds.

Keywords: azetidine , Hydrazones, Pignelli reaction, biological activity

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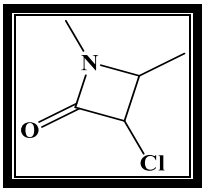
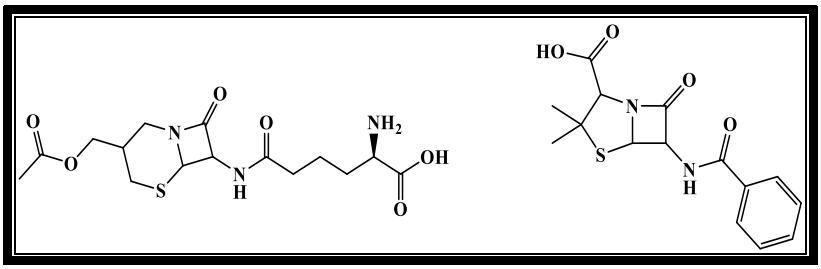
1. Introduction

There is a carbonyl team and a nitrogen atom at position two of these quadruple rings. They are also known as β-lactam compounds [1], [2].



Since azathiidine compounds are present in antibiotics like cephalosporin and penicillin, they are significant biologically cyclic compounds [3]. The following methods were used to create the two compounds, which have been used as anti-inflammatory agents [4], [5].



They are biologically active compounds. Studies have shown that they have efficacy antifungal [6], [7], antimicrobial [8], [9], antitumor [10], [11], antibacterial [12], [13], and antioxidant [14].

2. Materials and Methods

2.1. Material

All chemicals were used through this work and purchased from Fluka, BDH Companies.

2.2. Devices Used

The Stuart melting point apparatus recorded the uncorrected melting points in an open capillary tube. KBr discs and 1H NMR have been used to record infrared spectra on a Shimadzo FTIR-8100 spectrophotometer. DMSO-d6) was used as the solvent to measure spectra using an MHZ spectrometer. TLC was used to monitor the reaction and confirm the purity of the compounds (type 60 F254 Merck, Darmstadt, Germany) on alumni sheets percolated in silica gel.

2.3.Synthesis Of Azetidine (D57-D61) [15]

Dissolve a mixture of prepared hydrazones (0.001 Mol) in 10 ml of 4,1-dioxane and then add (0.002 Mol) of chloro acetyl chloride dissolved in 10 ml of 4,1-dioxane with (0.002 Mol) of triethylamine also dissolved in 4,1-dioxane solvent stir the solution for 24 hours (with a glass motor then the mixture was left at the laboratory temperature for 24 hours to complete the reaction, after which the solution was added to a beaker containing crushed ice, the precipitate was filtered, dried and recrystallized with ethanol 99.9%, As shown in Table.

