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Synthesis and study of biological activity of some new Imidazole derivatives

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Abstract:

In this work ester derivatives were synthesized by the reaction of imidazole derivatives (C1) with ethylchloroacetate in ethanol and NaOH to give the corresponding (C2) .While compound (C3) acetohydrazide was synthesized by the reaction of ester derivatives (C2) with hydrazine hydrat in ethanol. Compound (C3) from the reaction with different aromatic aldehydes in absolute ethanol gave the Schiff's bases (C4,C5). The product compounds were characterized by FT-IR, U.V and ^{1}HNMR spectra and the biological activities were studied as antibacterial.

Key words: acetohydrazide, Schiff's bases, Imidazole.

Introduction:

In recent years, heterocyclic compounds had been received considerable attention due to their pharmacological and pesticidal importance [1-9]. The simplest of five - membered heterocyclic compounds are pyrrole , furan and thiophene , each of which contains a single hetero atom [10]. Benzothiophene [11] a class of heterocyclic compounds containing a benzene ring fused with five membered aromatic ring made up of one sulfur as heteroatom with formula C_8H_6S. Benzothiophene undergoes electrophillic aromatic substitution at C-2 and C-3 equally [12] .

Materials and Methods:

Infrared spectra were recorded on (FTIR-8400s Fouriero Trans Form infrared Spectrophotometer Shimadzu). UV Spectra were recorded on UV-Visible spectrophotometer (VARIAN) UV-1650PC. ^{1}H-NMR spectra (Burker DMX -500 NMR spectrophotometer) were recorded on ultra shield 300 MHZ in Jordan, with tetra methyl silane as internal standerd and DMSO as a solvent. Melting points were determined in a(Gallen kamp MFB-600- Melting point apparatus) melting point apparatus with sample contained in open capillary glass tube in a electrically heated metal block apparatus ,and were uncorrected. All chemicalls were supplied from BDH, Merck, Fluka and used without further purification.

Synthesis of 1-amino-2-(3-chlorobe-nzo [b] thiophen-2-yl) -4-(4-(N,N-dimethylami-no) benzylidene)-1H-imidazol-5(4H)-one(C1)

Hydrazine hydrate (99%, 10 ml) was added to a mixture of compound (2-(3-chlorobenzo[b]thiophen-2-yl)-4-(4(dimethylamino)benzylidene)oxazol-5(4H)-one) (0.01 mol) in dry benzene (5 ml). The reaction mixture was refluxed for 20 hrs after cooling the sold product was obtained the desired compound. The physical properties are listed in Table(1) [13] .

Synthesis of ethyl (2-(3-chlorobenzo [b]thiophen-2-yl)-4-(4-(N,N-dimethy-lamino) benzylidene) -5-oxo-4,5-dihydro -1H-imidazol-1-yl)amino) acetate(C2)

The corresponding compound (C1) (3.94 g, 0.01 mol) was refluxed with an equivalent amount(0.04g , 0.01 mol) of NaOH in absolute ethanol for 2 hrs. Then, ethyl chloroacetate (1.36 g, 0.01 mol) was added and refluxed for an additional 5 hrs. After evaporating the solvent under reduced pressure, a solid was appeared and washed with distilled water and recrystallized from ethanol to afford the desired compound [14] .

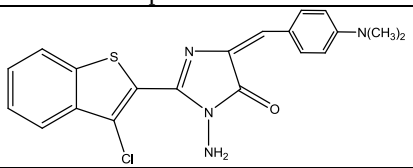
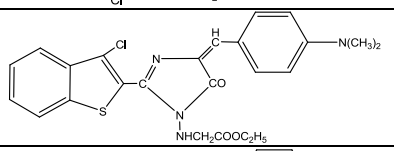
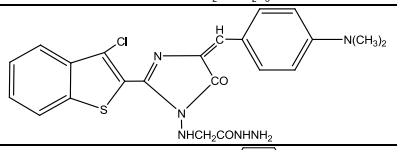
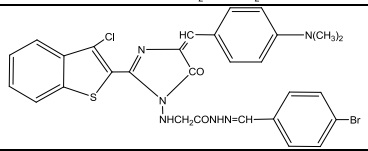
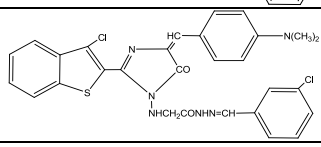
Synthesis of 2-(2-(3-chlorobenzo[b] thiophen-2-yl) -4-(4- (N,N-dimethyla-mino) benzylidene)-5-oxo-4,5-dihyd-ro-1H-imidazol-1-yl)amino)acetohy-drazide (C3)

A mixture of compound (C2) (4.80 g , 0.01mol) and hydrazine hydrate (99%, 0.32 g, 0.01 mole) in ethanol (25 ml) was refluxed for 8 hrs. Upon cooling the solution a solid appeared, and recrystallized from ethanol [15].

