

Preparation, Characterization, of Some Oxadiazol Derivatives Prepared from Different Carboxylic Acids

Selvana A. Yousif  

Department of Chemistry, College of Science for Women, University of Baghdad, Baghdad, Iraq

Received 30/03/2023, Revised 02/10/2024, Accepted 04/10/2024, Published Online First 20 /06/2024



© 2022 The Author(s). Published by College of Science for Women, University of Baghdad.

This is an open access article distributed under the terms of the [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

A series of Mefenamic acid derivatives were designed and synthesized and the products were characterized spectroscopically using FT-IR, ¹H NMR, and ¹³C NMR techniques. Series A included the transformation of six drugs (Mefenamic acid, Ampiciline, Noprofen, Benzilic acid, Diclofenac acid, and cephics) which are known to have highly medicinal effectiveness to acid chloride then react with thiosemicarbazide to synthesize series B. In the third stage, oxadiazole was prepared using POCl₃ as a ring-closing agent to compounds (B1-B6). The final step in the strategy was building new Mefenamic acid derivatives consisting of condensation of the Mefenamic acid chloride with the compounds (C1-C6) to give new compounds (D1-D6).

Keywords: Derivatives, Drugs, Mefenamic acid, Ring-closing, Synthesis oxadiazole.

Introduction

Mefenamic acid (MEF), which was first sold in the 1960s, is still one of the most often prescribed and reasonably priced non-steroidal anti-inflammatory (NSAIDs) medications in use today ^{1,2}, the mechanism of action of NSAIDs, such as diclofenac, ibuprofen, and Mefenamic acid, aided in the development of more NSAIDs³. Additionally, Mefenamic acid is developed as a new class of cancer chemopreventive therapies, together with other anti-inflammatory medications ⁴⁻⁶. However, NSAID-related adverse effects, particularly in the renal and gastrointestinal tract, frequently restrict its use. Because of this, significant attempts have been made to boost their activity while reducing negative effects ⁷. Mefenamic acid, an anthralinic acid derivative, is comparable to the NSAIDs tolfenamic and flufenamic acid ⁸. MFA has been clinically used to relieve pain brought on by musculoskeletal problems and primary dysmenorrhea ^{9,10}, antioxidant, bactericidal, and fungicidal activity,

anti-viral and used as an antipyretic, especially in pediatric cases ¹¹⁻¹⁴. Currently, Mefenamic acid is used as an efficient catalyst ¹⁵. 1,3,4-oxadiazoles were important for the development of heterocyclic chemistry theory and are exceedingly used in organic synthesis ¹⁶. Oxadiazole molecules have numerous properties that are useful in a variety of industries. These compounds have a broad range of biological activity, allowing them to be used as active agents in medicine and pharmacology, such as anti-inflammatory and analgesic agents. Because of their potential biological activity, these compounds are also used in agriculture as herbicides, insecticides, and plant protection agents against viruses, fungi, and bacteria¹⁷. In this paper, we synthesized and characterized new derivatives by making a combination of six drugs, the aim is to gain access to novel active biomolecules that may have potent antimicrobial activity.

Materials and Methods

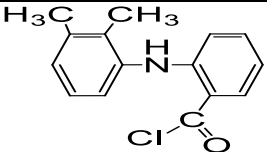
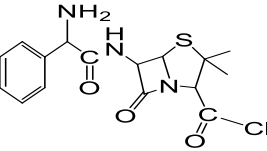
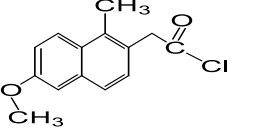
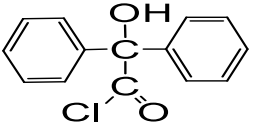
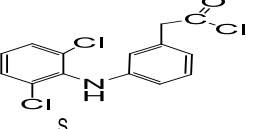
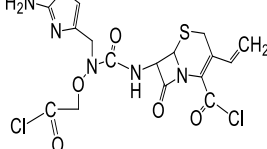
Materials and Physical Measurements:

All starting materials and solvents were obtained from Fluka and Sigma-Aldrich, and utilized without additional purification. Uncorrected measurements of the melting point were made using the Gallen Kamp melting point instrument. In the University of Al-Albyat in Jordan, ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker spectrosopin Ultra shield 300 MHZ instrument with (tetramethyl silane, TMS) as an internal standard and (DMSO-d₆) as a solvent. Shimadzu FT-IR 8400 Fourier Transformer infrared spectra were recorded as KBr disk.

Synthesis of Compounds(A1-A6)¹⁸

Carboxylic drugs (Mefenamic acid, Ampiciline, Noproxen, Benzilic acid, Diclofenic acid, cephics) (0.01mol) were dissolved in the smallest possible amount of CHCl₃, newly distilled thionyl chloride (0.01mol) was gently added to it. The mixture was refluxed at 60-70°C for 15 hours using a magnetic stirrer to continuously stir. The sticky liquid was quickly put into a petri dish and vacuum dried, yielding yellow crude Mefenamic acid chloride. The structural formula, physical data, and molecular formula of the compounds are illustrated in Table .1.

Table 1. Physical Characteristic of compounds (A1-A6).

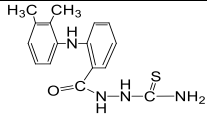
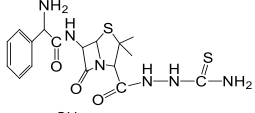
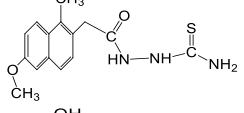
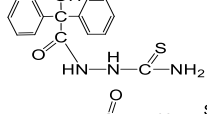
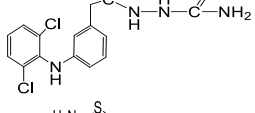
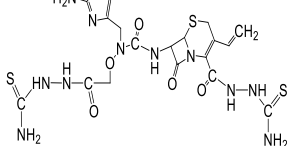
Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	M. P. °C	Yield %
A1		C ₁₅ H ₁₄ ClNO	259.73	Brown	110-112	75%
A2		C ₁₆ H ₁₈ ClN ₃ O ₃ S	367.85	Yellow	Oily	60%
A3		C ₁₄ H ₁₃ ClO ₂	248.70	Light Yellow	135-138	64%
A4		C ₁₄ H ₁₁ ClO ₂	246.69	Brown	Oily	55%
A5		C ₁₄ H ₁₀ Cl ₃ NO	314.59	Brown	105-106	45%
A6		C ₁₆ H ₁₅ Cl ₂ N ₅ O ₅ S ₂	492.36	Dark Red	Oily	55%

Synthesis of Compounds(B1-B6)¹⁹

Anhydrous sodium carbonate (0.005mol) and carbon disulfide were added to thiosemicarbazide (0.005mol), and compounds (A1-A6) (0.005mol) were suspended in anhydrous ethanol (20 ml). For 1 hour, the mixture was warmed by stirring under reflux. Next, it was heated for 4 hours in a steam

bath. The solvent was mostly removed, and the residue was then dissolved in water (15 ml) and slightly acidified with concentrated hydrochloric acid to yield the product. The structural formula, physical data, and molecular formula of the compounds are shown in Table 2.

Table 2. Physical Characteristic of compounds (B1-B6).