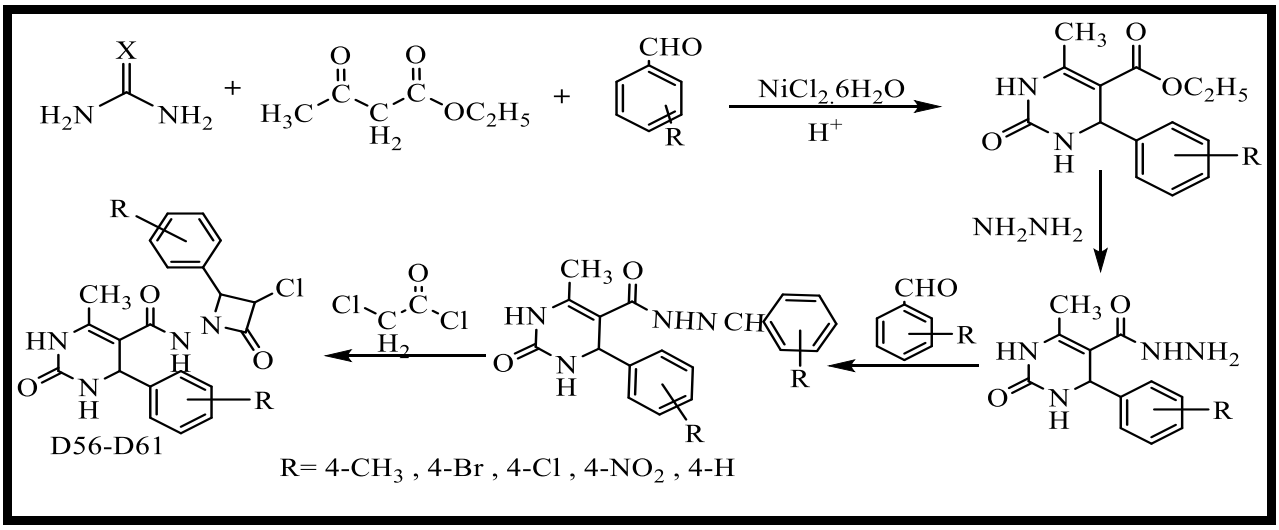
2.4. Evaluation Of Biological Activity

Unlike the Kirby Bauer movement [16, 17], which uses the propagation method to measure biological activity, [18, 19] involves adding 0.1 ml of bacterial suspension to ager Muller Hinton dishes and letting them absorb it for five minutes. The dishes were then incubated for twenty-four hours at 37 °C after holes were made in each one using a cork plunger and a diameter of five mm per hole (0.1 ml) of the prepared solutions of the fourth hole using (Amoxicillin) as a control sample. Using Prescott's method [20], the inhibition zone diameters surrounding each hole have been measured in millimetres.

3. Results and Discussion

Preparing a set of compounds, producing new ester derivatives through a biogenic reaction, and converting the end product of that reaction into hydrazide by reacting with hydrazine, benzaldehyde, and hydrazone, which in turn responded with chloro acetyl chloride acid to produce derivatives of azetidine were all part of this study. Spectral

methods were used to validate the compounds in this investigation. Scheme (1) illustrates the described sequence of events.



Scheme 1. Route of prepared compounds (D_{57}-D_{61})

3.1.Characterization of azetidine

When studying the ultraviolet and visible (Vis-UV) spectra of quinazoline derivatives[D51-D61] using ethanol (95%) as a solvent and with a concentration ranging from [10-5-10-3] molar, an absorption beam at (284-224) Nm due to transitions (*π←π) and an absorption beam at (387-328) Nm due to electronic transitions of type (*π←n) appeared.

And when studying the infrared (IR) spectrum of azetidine-2 derivatives- On [D57-D61] the disappearance of the azomethine elastic band (C=N) of hydrazone was observed, the appearance of absorption bands at the frequency (3161-3326) cm-1 belonging to the elastic band (NH), the appearance of an absorption band at the frequency (3054-3085) cm-1 belonging to the aromatic elastic band (CH), as well as the appearance of absorption at the frequency (2927-2989) cm-1 belongs to the aliphatic (c-h) sphincter, an absorption beam appeared at the frequency (1677-1695) cm-1 belongs to the carbonyl (C=O) team adjacent to the chlorine team, and an absorption beam appeared at the frequency (1635-1657) cm-1 belongs to the carbonyl(c=o) amide sphincter, also two absorption beams were observed at the frequency (1454-1542) cm-1 and(1406-1472) cm-1 belonged to the Metropolitan of Asser (C=C) aromatization, and an absorption beam appeared at the frequency (752-796) cm-1 belonging to the sphincter (C-Cl [21], as shown in Table (2) and Figure (1,2).

When studying the (^{1}H-NMR) spectrum of the compound [D58], the appearance of a single signal in the range (8.82) ppm attributable to the Proton team (NH), the appearance of a multiple signal in the range (7.51-8.09) ppm attributable to the protons of the aromatic ring, the appearance of a binary signal in the range (5.34 - 5.35) ppm attributable to the Proton Team (CH-Cl) in the azetidine quad ring, the appearance of a binary signal in in the range (5.91 - 5.93) ppm attributed to the Proton Team (CH-N) in the azetidine quaternary ring, and the appearance of a single signal in the range (4.98) ppm attributed to the Proton Team (CH) of the pyrimidine ،[22], as shown in Figure (3).

When studying the (^{13}C-NMR) spectrum of the compound [D58], the appearance of a signal in the range (12.54) ppm attributable to the carbon Team (C-Cl) in the azetidine quaternary ring, the appearance of a signal in the range (45.63) ppm attributable to the

carbon Team (C-N) in the azetidine quaternary ring, the appearance of signals in the range (64.115-16.147) ppm attributable to the carbons of the benzene aromatic ring, the as well as the appearance of a signal in the range (165.51) ppm attributed to the carbon of the carbonyl team (CO-CCL), the appearance of a signal in the range (152.22) ppm attributed to the carbon of the carbonyl team of the pyrimidine, as well as the appearance of a signal in the range (170.04) part of The millionth is attributed to the carbon of the amide carbonyl team [23], as shown in figure (4).