Synthesis of N'-(4-bromobenzylidene) -2-(2- (3-chlorob- enzo[b] thiophen-2-yl) -4-(Arylidene) -5-oxo-4,5- dihydro-1H-imidazol-1-yl)amino) acetohydrazide(C4,C5)

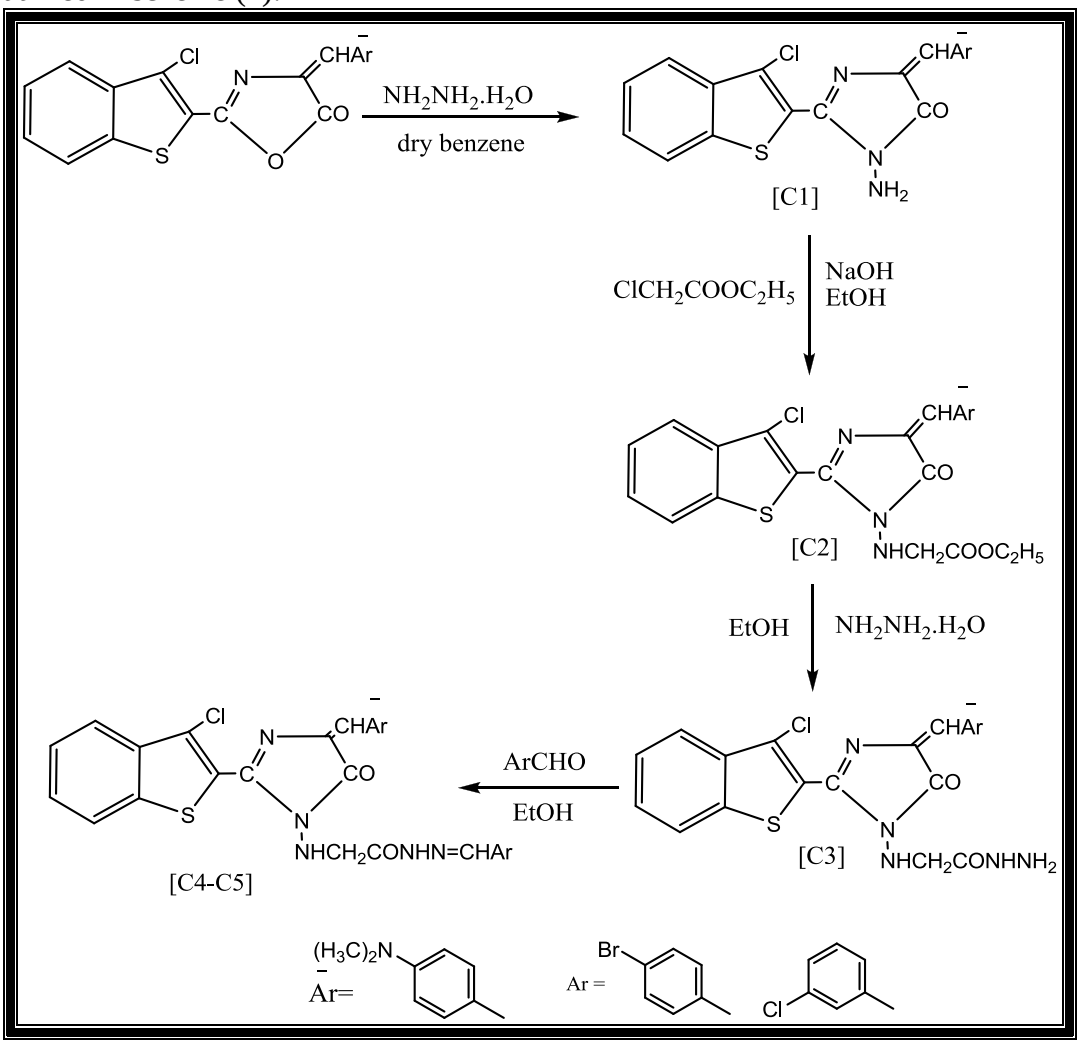
The corresponding aryl aldehyde (0.01 mol) was added to a stirred solution of compound (C3) (4.76 g, 0.01mol) in absolute ethanol (20 ml) and the mixture was refluxed for 8 hrs. After cooling, the mixture was filtered and the solid recrystallized from ethanol to afford the desired compound. The physical properties were listed in Table(1) [16] .