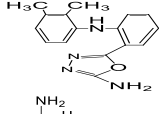
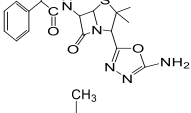
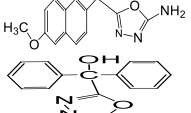
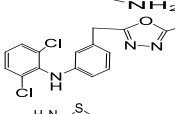
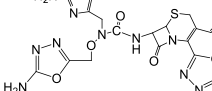

Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	M. P. °C	Yield %
B1		C ₁₆ H ₁₈ N ₄ OS	314.41	Light Brown	Oily	60%
B2		C ₁₇ H ₂₂ N ₆ O ₃ S ₂	422.52	Dark Yellow	196-198	70%
B3		C ₁₅ H ₁₇ N ₃ O ₂ S	303.38	Dark Brown	Oily	50%
B4		C ₁₅ H ₁₅ N ₃ O ₂ S	301.36	White	188-190	80%
B5		C ₁₅ H ₁₄ Cl ₂ N ₄ OS	369.27	Redish Brown	Oily	65%
B6		C ₁₈ H ₂₃ N ₁₁ O ₅ S ₄	601.71	Yellowish Brown	105-106	58%

Synthesis of Compounds [C1-C6] ²⁰

Synthesis of compounds C1-C6 was conducted by using POCl₃ (0.001mol) which was added drop wise to an ice-stirred solution of compound [B1-B6] (0.001mol) in dry DMF (15 ml), and the mixture was allowed to be at room temperature and then heated at 80 C for (4 hours), using a water bath, the

mixture was then poured onto ice water, neutralized with dilute sodium hydroxide, and allowed to stand for 24 hours before recrystallization with ethyl acetate. The structural formula, physical data, and molecular formula of the compounds are exhibited in Table 3.

Table 3. Physical Characteristic of compounds (C1-C6).

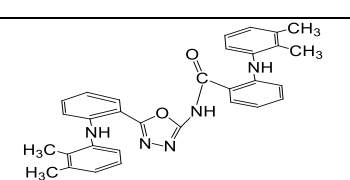
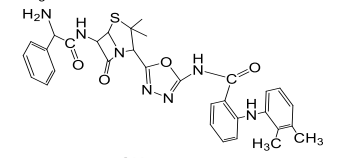
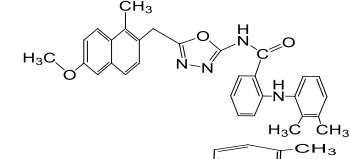
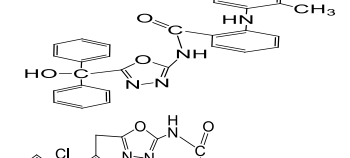
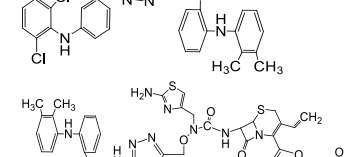
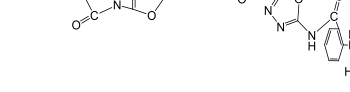
Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	M. P. °C	Yield %
C1		C ₁₈ H ₁₈ N ₂ O	278.35	Light Brown	Oily	40%
C2		C ₁₉ H ₂₂ N ₄ O ₃ S	386.47	Brown	Oily	70%
C3		C ₁₇ H ₁₇ NO ₂	267.32	Dark Brown	Oily	60%
C4		C ₁₇ H ₁₅ NO ₂	265.31	Dark Brown	Oily	45%
C5		C ₁₇ H ₁₄ Cl ₂ N ₂ O	333.21	Redish Brown	Oily	30%
C6		C ₂₂ H ₂₃ N ₇ O ₅ S 2	529.59	Dark Brown	Oily	78%

Synthesis of Compounds [D1-D6] ²¹

To a stirred solution of an acid chloride (0.001 mol in THF (15 mL) at 0 °C, trimethylamine (0.001 mol,) and a primary amine (0.001 mol.) were added. The resultant mixture was allowed to warm to rt. over 2 hours. After adding 8 mL of water, the

mixture was stirred until the product precipitated. To obtain pure amide, the precipitate was filtered and washed with water. Table 4, shows the structural formula, physical data, and molecular formula of the compounds (D1-D6) .

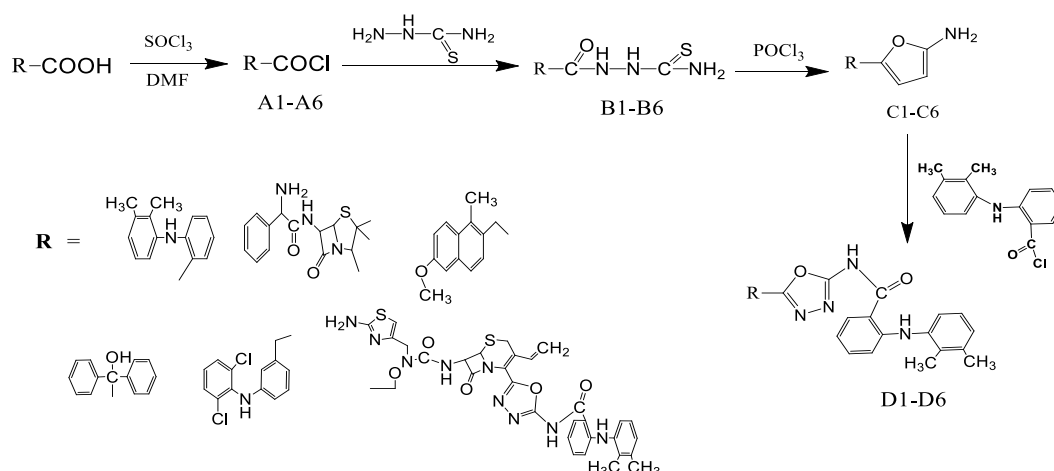
Table 4. physical Characteristic of compounds (D1-D6).

Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	M. P. °C	Yield %
D1		C ₃₃ H ₃₁ N ₃ O ₂	501.62	Redish Brown	Oily	40%
D2		C ₃₄ H ₃₅ N ₅ O ₄ S	609.74	Dark Yellow	Oily	35%
D3		C ₃₂ H ₃₀ N ₂ O ₃	490.59	Lead	235-238	70%
D4		C ₃₂ H ₂₈ N ₂ O ₃	488.58	Light Brown	Oily	65%
D5		C ₃₂ H ₂₇ C ₁₂ N ₃ O ₂	556.48	Light Orange	Oily	65%
D6		C ₅₂ H ₄₉ N ₉ O ₇ S 2	976.13	Brown	Oily	40%

Results and discussion

Six drugs were combined to create new Mefenamic acid derivatives. These compounds are used as a starting material to design new drugs system. These derivatives are synthesized via reaction with different carboxylic drugs (Mefenamic acid, Ampiciline, Noproxen, Benzilic acid, Diclofenic acid, cephics) respectively, the proposed structures

of the compounds were confirmed on the basis of spectroscopic data (IR, ¹H NMR, and ¹³C NMR). The first step included preparing six new compounds (A1-A6) prepared from the reaction of different carboxylic drugs with thionyl chloride in chloroform according to Scheme 1.



Scheme 1. Synthesis of all compounds

FTIR spectra of the prepared derivatives [A1-A6] showed the disappearance of $\nu(\text{C}=\text{O})$ of acid absorption bands indicating the success of the reaction and the acid chloride formation. The spectra showed clear absorption bands due to $[\nu(\text{C}-\text{H aromatic}), \nu(\text{C}=\text{O}), \nu(\text{N}-\text{H})]$ appeared about at $[(3001-3085)\text{cm}^{-1}, (1650-1757)\text{cm}^{-1}$ and $(3282-3323)\text{cm}^{-1}]$ respectively, others bands are listed in Table 5 and shown in Fig. 1,2. $^1\text{H-NMR}$ spectrum

of compound [A3] showed signals at $\delta 1.23$ ppm of (s, 3H, CH_3), $\delta 2.09$ ppm of (s, 3H, CH_3), $\delta 4.23$ ppm of (s, 1H, NH), $\delta 6.69-8.78$ ppm of (m, 7H, ArH) as listed in Table 9 and shown in Fig. 7,8,9, while $^{13}\text{C-NMR}$ spectrum in δ (ppm) of compound (A4), Table 10, exhibited the signals for carbon ($\text{C}=\text{O}$) in 178 and twelve aromatic carbon appeared at 118-139 ppm.

