

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

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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, Noproxen, 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 POC13 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

acid (MEF), which was first sold in Mefenamic the 1960s, is still one of the most often prescribed reasonably and priced non-steroidal antiinflammatory (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, 1HNMR and 13C-NMR spectra were recorded on a Bruker specrospin Ultra shield 300 MHZ instrument with (tetramethyl silane, TMS) as an internal standard and (DMSOd6) 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.

~		ical Characterist			· ·	
Comp.	Structure	Chemical	Molecular	Color	M. P. °C	Yield %
No.		Formula	Weight			
A1	H_3C CH_3 H_3C H_3 H_3C H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3 H_3	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	CH ₃ CH ₃ CH ₃	$C_{14}H_{13}ClO_2$	248.70	Light Yellow	135-138	64%
A4	CI O OH CI O	$C_{14}H_{11}ClO_2$	246.69	Brown	Oily	55%
A 5		C14H10Cl3NO	314.59	Brown	105-106	45%
A6	$\begin{array}{c} H_2N,S\\ N&O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ O\\ CI-C\\ O\\ O\\ O\\ O\\ O\\ CI-C\\ O\\ O\\$	C ₁₆ H ₁₅ Cl ₂ N ₅ O ₅ S 2	492.36	Dark Read	Oily	55%

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

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.

Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	М. Р. °С	Yield %
B1	$ \begin{array}{c} H_3C CH_3 \\ \swarrow - H \swarrow \\ O = C H NH_2 \\ H H NH_2 \end{array} $	$C_{16}H_{18}N_4OS$	314.41	Light Brown	Oily	60%
B2		$C_{17}H_{22}N_6O_3S_2\\$	422.52	Dark Yellow	196-198	70%
В3	CH ₃ CH ₃	$C_{15}H_{17}N_3O_2S$	303.38	Dark Brown	Oily	50%
B4	$\dot{C}H_3$ $\langle D - \dot{C} - \langle D - \dot{C} \rangle$ $\langle C - \langle D - \dot{C} \rangle$ $HN - N - C - NH_2$	$C_{15}H_{15}N_3O_2S$	301.36	White	188-190	80%
B5	CI H H N C NH2	$C_{15}H_{14}Cl_2N_4OS$	369.27	Redish Brown	Oily	65%
		$C_{18}H_{23}N_{11}O_5S_4$	601.71	Yellowish Brown	105-106	58%
B6						

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

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 (CI-C6).										
Comp.	Structure	Chemical	Molecular	Color	M. P. °C	Yield %				
No.		Formula	Weight							
C1		$C_{18}H_{18}N_2O$	278.35	Light Brown	Oily	40%				
C2		$C_{19}H_{22}N_4O_3S$	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		$\begin{array}{c} C_{17}H_{14}Cl_2N_2\\ O\end{array}$	333.21	Redish Brown	Oily	30%				
C6	H_2N , S N, N , O , SH_2N, CH_2N, C	C ₂₂ H ₂₃ N ₇ O ₅ S	529.59	Dark Brown	Oily	78%				

Table 3. Physical	Characteristic of	of com	oounds (C1-C6).
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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).

Comp. No.	Structure	Chemical Formula	Molecular Weight	Color	M. P. °C	Yield %
D1	NH NH H ₃ C	C ₃₃ H ₃₁ N ₃ O ₂	501.62	Redish Brown	Oily	40%
D2	H_3C^{-1} H_2N H_2N H	$C_{34}H_{35}N_5O_4S$	609.74	Dark Yellow	Oily	35%
D3		C ₃₂ H ₃ 0N ₂ O ₃	490.59	Lead	235-238	70%
D4		$C_{32}H_{28}N_2O_3$	488.58	Light Brown	Oily	65%
D5	$ \begin{array}{c} & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & $	C ₃₂ H ₂₇ C ₁₂ N ₃ O ₂	556.48	Light Orange	Oily	65%
D6	$\begin{array}{c} H_{3}C,CH_{3}\\ & \begin{array}{c} H_{2}N-N\\ & \end{array} \\ & \begin{array}{c} \\ \\ \end{array} \\ & \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \end{array} \\ & \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \end{array} \\ & \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \end{array} \\ \\ & \end{array} \\ & \begin{array}{c} \\ \\ \end{array} \\ \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \end{array} \\ & \begin{array}{c} \\ \\ \end{array} \\ \\ \end{array} \\ \\ \\ \end{array} \\ \\ \\ \end{array} \\ \\ \\ \end{array} \\ \\ \\ \\ \end{array} \\ \\ \\ \end{array} \\ \\ \\ \end{array} \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	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 v(C=O) of acid absorption bands indicating the success of the reaction and the acid chloride formation. The spectra showed clear absorption bands due to [v (C-H aromatic), v (C=O), v (N-H)] appeared about at [(3001-3085)cm⁻¹, (1650-1757)cm⁻¹ and (3282-3323)cm⁻¹] respectively, others bands are listed in Table 5 and shown in Fig. 1,2 .¹H-NMR spectrum