Table (1): Physical properties of compounds (C1 – C5)

Comp. No	Compound structure	Colour	Yield %	M.P
C1		Deep red	86	138-140
C2		brown	87	209-211
C3		orange	73	202-204
C4		yellow	80	213-215
C5		Green-yellow	67	205-207

Results and Discussion:

For the synthesis of the targeted compounds (C1- C5), the reaction sequences are outlined in scheme (1):



Scheme (1): Synthesis imidazole derivatives

Synthesis of 1-amino-2-(3-chlorob-enzo[b] thiophen-yl) -4-(Arylidene) -1H-imidazol -5(4H)-one(C1)

This compound was synthesized when hydrazine hydrate in dry benzene was refluxed with oxazole to give (C1). Titled compound was indicated by the appearance of the stretching vibration bands at(3348) cm^{-1} to NH_2 groups and decreasing of stretching vibration bands at(1664) cm^{-1} to carbonyl group .The product(C1) was confirmed by FT-IR and U.V. spectra. FT-IR spectrum(Fig.1), Table (2) shows the stretching vibration bands at(3348-3229) cm^{-1} due to stretching vibration (asymmetric and symmetric)for (NH_2) group ,band at (3117) cm^{-1} due to for (=CH) group ,band at (3030) cm^{-1} due to aromatic (C-H), band at (1664) cm^{-1} due to(C=O) group, band at(1627) cm^{-1} due to (C=N) group and band at (1599-1525) cm^{-1} due to for aromatic (C=C) . UV spectrum of compound (C1) shows intense maxima at (269 nm) and (327 nm) due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transition, respectively.

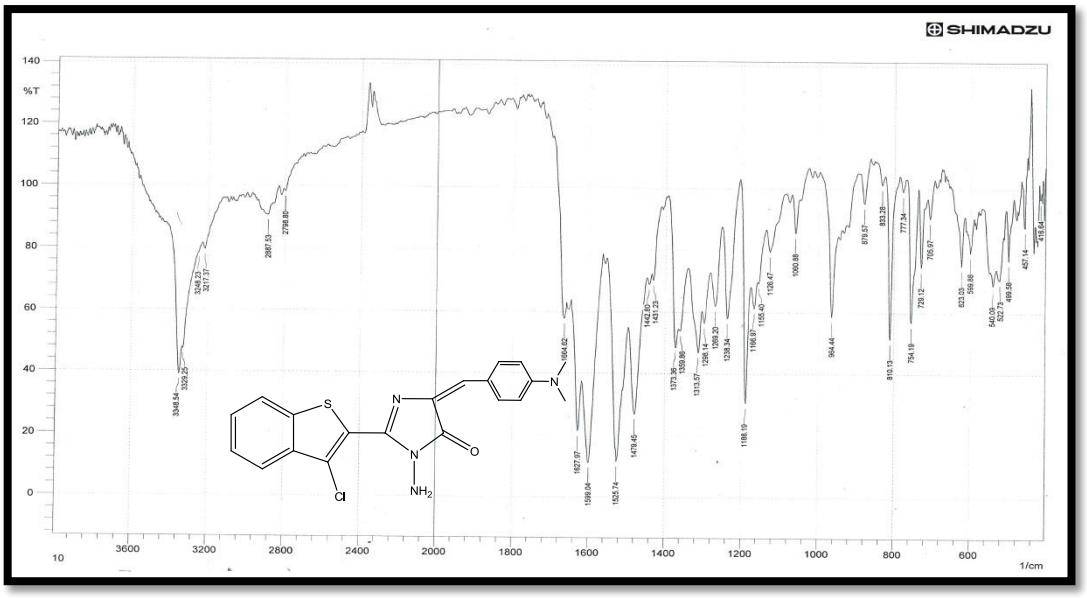


Fig. 1: The FT-IR spectrum of compound (C1)