Table 5. FT-IR Spectral data of synthesized compounds (A1-A6) in cm^{-1}

Comp. No.	$\nu\text{N-H}$	$\nu\text{C-H}$ Aromatic	$\nu\text{C-H}$ Aliphatic	$\nu\text{C}=\text{O}$ of acid	$\nu\text{C}=\text{C}$ aromatic	$\nu\text{C-N}$	Others
A2	3323	3042	2970, 2840	1743	1572, 1440	1338	NH ₂ 4115, 3342 C=O lactam 1679
A3	3001	2974, 2939	1728	1604, 1485	1394	C-O 1228, 1159
A4	3045	2957, 2845	1752	1583	1384	ν OH 3412
A5	3323	3085	2953, 2885	1731	1593, 1456	1396	C-Cl 1084
A6	3282	3047	2979, 2939	1749	1573	1332	NH ₂ 3407, 3350 C=O lactam 1677 C=N 1627

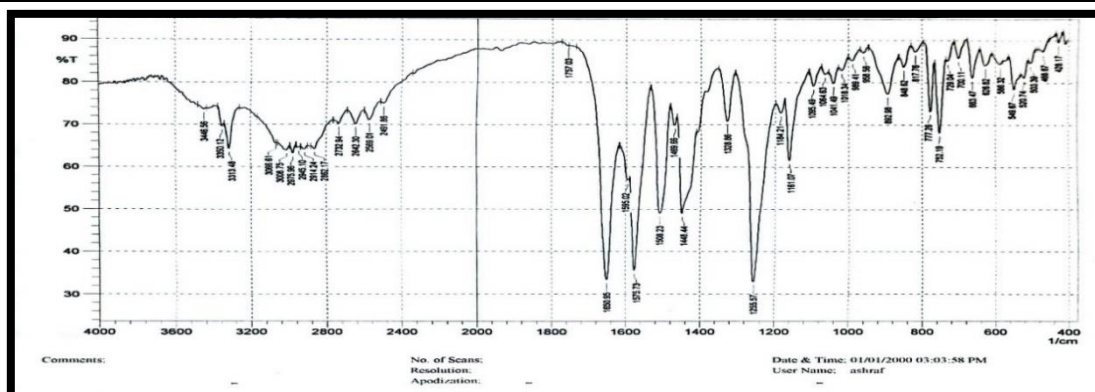


Figure 1. FTIR spectrum for compound (A1)

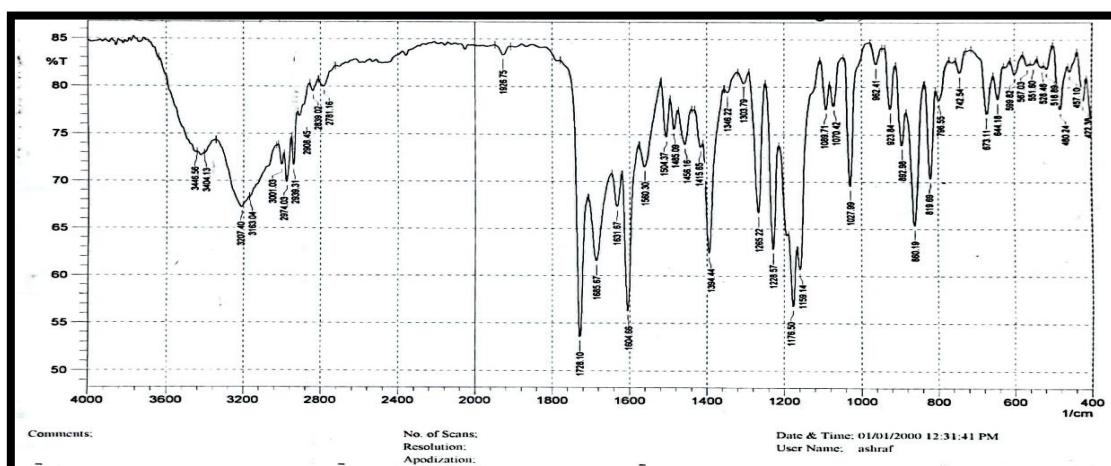


Figure 2. FTIR spectrum for compound (A3)

The second step in this strategy involved a reaction between acyl chloride and thiosemicarbazide which underwent (nucleophilic addition-elimination) mechanism by attacking amine from the thiosemicarbazide group on carbonyl group in acyl chloride; then followed by leaving the chloride ion to form the acyl thiosemicarbazide¹⁹. Spectral data for this set of compounds indicates the synthesis of the amide group, and the FT-IR spectra of compounds (B1-B6) confirm the synthesis of amide by the presence of N-H absorption in the region of 3456-3340 cm^{-1} . Moreover, $\nu(\text{C}=\text{O})$ shifted from the acid chloride region 1775 and 1728 cm^{-1} to the amide carbonyl region 1643-1635 cm^{-1} , these results agreed with the data presented in the literature^{22,23}. Other bands are listed in Table 6 and Fig. 3,4. $^1\text{H-NMR}$ spectrum of compound [B3] showed signals at δ 1.44 ppm of (s, 3H, CH_3), δ 2.72 ppm of (s, 3H, $\text{CH}_3\text{-O}$), δ 4.23ppm of (s, 1H, NH), δ 5.43ppm of (s, 2H, NH_2), δ 8.47ppm of (1H, s, $\text{NH-C}=\text{S}$), δ 8.57ppm of (1H, s, $\text{NH-C}=\text{O}$), δ 7.07-7.72 ppm of (m, 5H, ArH), in Fig. 10, while ^{13}C NMR in δ (ppm) spectrum proved the synthesis of

compound (B3) by the presence of ($\text{C}=\text{S}$) in 157 ppm, ($\text{C}=\text{O}$) in 175 ppm, and ten aromatic carbon appeared at 118-136 ppm, Fig. 11. The NMR spectrum of other compounds is displayed in Table 9 and Table 10. A new series of substituted Oxadiazole was prepared in this part by the cyclization reaction of compounds (B1-B6) using POCl_3 as a ring-closing agent. The general reaction was shown in Scheme 1. The FT-IR spectra of compounds (C1-C6) confirm the synthesis of Oxadiazole ring by the disappearance of ($\text{C}=\text{O}$) absorption and the presence of (C-O-C Oxadiazole) absorption in the region of (1124,1114-1062,1037 cm^{-1}). Other bands are listed in Table 7 and Fig. 5. $^1\text{H-NMR}$ spectrum of compound [C3] showed signals at δ 1.85 ppm of (s, 3H, CH_3), δ 3.45 ppm of (s, 2H, CH_2), δ 3.12ppm of (s, 3H, $\text{CH}_3\text{-O}$), δ 5.34ppm of (s, 2H, NH_2), δ 7.10-7.89 ppm of (m, 5H, ArH). $^{13}\text{C-NMR}$ spectrum in δ (ppm) of compound (C1) exhibited the signals for carbon Oxadiazole in 162.-168 ppm, and aromatic carbon appeared at 115-141 ppm, other bands are listed in the Table 10.