of compound [A3] showed signals at $\delta 1.23$ ppm of (s, 3H, CH₃), δ 2.09 ppm of (s, 3H, CH₃), δ 4.23ppm of (s, 1H, NH), δ 6.69-8.78ppm of (m, 7H, ArH) as listed in Table 9 and shown in Fig. 7,8,9, while ¹³C-NMR spectrum in δ (ppm) of compound (A4), Table 10, exhibited the signals for carbon (C=O) in 178 and twelve aromatic carbon appeared at 118-139 ppm.

	140		peetial aata of	sy nemesized	. compounds (i	·····	
Comp.	υN-H	vC-H	υС-Н	vC=O of	vC=C	υC-N	Others
No.		Aromatic	Aliphatic	acid	aromatic		
A1	3313	3066	2975, 2862	1650	1575,1448	1328	
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-0
							1228, 1159
A4		3045	2957, 2845	1752	1583	1384	υOH
							3412
A 5	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

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



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) by attacking amine from mechanism the thiosemicarbazide group on carbonyl group in acyl chloride; then followed by leaving the chloride ion to form the acyl thiosemicarbazide ¹⁹. 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 $3456-3340 \text{ cm}^{-1}$. Moreover, v(C=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. ¹H-NMR spectrum of compound [B3] showed signals at δ 1.44 ppm of (s, 3H, CH₃), δ 2.72 ppm of (s, 3H, CH₃-O), δ 4.23ppm of (s, 1H, NH), δ 5.43ppm of (s, 2H, NH₂), δ 8.47ppm of (1H, s, NH-C=S), δ 8.57ppm of (1H, s, NH-C=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 (C=S) in 157 ppm, (C=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 POCl₃ 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 (C=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. ¹H-NMR spectrum of compound [C3] showed signals at δ 1.85 ppm of (s, 3H, CH₃), δ 3.45 ppm of (s, 2H, CH₂), δ 3.12ppm of (s, 3H, CH3-O), δ 5.34ppm of (s, 2H, NH₂), δ 7.10-7.89 ppm of (m, 5H, ArH). ¹³C-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.

Comp. No.	υN-H	vNH2	υC-H Aromatic	υC-H Aliphatic	vC=O of amide	vC=C aromatic	υC-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	О-Н 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

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





Figure 3. FTIR spectrum for compound (B4)



Figure 4. FTIR spectrum for compound(B6)

Comp.	υN- H	vNH2	vC-H	υС-Н	υC=N	vC=C	С-О-С	Others
No.			Aromatic	Aliphatic		aromatic	Oxadiazol	
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	υ O-H, 3438
C5	3433	3310,3191	3012	2935,2887	1633	1575	1118	υ C-Cl, 1108
C6	3436	3415,3259	3001	2978,2890	1631	1575	1118,1060	υ C=O _{lactam} 1697

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Figure 5. FTIR spectrum for compound (C4)