3.2. Evaluation of Biological activity:

Bacteria with Gram-positive status Tests were conducted on D57, D58, and D59, three of the synthesized compounds, against Streptococcus faecalis and gram-negative bacteria. The agar diffusion method uses a Proteus cup plate [24]. After the microbial cultures were incubated for eight hours at 37 °C, 0.8% sterile saline was added [25]. The concentration of the drug solution in DMSO was maintained at 100µg/mL. As a negative control, amoxicillin was utilized. The inhibition diameter of bacterial growth surrounding the in-use disk served as a proxy for biological activity[26]. as shown in Table (3).

Table 1. Physical properties of the prepared compounds (D_{57}-D_{61})

Com. No.	R	Molecular formula	m.p. °C	Yield%	R.f	Color
D_{57}	Cl	$C_{21}H_{17}N_4O_3Cl_2S$	(159-161)	52%	0.69	Brown
D_{58}	Br	$C_{21}H_{17}N_4O_3Br_2S$	(120-123)	48%	0.72	Brown
D_{59}	H	$C_{21}H_{19}N_4O_3S$	250dec.	86%	0.88	Brown
D_{60}	NO2	$C_{21}H_{17}N_6O_7S$	(151-153)	45%	0.68	Brown
D_{61}	CH3	$C_{23}H_{23}N_4O_3S$	(127-129)	70%	0.80	Brown

Table 2. FT-IR data of prepared compounds (D_{65}-D_{69}) cm^{-1}

Comp. No.	λ max1 λ max2 EtOH Nm	R	νNH	νC-H Arom.	νC-H Aliph.	νC=O	ν C=C Arom.	ν (C-Cl)	Others
D_{57}	262 387	Cl	3161 3226 3303	3078	2972	1637 1695	1454 1406	796	ν(C-Cl) 756
D_{58}	237 370	Br	3193 3232 3312	3069	2981	1646 1681	1531 1472	759	ν(C-Br) 657

			3262						
	282					1635	1542		
D59		H	3281	3051	2964				---
	337					1672	1465	765	
			3317						
			3169						
	231					1641	1510		asy.1314
D60		NO2	3274	3045	2955				
	351					1678	1426	783	sym.1538
			3325						
			3197						
	284					1656	1512		
D61		CH3	3245	3085	2974				---
	342					1677	1454	752	
			3326						

Table 3. Inhibitory effectiveness of some prepared compounds (D_{57}, D_{58}, D_{59}) and control treatments (antibiotics) on the growth of a number of positive and negative bacteria

Com. No.	*Escherichia coli*			*Staphylococcus epidermidis*		
	0.001	**0.01**	**0.01**	**0.001**	**0.01**	**0.1**
D57	1.3	1.2	1.2	4.4	4.7	5.1
D58	3.1	2	3.2	3.1	3.2	3
D59	2.7	2.6	4.1	4.0	4.4	5.1
Ciprofloxacin	0.5	2.5	1.5	0.8	1.8	1.8