Table 6. FT-IR Spectral data of synthesized compounds (B1-B6) in cm^{-1}

Comp. No.	$\nu\text{N-H}$	νNH_2	$\nu\text{C-H}$ Aromatic	$\nu\text{C-H}$ Aliphatic	$\nu\text{C=O}$ of amide	$\nu\text{C=C}$ aromatic	$\nu\text{C-N}$	Others
B1	3456	3340,3305	3012	2848,2823	1640	1546	1361	
B2	3367	3263,3179	3005	2982,2880	1643	1600,1492	1345	C=O lactam 1670
B3	3452	3350,3302	3140,3012	2920,2868	1635	1597,1496	1361	C-O 1215,1130
B4	3340	3305, 3159	3012	2980,2846	1640	1548,1496	1391	O-H 3448
B5	3435	3385, 3302	3107	2935,2845	1635	1548	1365	C-Cl 1120
B6	3433	3340, 32	3012	2930,2845	1641	1554	1387	C=O lactam 1678 C=N 1627

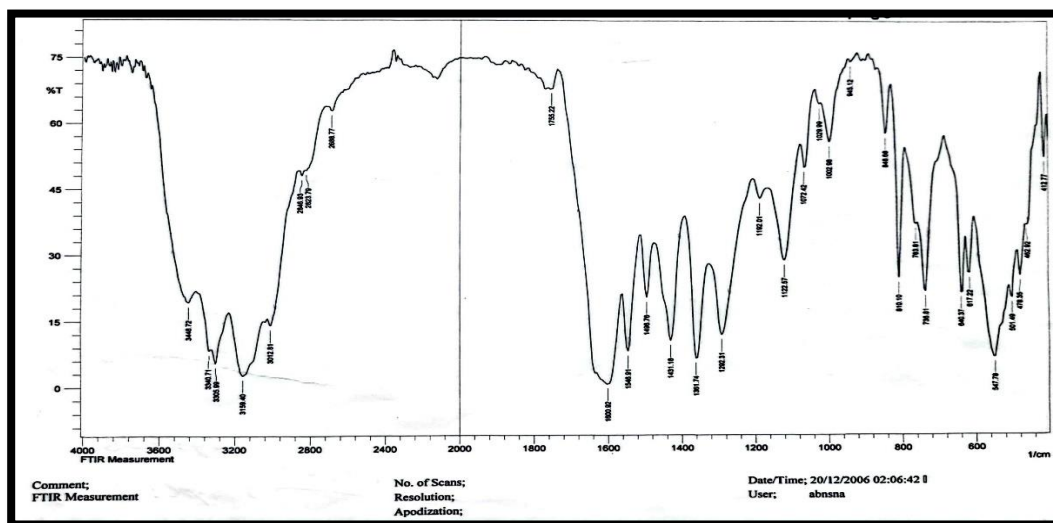


Figure 3. FTIR spectrum for compound (B4)

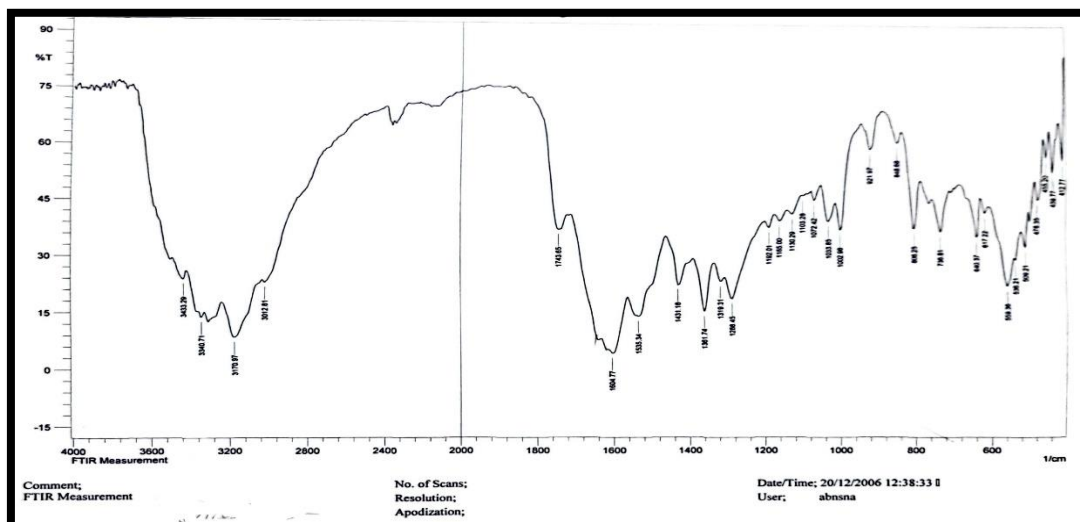


Figure 4. FTIR spectrum for compound(B6)

Table 7. FT-IR Spectral data of synthesized compounds (C1-C6) in cm^{-1}

Comp. No.	$\nu\text{N-H}$	νNH_2	$\nu\text{C-H}$		$\nu\text{C=N}$	$\nu\text{C=C}$	C-O-C	Others
			Aromatic	Aliphatic				
C1	3431	3281, 3198	3002	2975, 2842	1637	1558	1118, 1037
C2	3433	3404, 3259	3010	2977, 2891	1635	1573	1114, 1056	C=O lactam 1676
C3	3421, 3369	3004	2995, 2892	1629	1568	1122
C4	3377, 3211	3008	2990, 28	1633	1568	1124, 1062	ν O-H, 3438
C5	3433	3310, 3191	3012	2935, 2887	1633	1575	1118	ν C-Cl, 1108
C6	3436	3415, 3259	3001	2978, 2890	1631	1575	1118, 1060	ν C=O lactam 1697

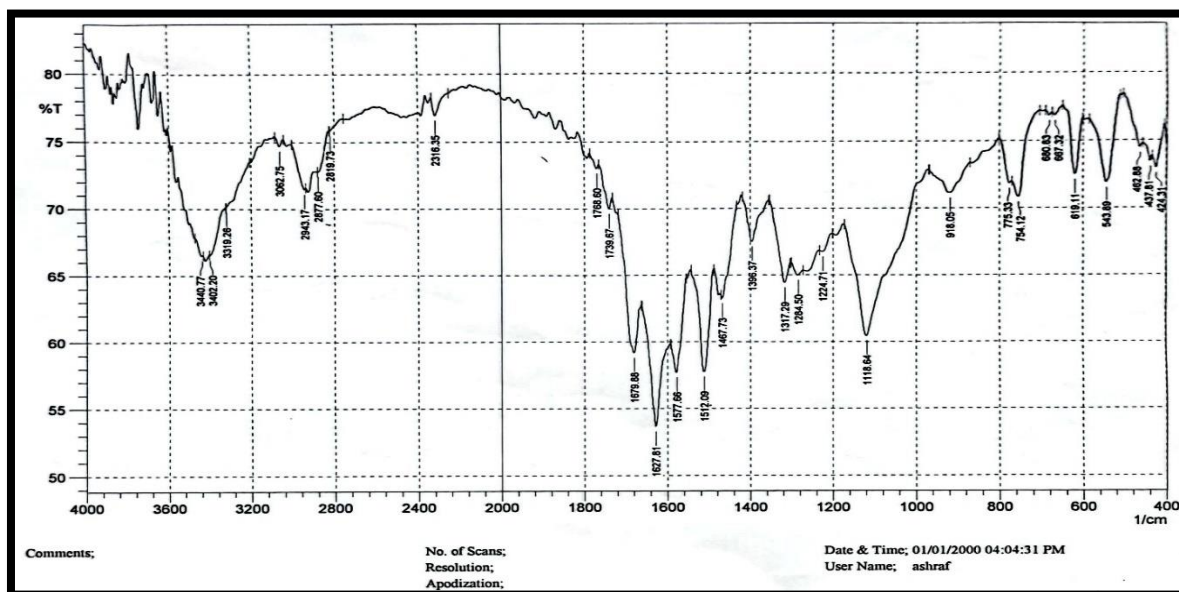


Figure 5. FTIR spectrum for compound (C4)