Synthesis of ethyl 2-(2-(3-chlorobenzo[b]thiophen-2-yl)-4-(4-(dimethylamino) benzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-ylamino)acetate (C2)

Imidazole derivative was synthesized by reaction of compound (C1) with ethylchloroacetate in ethanol to give the corresponding (C2). The formation of titled compounds were indicated by the appearance of the NH stretching vibration band , two carbonyl stretching vibration bands and disappearance of the stretching vibration bands (asymmetric and symmetric) for (NH_2) group. The structure of (C2) was confirmed by FT-IR , U.V and ^{1}HNMR spectrum . FT-IR spectrum (Fig .2) ,Table (2) showed the stretching vibration band at (3340) cm^{-1}due to (NH) group, band at(3064) cm^{-1} due to aromatic (C-H) , band at (2926-2868) cm^{-1} due to aliphatic (CH), band at(1683)cm^{-1} due to(C=O) ,band at (1635) cm^{-1} due to (C=N) and band at (1599-1516) cm^{-1} due to aromatic (C=C) group.UV spectrum of compound (C2) shows intense maximum at (258 nm) and (327 nm) due to $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ electronic transition, respectively.The ^{1}H-NMR of compound (C2) (Fig.3), Table(2) shows the following signals:

- Doublet at(7.89-7.91) ppm due to aromatic proton near $N(CH_3)_2$.
- Doublet at(7.76-7.79) ppm due to aromatic proton far $N(CH_3)_2$.
- Multiplet at (7.34-7.65) ppm due to aromatic proton for benzo[b] thiophene ring.
- Singlet at (6.53) ppm assigned to (=CH) proton.
- Singlet at (5.83) ppm due to ($N-CH_2$) proton.
- Quartet at (5.14) ppm due to (OCH_2) proton.
- Singlet at(4.44) ppm due to (NH) proton.
- Singlet at(2.96) ppm due to aliphatic [$N(CH_3)_2$] proton.
- Triplet (0.9) ppm due to aliphatic(CH_3) proton.

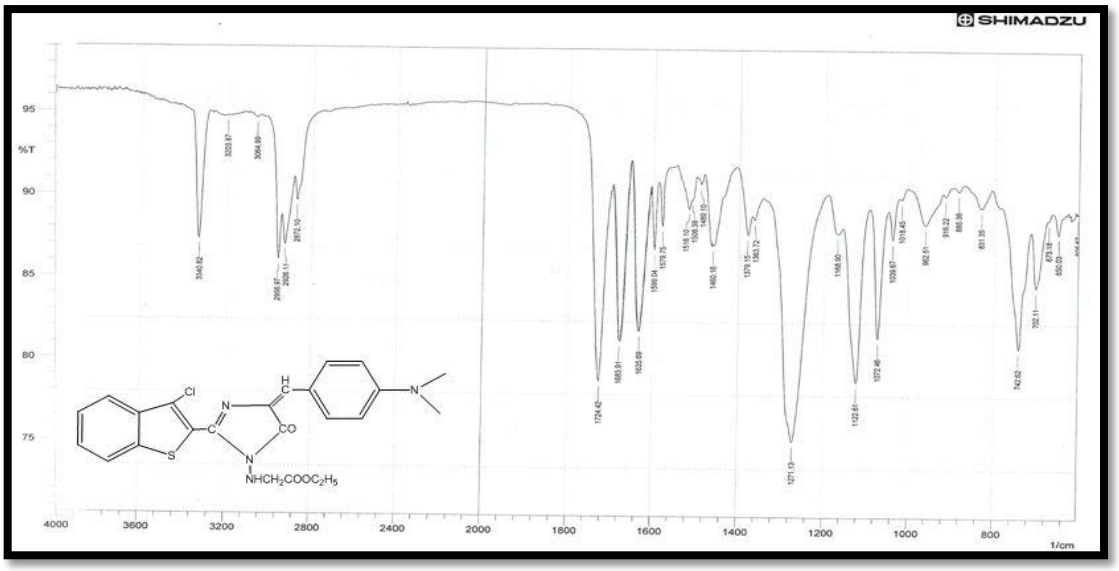


Fig. 2: The FT-IR spectrum of compound (C2)