Table 8. FT-IR Spectral data of synthesized compounds (D1-D6) in cm ⁻¹										
Comp.	υN-H	υС-Н	υC-H	υ C=O	vC=C	С-О-С	Others			
No.		Aromatic	Aliphatic		aromatic	Oxadiazol				
D1	3396	3072	2941, 2870	1681	1577, 1473	1120				
D2	3286	3060	2923,2881	1679	1577,1465	1108,1046	υ NH ₂ , 3367,3309 υ C=O _{lactam} , 1724			
D3	3236	3058	2920,2889	1674	1573,1473	1118				
D4	3218	3072	2947, 2872	1679	1573, 1512	1089	υ O-H, 3422			
D5	3402	3062	2943, 2877	1679	1577, 1512	1118	C-Cl overlap with(C-O-C)			
D6	3278	3037	2943,2879	1676	1579,1473	1116	v NH ₂ , 3409, 3355 C=O _{lactam} 1720			



Figure 6. FTIR spectrum for compound (D5)

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Comp.	Compound	<u>le 9. ¹H-NMR data fo</u> ¹ H-NMR data in	Comp.		¹ H-NMR data in ppm
No.	structure	ppm	No.	Compound structure	
A1		δ1.23(s, 3H, CH ₃), δ2. 09 (s, 3H, CH ₃), δ 4.23 (s, 1H, NH) δ 6.69-8.78(m, 7H, ArH),	B3	CH_3 CH_3 CH_2 CH_3 O HN-NH-C NH_2 O H_2 CH_3	$δ1.44(s, 3H, CH_3),$ $δ2.72(s, 3H, CH_3-O),$ $δ3.38(s, 2H, CH_2), δ$ $5.43(s, 2H, NH_2, δ8.47$ (1H, s, NH-C=S), δ 8.57 (1H, s, NH-C=O) , $δ7.07-7.72$ (m, 5H, ArH), δ1.24 + 21(m, 2H
A3	CH ₃ CH ₃	δ1.45(s, 3H, CH ₃), δ2.40 (s, 3H, CH ₃ -O), δ 3.81 (s, 2H, CH ₂) δ 7.13-7.81(m, 5H, ArH),	B6	$H_2N \xrightarrow{S} H_2N \xrightarrow{S} C = C$	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), $δδ$ 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)
A6	$\begin{array}{c c} H_2N & S \\ N & 0 \\ N & 0 \\ 0 \\ N & C \\ 0 \\ N \\ C \\ C \\ C \\ 0 \\ 0 \\ C \\ C \\ 0 \\ C \\ C$	$\begin{array}{c} \delta \ 1.33\text{-}1.75(\text{m}, 2\text{H},\\ \text{CH}_2\text{-}\text{S}), \ \delta \ 3.38 \ (\text{s},\\ 2\text{H}, \text{CH}_2\text{-}\text{N}), \ \delta \ 3.88(\text{s},\\ 2\text{H}, \text{CH}_2\text{-}\text{C}\text{=}\text{O}), \ \delta \\ 4.81(\text{s}, 1\text{H}, \text{C}\text{H}\text{-}\\ \text{C}\text{=}\text{O}), \ \delta \ 3.90(\text{s}, 1\text{H},\\ \text{C}\text{H}\text{-}\text{N}), \ 4.10 \ (\ dd, 1\text{H},\\ \text{H}\text{-}2), \ 4.96(\text{dd}, 1\text{H}, \text{H}\text{-}\\ 3),\\ \delta \ 7.33(\text{dd}, 1\text{H}, \text{H}\text{-}1),\\ \delta \ \delta \ 7.5(\text{s}, \text{C}\text{H}\text{-}\text{S}), \ \delta \\ 7.71(\text{s}, 1\text{H}, \text{N}\text{H}_2)\\ \delta 9.71(\text{s}, 1\text{H}, \text{N}\text{H}\text{-}\\ \text{C}\text{=}\text{O}) \end{array}$	C1	H_3C CH_3 H_3 H_2 H_3 H_3 H_3 H_3 H_3 H_3 H_2	δ2.10(s, 3H, CH ₃), δ2. 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	$H_{3}C CH_{3}$ $H_{3}C H_{3}$ $H_{3}C H_{3}$ $H_{3}C H_{3}$ $H_{3}C H_{3}$ $H_{3}C H_{3}$ $H_{3}C H_{3}$	$δ2.24(s, 3H, CH_3),$ $δ3.33(s, 3H, CH_3),$ δ4.49(s, 1H, NH), δ (s, 1H, NH2) $δ8.78$ (1H, s, NH-C=S), δ 9.47 (1H, s, NH- C=O), δ 6.69- 8.45(m, 7H, ArH),	C3	H_3C_0 NH_2 NH_2	$\begin{array}{l} \delta 1.85(s,3H,CH_3),\\ \delta 3.45(s,2H,CH_2),\delta\\ 3.12(s,3H,CH_3\text{-}O),\\ \delta 5.84(s,2H,NH_2,\delta\\ 7.10\text{-}7.89(m,5H,ArH) \end{array}$