Table 8. FT-IR Spectral data of synthesized compounds (D1-D6) in cm^{-1}

Comp. No.	$\nu\text{N-H}$	$\nu\text{C-H}$ Aromatic	$\nu\text{C-H}$ Aliphatic	$\nu\text{C=O}$	$\nu\text{C=C}$ aromatic	C-O-C Oxadiazol	Others
D1	3396	3072	2941, 2870	1681	1577, 1473	1120
D2	3286	3060	2923, 2881	1679	1577, 1465	1108, 1046	νNH_2 , 3367, 3309 $\nu\text{C=O}$ lactam, 1724
D3	3236	3058	2920, 2889	1674	1573, 1473	1118
D4	3218	3072	2947, 2872	1679	1573, 1512	1089	$\nu\text{O-H}$, 3422
D5	3402	3062	2943, 2877	1679	1577, 1512	1118	C-Cl
D6	3278	3037	2943, 2879	1676	1579, 1473	1116	overlap with (C-O-C) νNH_2 , 3409, 3355 C=O lactam 1720

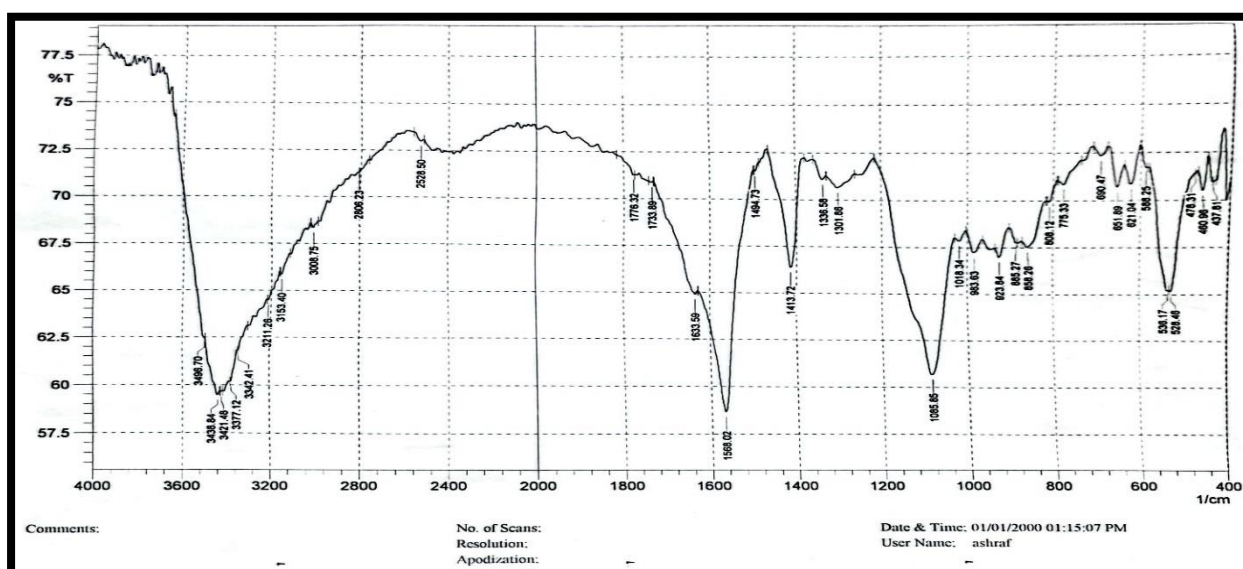
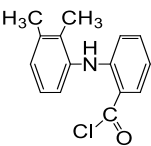
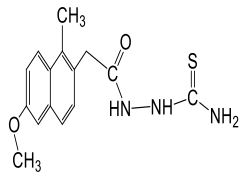
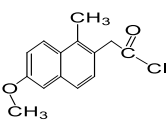
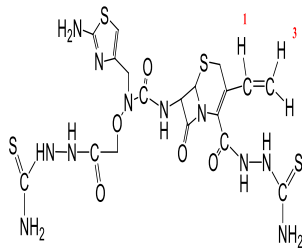
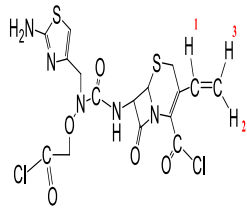
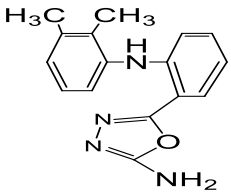
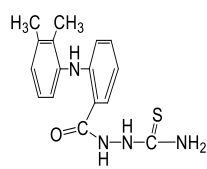
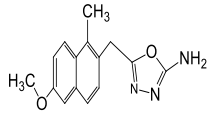


Figure 6. FTIR spectrum for compound (D5)

Table 9. ¹H-NMR data for some compounds in ppm.

Comp. No.	Compound structure	¹ H-NMR data in ppm	Comp. No.	Compound structure	¹ H-NMR data in ppm
A1		δ 1.23(s, 3H, CH ₃), δ 2.09 (s, 3H, CH ₃), δ 4.23 (s, 1H, NH) δ 6.69-8.78(m, 7H, ArH),	B3		δ 1.44(s, 3H, CH ₃), δ 2.72(s, 3H, CH ₃ -O), δ 3.38(s, 2H, CH ₂), δ 5.43(s, 2H, NH ₂), δ 8.47 (1H, s, NH-C=S), δ 8.57 (1H, s, NH-C=O) , δ 7.07-7.72(m, 5H, ArH), δ 1.24-1.31(m, 2H, CH ₂ -S), δ 3.11 (s, 2H, CH ₂ -N), δ 3.32(s, 2H, CH ₂ -C=O), δ 4.22(s, 1H, CH-C=O), δ 4.40(s, 1H, CH-N), δ 4.20 (dd, 1H, H-2), 4.49(dd, 1H, H-3), δ 7.18(dd, 1H, H-1), δ 7.25(s, CH-S), δ 7.54(s, 1H, NH ₂ - C=S), δ 7.59 (s, 1H, NH ₂) δ 8.62 (s, 1H, NH- C=S) δ 9.62 (s, 1H, NH- C=O)
A3		δ 1.45(s, 3H, CH ₃), δ 2.40 (s, 3H, CH ₃ -O), δ 3.81 (s, 2H, CH ₂) δ 7.13-7.81(m, 5H, ArH),	B6		δ 1.33-1.75(m, 2H, CH ₂ -S), δ 3.38 (s, 2H, CH ₂ -N), δ 3.88(s, 2H, CH ₂ -C=O), δ 4.81(s, 1H, CH- C=O), δ 3.90(s, 1H, CH-N), 4.10 (dd, 1H, H-2), 4.96(dd, 1H, H- 3), δ 7.33(dd, 1H, H-1), δ δ 7.5(s, CH-S), δ 7.71(s, 1H, NH ₂) δ 9.71(s, 1H, NH- C=O)
A6		δ 7.33(dd, 1H, H-1), δ δ 7.5(s, CH-S), δ 7.71(s, 1H, NH ₂) δ 9.71(s, 1H, NH- C=O)	C1		δ 2.10(s, 3H, CH ₃), δ 2. 25 (s, 3H, CH ₃), δ 4.12 (s, 1H, NH), δ 5.05 (s, 1H, NH ₂) δ 7.05- 8.11(m, 7H, ArH),
B1		δ 2.24(s, 3H, CH ₃), δ 3.33(s, 3H, CH ₃), δ 4.49(s, 1H, NH), δ (s, 1H, NH ₂) δ 8.78 (1H, s, NH-C=S), δ 9.47 (1H, s, NH- C=O), δ 6.69- 8.45(m, 7H, ArH),	C3		δ 1.85(s, 3H, CH ₃), δ 3.45(s, 2H, CH ₂), δ 3.12(s, 3H, CH ₃ -O), δ 5.84(s, 2H, NH ₂), δ 7.10-7.89(m, 5H, ArH)