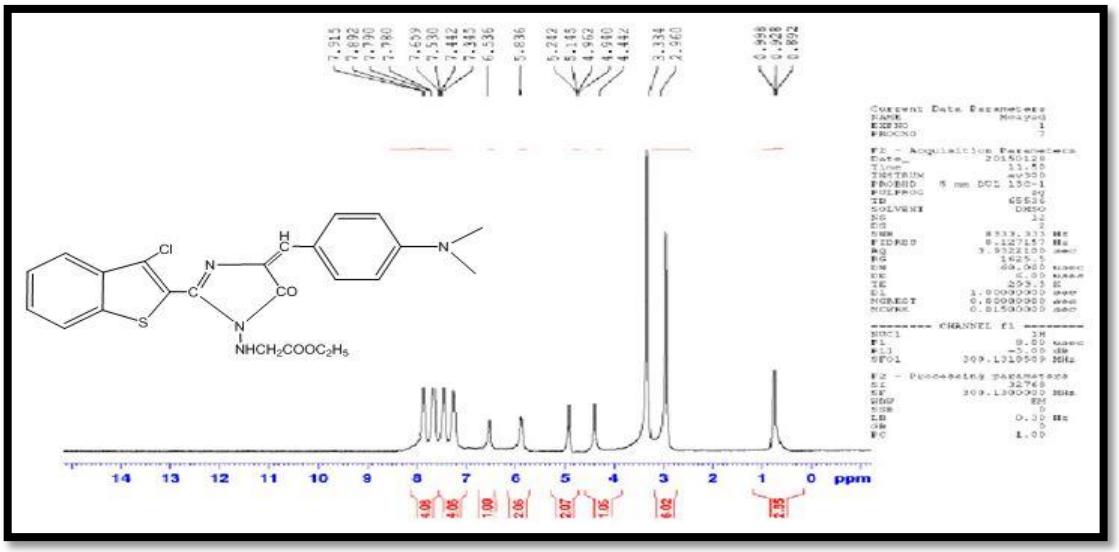


Fig. 3: The ^{1}H-NMR spectrum of compound (C2)

Synthesis of 2-(2-(3-chlorobenzo [b] thiophen-2-yl)-4-(4-(dimethylamino) benzylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-ylamino) acetohydrazide (C3)

Hydrazide was synthesized by the reaction of ester (C2) with hydrazine hydrate in ethanol to give the corresponding (C3). The formation of title compounds was indicated by the appearance of the two NH stretching vibration bands , amidic carbonyl stretching vibration bands and appearance of the NH_2 stretching vibration bands . The structure of (C3) was confirmed by FT-IR and U.V spectra. FT-IR spectrum (Fig .4), Table (2) shows the stretching vibration bands at (3385-3350)cm^{-1} due to (NH_2) groups, band at(3290-3180) cm^{-1} due to(NH) ,band at (3024) cm^{-1} due to aromatic (C-H) ,band at(2990-2835) cm^{-1} due to aliphatic (CH),band at (1681-1668) cm^{-1} due to (C=O) ,band at (1626) cm^{-1} due to (C=N) and band at (1589-1510) cm^{-1} due to aromatic (C=C) group.UV spectrum of compound (C3) shows intense maxima at (238 nm) and (276 nm) due to $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ electronic transition, respectively.