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Figure 7. ¹HNMR spectrum for compound (A1)



Figure 8. ¹HNMR spectrum for compound (A3)



Figure 9. ¹HNMR spectrum for compound (A6)





Figure 10. ¹HNMR spectrum for compound (B3)



Figure 11. ¹³CNMR spectrum for compound (B3)

Table 10	. ¹³ C NMR	data f	or some	compounds	in p	pm.
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Comp. No.	Compound structure	¹³ CNMR data in ppm	Comp. No.	Compound structure	¹³ CNMR data in ppm
B1	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	C1=18.44,C2=22.32,[C 3,C4,C5,C6,C7,C8,C9, C10.C11,C12,C13.C14]=117.89- 132.79,C15=162.45,C1 6-169.56	A4	$12 \qquad 13 \qquad OH \qquad 3 \qquad 4 \\ 11 \qquad 9 \qquad CI \qquad 0 \qquad 5$	C1=98.32,C2,C3,C4,C5,C 6,C7,C8,C9,C10,C11,C12 ,C13=118.22- 1339.87,C14=178.45
C1	$\begin{array}{c}1 & 2 \\ H_{3}C \\ 3 \\ 4 \\ 7 \\ 6 \\ 10 \\ 16 \\ 16 \\ 16 \\ 12 \\ 12 \\ 12 \\ 12 \\ 12$	C1=13.64; C2=20.11; [C3, C4,C5,C6,C7, C8,C9,C10,C11,C12,C 13, C14] =115.15- 141.69, C15=162.51,C16=168. 09	B3	1 1 1 1 1 1 1 1 1 1 1 1 1 1	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

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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

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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 republication, which is attached to the manuscript.
- Authors sign on ethical consideration's approval.

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and the spectra showed clear absorption bands due to υ (C-H aromatic), υ (N-H) and υ (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.

POC13 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.

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تحضير وتشخيص بعض مشتقات الاوكساديازول المحضرة من حوامض كاربوكسيلية مختلفة

سلفانا أدور يوسف

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

الخلاصة

تم تصميم وتصنيع سلسلة من مشتقات حامض الميفيناميك وتم وصف المنتجات طيفيًا باستخدام تقنيات (FT-. ¹³CNMR, ¹HNMR) تم تصميم وتصنيع سلسلة أ تحويل ستة عقاقير (حمض الميفيناميك ، الأمبيسيلين ، النوبروكسين ، حمض البنزيلك ، حمض الديكلوفينك ، والكيفيكس) و المعروفة بفعاليتها الطبية العالية الى كلوريد الحامض ومن ثم تتفاعل مع ثيوسيميكارباز ايد لتكوين السلسلة ب وفي المرحلة (الكيفيكس) و المعروفة بفعاليتها الطبية العالية الى كلوريد الحامض ومن ثم تتفاعل مع ثيوسيميكارباز ايد لتكوين السلسلة ب وفي المرحلة (الكيفيكس) و المعروفة بفعاليتها الطبية العالية الى كلوريد الحامض ومن ثم تتفاعل مع ثيوسيميكارباز ايد لتكوين السلسلة ب وفي المرحلة الثالثة ، تم تحضير حلقة الأوكساديازول باستخدام POCI 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) لإعلام عالم عالم عنه تكثيف كلوريد حمض الميفيناميك مع المركبات. (20-10).

الكلمات المفتاحية: اوكساديازول, ادوية كاربوكسيلية,تخليق,حامض المينافيمك,غلق حلقي,تخليق.