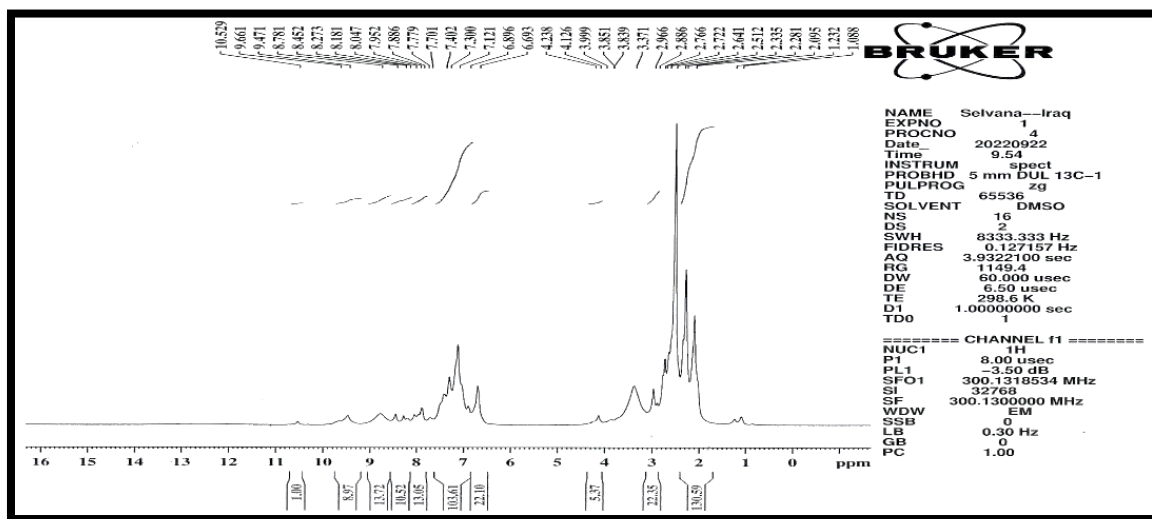


Figure 7. ¹H NMR spectrum for compound (A1)

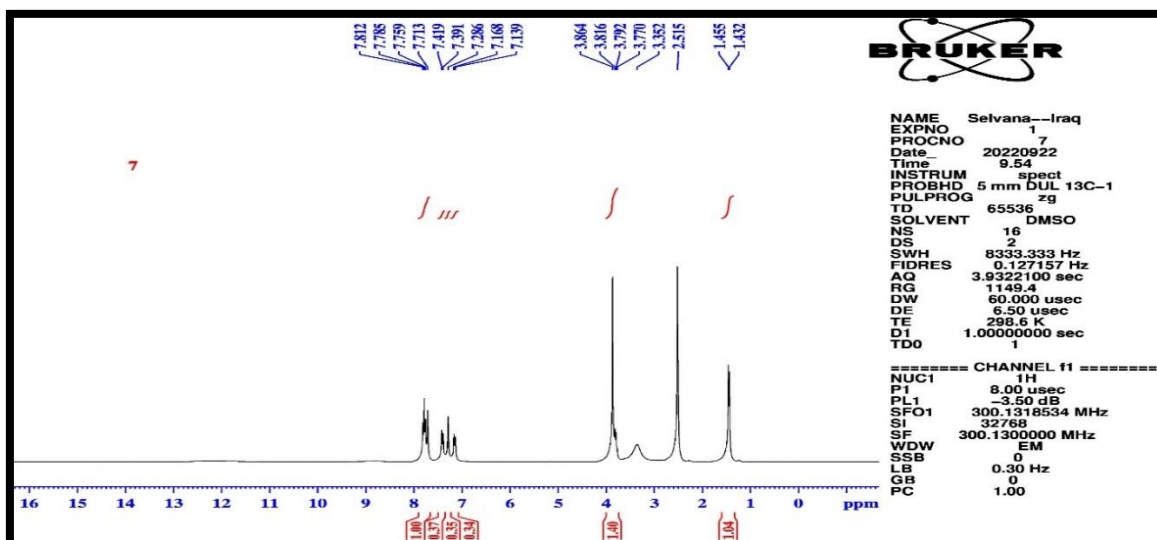


Figure 8. ¹H NMR spectrum for compound (A3)

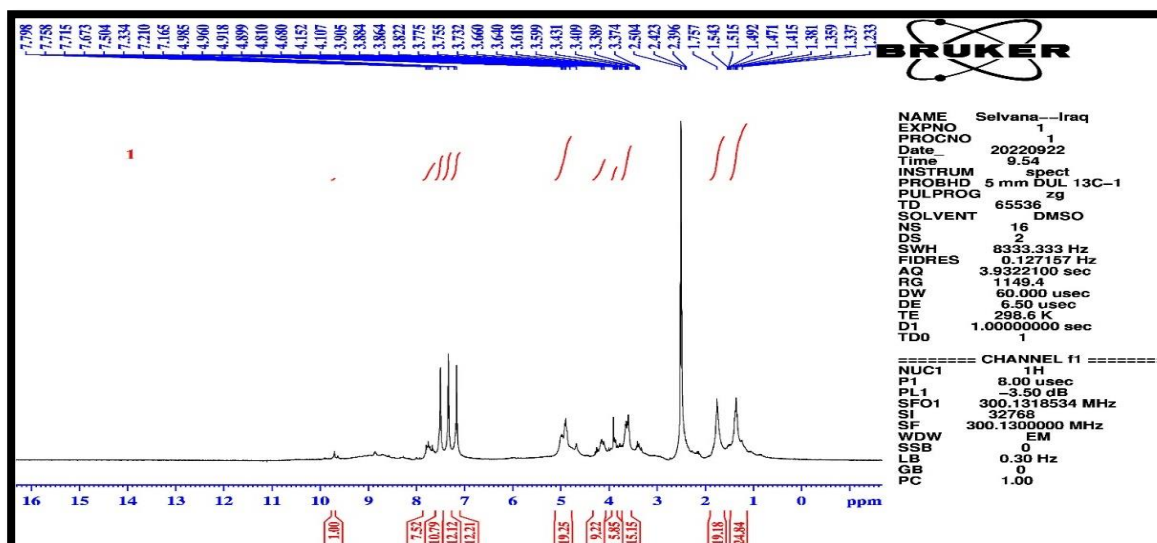


Figure 9. ¹H NMR spectrum for compound (A6)

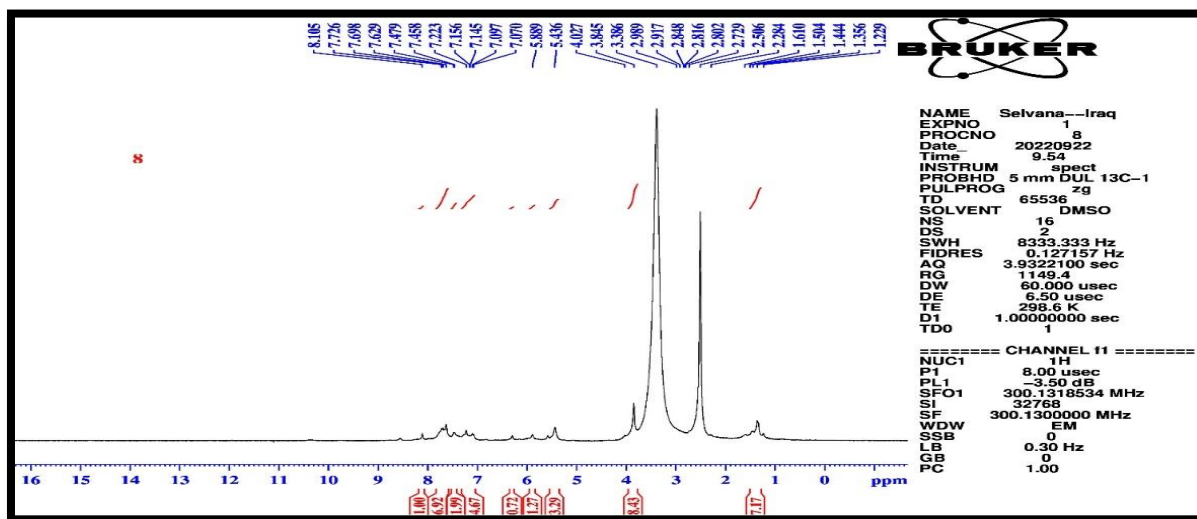


Figure 10. ¹H NMR spectrum for compound (B3)