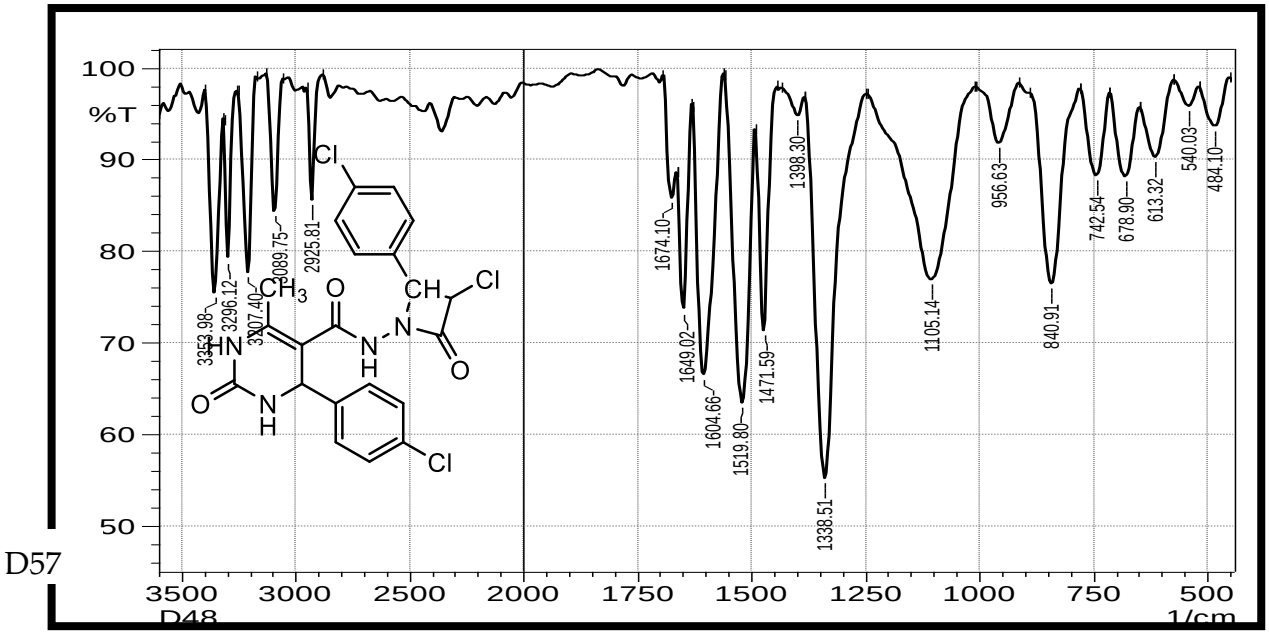
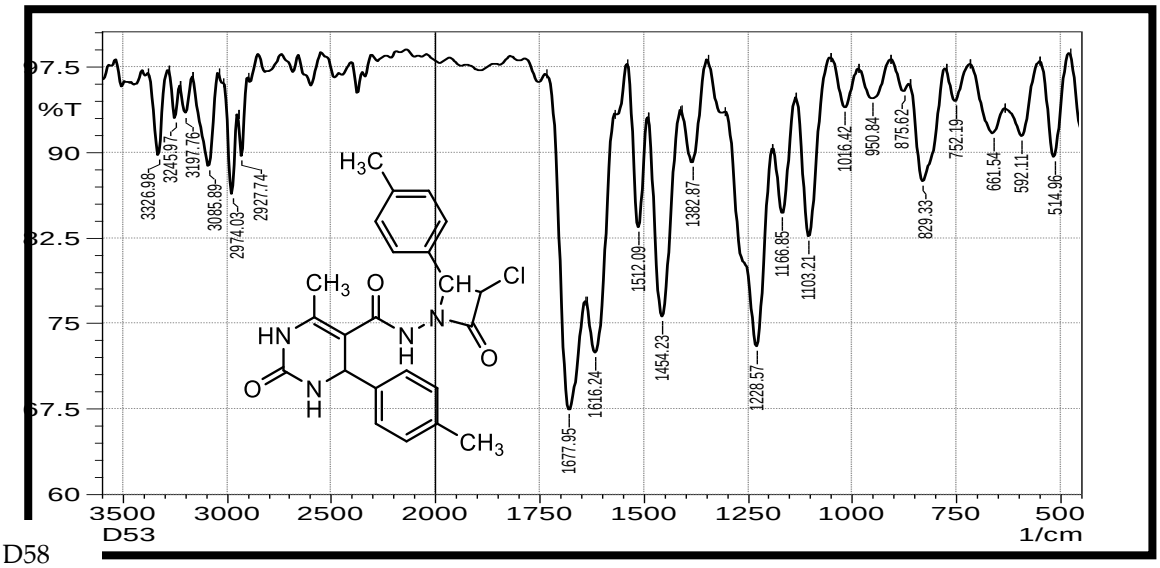


Figure 11. The infrared spectrum of the compound (D57)



D58

Figure 12. The infrared spectrum of the compound (D58)