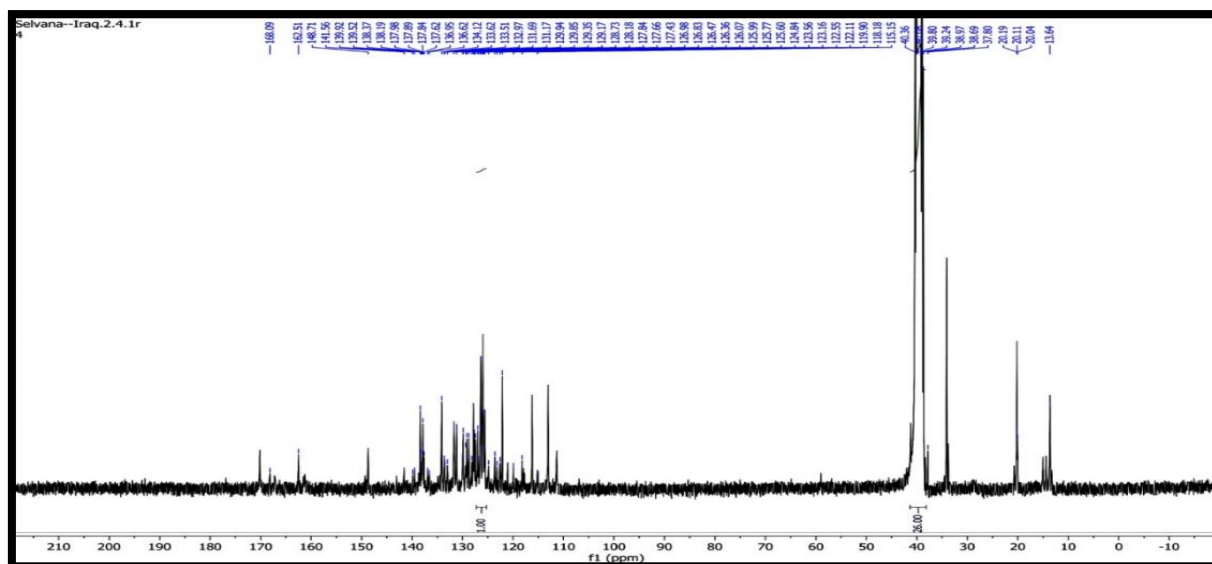


Figure 11. ¹³C NMR spectrum for compound (B3)

Table 10. ¹³C NMR data for some compounds in ppm.

Comp. No.	Compound structure	¹³ C NMR data in ppm	Comp. No.	Compound structure	¹³ C NMR data in ppm
B1		C1=18.44, C2=22.32, [C3, C4, C5, C6, C7, C8, C9, C10, C11, C12, C13, C14] =117.89-132.79, C15=162.45, C16=169.56	A4		C1=98.32, C2, C3, C4, C5, C6, C7, C8, C9, C10, C11, C12, C13=118.22-1339.87, C14=178.45
C1		C1=13.64; C2=20.11; [C3, C4, C5, C6, C7, C8, C9, C10, C11, C12, C13, C14] =115.15-141.69, C15=162.51, C16=168.09	B3		C1=18.41; C2=39.50; C3=44.97; [C4, C5, C6, C7, C8, C9, C10, C11, C12, C13] =118.64-136.30, C14=157.08, C15=175.41

The final step in the strategy is building is the creation of new Mefenamic acid derivatives consisting of condensation of the Mefenamic acid chloride with the compounds (C1-C6). Spectral data for this set of compounds indicates the synthesis of a new amide group that corresponds to the (C=O) by the presence in the region of (1681-1674 cm^{-1})

Conclusion

In this study, a facile method for the modification of six drug derivatives by incorporating the oxadiazole ring within the formulation of the drug. Oxadiazol derivatives prepare by the cyclization reaction of (B1-B6) using

and the spectra showed clear absorption bands due to ν (C-H aromatic), ν (N-H) and ν (C-O-C) appeared about at [(3001-3085 cm^{-1}), (3218-3402 cm^{-1}) and (1118-1124), (1037-1062) cm^{-1}] respectively, others bands are listed in Table 8 and shown in Fig. 6.

Acknowledgment

I would like to express my sincere gratitude to the College of Science for Women.

Author's Declaration

- Conflicts of Interest: None.
- I hereby confirm that all the Figures and Tables in the manuscript are mine. Furthermore, any Figures and images, that are not mine, have been included with the necessary permission for re-publication, which is attached to the manuscript.
- Authors sign on ethical consideration's approval.

POCl₃ as a ring-closing agent. It should be noted that the chemical structure of these modification drugs may be important in creating different effects in some biological models.

- Ethical Clearance: The project was approved by the local ethical committee at University of Baghdad.
- No animal studies are present in the manuscript.
- No human studies are present in the manuscript.
- No potentially identified images or data are present in the manuscript.

References

1. Al-Bayati Y K, Aljabari F I. Mefenamic Acid Selective Membranes Sensor and Its Application to pharmaceutical Analysis. *Baghdad Sci J* 2016; 13(4): 829-837. <http://dx.doi.org/10.21123/bsj.2016.13.4.0829>.
2. Lago EM, Silva MP, Queiroz TG, Mazloum SF, Rodrigues VC, Carnaúba PU, et al. Phenotypic screening of nonsteroidal anti-inflammatory drugs identified Mefenamic acid as a drug for the treatment of schistosomiasis. *EbioMedicine*. 2019; 43: 370-379. <https://doi.org/10.1016/j.ebiom.2019.04.029>.
3. Amanullah A, Upadhyay A, Dhiman R, Singh S, Kumar A, Ahirwar DK, et al. Development and Challenges of Diclofenac-Based Novel Therapeutics: Targeting Cancer and Complex Diseases. *Cancers*. 2022; Sep 9; 14(18): 4385. <https://doi.org/10.3390/cancers14184385>.
4. Patel SS, Tripathi R, Chavda VK, Savjani JK. Anticancer potential of Mefenamic acid derivatives with platelet-derived growth factor inhibitory property. *Anti-Cancer Agents in Medicinal Chemistry*. *Anti-Cancer Agents Med*. 2020 May 1; 20(8): 998-1008. <https://doi.org/10.2174/1871520620666200415100614>.
5. Mohammed IA, Kareem, MM. Synthesis, characterization and study of some of new Mefenamic acid derivatives as cytotoxic agents. *Int J Phys Conf Ser: Conf Ser*. 2020; 1664(1): 012081. IOP Publishing. <https://doi.org/10.1088/1742-6596/1664/1/012081>.
6. Thiruchenthooran V, Sánchez-López E, Gliszczyńska A. Perspectives of the Application of Non-Steroidal Anti-Inflammatory Drugs in Cancer Therapy: Attempts to Overcome Their Unfavorable Side Effects. *Cancers*. 2023 Jan; 15(2): 475. <https://doi.org/10.3390/cancers15020475>.
7. Thiruchenthooran V, Sánchez-López E, Gliszczyńska A. Perspectives of the Application of Non-Steroidal Anti-Inflammatory Drugs in Cancer Therapy: Attempts to Overcome Their Unfavorable Side Effects. *Cancers*. 2023 Jan; 15(2): 475. <https://doi.org/10.3390/cancers15020475>.
8. Qassim B, Motelica-Heino M, Morabito D. Uptake of Three Pharmaceuticals by Beans (*Phaseolus vulgaris* L.) from Contaminated Soils. *Baghdad Sci J*. 2020 Sep 1; 17(3): 0733-742. <http://dx.doi.org/10.21123/bsj.2020.17.3.0733>.