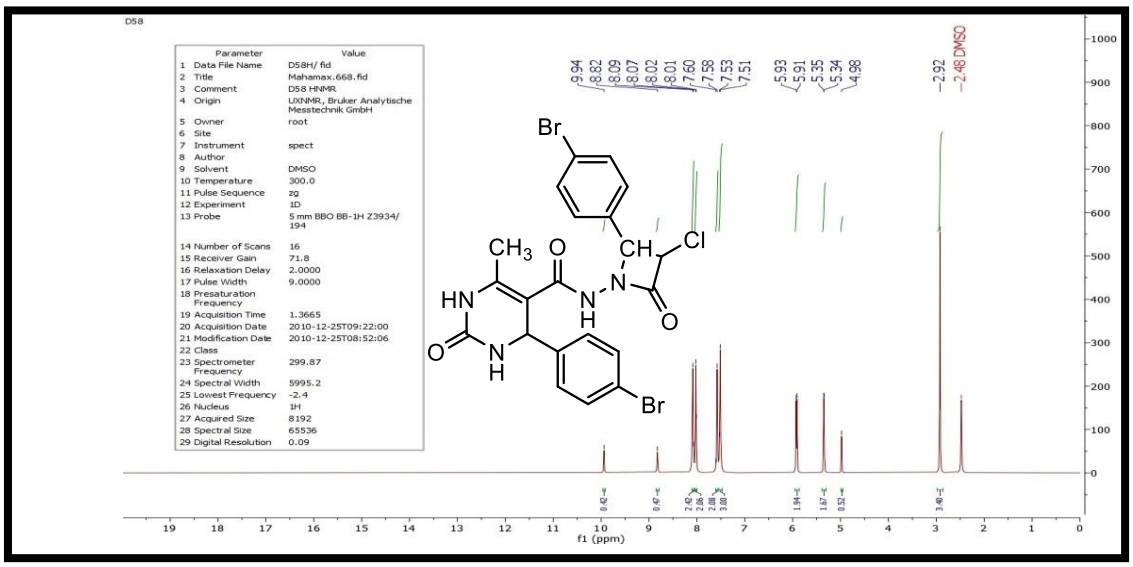


Figure 13. The ^{1}H-NMR spectrum of the compound (D58)

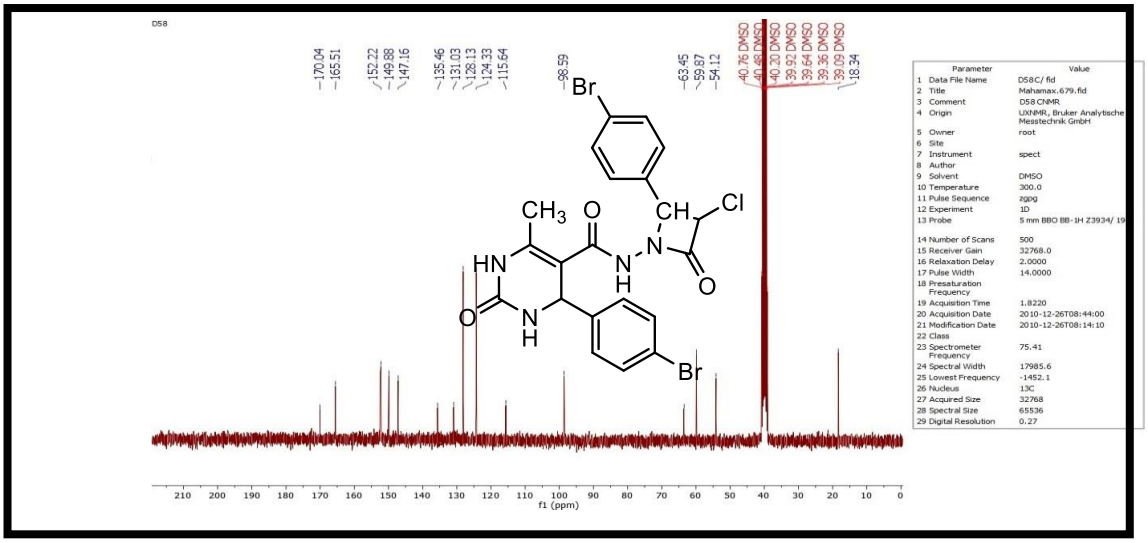


Figure 14. The ^{13}C-NMR spectrum of the compound (D_{58})

4. Conclusion

The prepared compounds demonstrated good efficacy against two types of positive and negative bacteria when tested against cram dye. These methods included physical and spectroscopic methods where the active aggregates were visible in the infrared spectrum, as well as confirmation of the proton and carbon NMR spectra.

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