9. Al-Jabari M, Khalid I, Sulaiman S, Alawi I, Shilo J. Synthesis, characterization, kinetic and thermodynamic investigation of silica nanoparticles and their application in Mefenamic acid removal from aqueous solution. *Desalin.* 2018 Oct 1; 129: 160-7. <https://doi.org/10.5004/dwt.2018.23083>.
10. Ayoub R, Jarrar Q, Ali D, Moshawih S, Jarrar Y, Hakim M, et al. Synthesis of novel esters of Mefenamic acid with pronounced anti-nociceptive effects and a proposed activity on GABA, opioid and glutamate receptors. *Eur J Pharm Sci.* 2021 Aug 1; 163: 105865. <https://doi.org/10.1016/j.ejps.2021.105865> [Get rights and content.](#)
11. Tarushi A, Geromichalos GD, Kessissoglou DP, Psomas G. Manganese coordination compounds of Mefenamic acid: In vitro screening and in silico prediction of biological activity. *J Inorg.* 2019 Jan 1; 190: 1-4. <https://doi.org/10.1016/j.jinorgbio.2018.09.017>
12. Smolková R, Zeleňák V, Gyepes R, Sabolová D, Imrichová N, Hudecová D, et al. Synthesis, characterization, DNA binding, topoisomerase I inhibition and antimicrobial activity of four novel zinc (II) fenamates. *Polyhedron.* 2018 Feb 15; 141: 230-8. <https://doi.org/10.1016/j.poly.2017.11.052>.
13. Tarushi A, Totta X, Papadopoulos A, Kljun J, Turel I, Kessissoglou DP, et al. Antioxidant activity and interaction with DNA and albumins of zinc-tolfenamato complexes. Crystal structure of [Zn (tolfenamato) 2 (2, 2'-dipyridylketoneoxime) 2]. *Eur J Med Chem.* 2014 Mar 3; 74: 187-98. <https://doi.org/10.1016/j.ejmech.2013.12.019>.
14. Pareek RP. Use of Mefenamic acid as a supportive treatment of COVID-19: a repurposing drug. *Int J Sci Res.* 2020; 9(6): 69. <https://doi.org/10.21275/SR20530150407>
15. Asadpour Behzadi S, Sheikhhosseini E, Ali Ahmadi S, Ghazanfari D, Akhgar M. Mefenamic acid as Environmentally Catalyst for Threecomponent Synthesis of Dihydropyrano [2, 3-c] Chromene and Pyrano [2, 3-d] Pyrimidine Derivatives. *J Appl Chem Res.* 2020 Jul 1; 14(3): 63-73. <https://doi.org/10.1001.1.20083815.2020.14.3.6.2>
16. Alkalidi RAA, Al-Tamimi EO, Al-Shammaree SAW. Synthesis and Identification of New 2-Substituted-1,3,4-Oxadiazole Compounds from Creatinine and Study Their Antioxidant Activities. *J Med Chem Sci.* 2023; 6(6): 1216-122. <https://doi.org/10.26655/JMCHEMSCI.2023.6.2>.
17. uczynski M, Kudelko A. Synthesis and Biological Activity of 1, 3, 4-Oxadiazoles Used in Medicine and Agriculture. *Appl Sci.* 2022 Apr 8; 12(8): 3756. <https://doi.org/10.3390/app12083756>.
18. Rasheed A, Ashok Kumar CK. Tyrosine and glycine derivatives as potential prodrugs: design, synthesis, and pharmacological evaluation of amide derivatives of Mefenamic acid. *J Enzyme Inhib Med Chem.* 2010 Dec 1; 25(6): 804-11. <https://doi.org/10.1080/87559129.2021.2014861>.
19. Khammas SJ, Hamood AJ. Synthesis, Cytotoxicity, Xanthine Oxidase Inhibition, Antioxidant of New Pyrazolo {3, 4 d} Pyrimidine Derivatives. *Baghdad Sci J.* 2019 Jul 2; 16(4 Supplement): 1003-9. [https://doi.org/10.21123/bsj.2019.16.4\(Suppl.\).1003](https://doi.org/10.21123/bsj.2019.16.4(Suppl.).1003)
20. Amer A, El-Eraky WI, Mahgoub S. Synthesis, characterization and antimicrobial activity of some novel quinoline derivatives bearing pyrazole and pyridine moieties 14th Ibn Sina Arab py moieties Conf Heterocycl Chem Appl, 30 March-2 April 2018; 1-8. Hurgada, Egypt. <https://doi.org/10.21608/ejchem.2018.3941.1345>
21. Bousfield TW, Pearce KP, Nyamini SB, Angelis-Dimakis A, Camp JE. Synthesis of amides from acid chlorides and amines in the bio-based solvent Cyrene™. *Green Chem.* 2019; 21(13): 3675-81. <https://doi.org/10.1039/C9GC01180C>.
22. Zahra U, Saeed A, Fattah TA, Flörke U, Erben MF. Recent trends in chemistry, structure, and various applications of 1-acyl-3-substituted thioureas: a detailed review. *RSC Adv.* 2022; 12(20): 12710-45. <https://doi.org/10.1039/D2RA01781D>.
23. Gandhaveeti R, Konakanchi R, Jyothi P, Bhuvanesh NS, Anandaram S. Unusual coordination mode of aroyl/acyl thiourea ligands and their π -arene ruthenium (II) piano-stool complexes: Synthesis, molecular geometry, theoretical studies and biological applications. *Appl Organomet.* 2019 May; 33(5): e4899. <https://doi.org/10.1002/aoc.4899>.

تحضير وتشخيص بعض مشتقات الاوكساديازول المحضرة من حوامض كربوكسيلية مختلفة

سلفانا أدور يوسف

قسم الكيمياء, كلية العلوم للبنات, جامعة بغداد, بغداد, العراق.

الخلاصة

تم تصميم وتصنيع سلسلة من مشتقات حامض الميفيناميك وتم وصف المنتجات طيفياً باستخدام تقنيات (FT-, ¹³CNMR, ¹HNMR) IR تضمنت السلسلة أ تحويل ستة عقاير (حمض الميفيناميك، الأمبسيلين، النوبروكسين، حمض البنزليك، حمض الديكلوفيناك، والكيفيكس) و المعروفة بفعاليتها الطبية العالية الى كلوريد الحامض ومن ثم تتفاعل مع ثيوسيميكاربازايد لتكوين السلسلة ب وفي المرحلة الثالثة، تم تحضير حلقة الأوكساديازول باستخدام POCl₃ كعامل إغلاق حلقي للمركبات (B1-B6). كانت الخطوة الأخيرة في الاستراتيجية هي بناء مشتقات حامض الميفيناميك الجديدة التي تتكون من تكثيف كلوريد حمض الميفيناميك مع المركبات (C1-C6) لإعطاء مركبات جديد (D1-D6).

الكلمات المفتاحية: اوكساديازول, ادوية كربوكسيلية, تخليق, حامض المينافيمك, غلق حلقي, تخليق