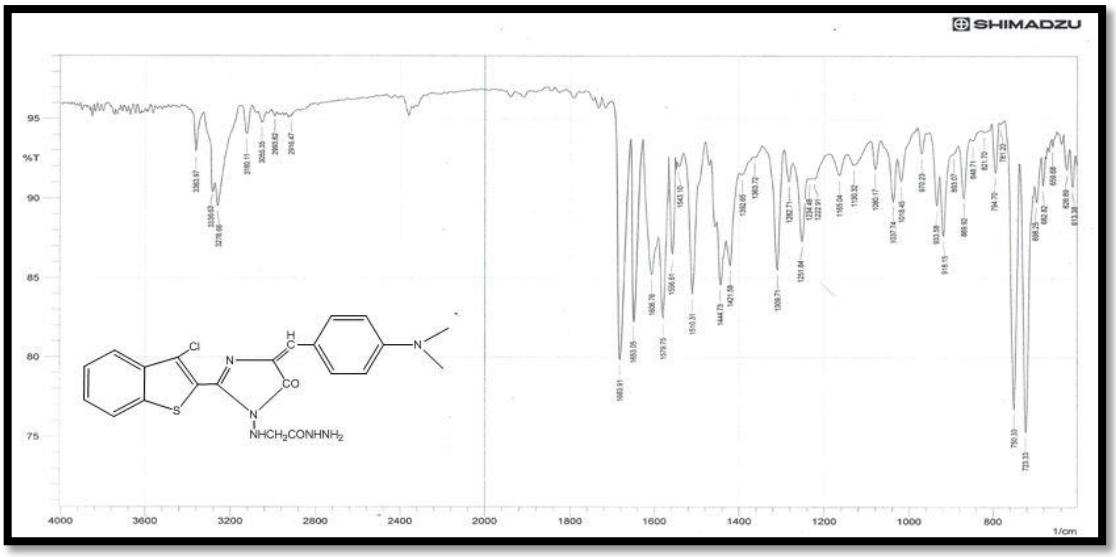


Fig. 4: The FT-IR spectrum of compound (C3)

Synthesis of N'-(4-bromobenzylidene)-2-(2-(3-chlorob-enzo[b]thiophen-2-yl)-4-(Arylidene)-5-oxo-4,5-dihydro-1H-imidazol-1-ylamino)acetohydrazide (C4,C5)

Compound (C3) undergoes the character condensation reaction with different aromatic aldehyde in absolute ethanol to give the Schiff's bases (C4-C5) The formation of these Schiff's bases was indicated by the disappearance of the NH_2 stretching vibration bands.The structure of (C4) was confirmed by FT-IR and U.V spectra . FT-IR spectrum (Fig .5) , Table (2)shows the stretching vibration band at (3265-3235) cm^{-1} due to(NH) , band at (3169) cm^{-1}due to (N=CH),band at (3095) cm^{-1} due to (=CH),band at (3057) cm^{-1} due to aromatic (C-H) ,band at (2935-2870) cm^{-1} due to aliphatic (CH), band at(1688-1660) cm^{-1} due to(C=O) ,band at (1618) cm^{-1} due to(C=N) ,band at (1593-1560) cm^{-1} due to aromatic (C=C) group and band at (858) cm^{-1} due to for (C-Br) group. Spectrum also shows other characteristic bands in Table (2). UV spectrum of compound (C4) shows intense maxima at (255 nm) and (314 nm) due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transition, respectively.

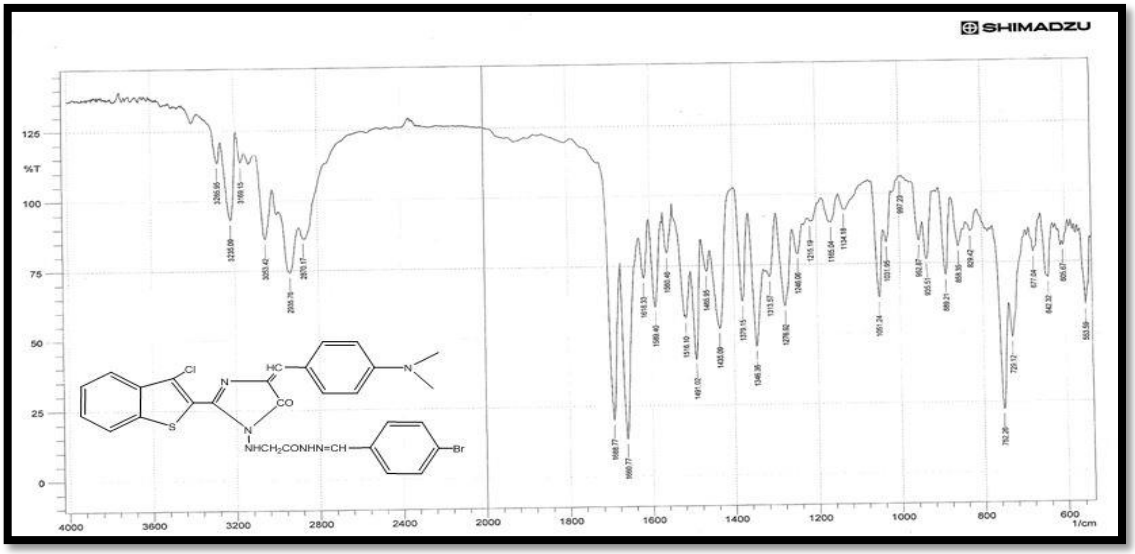


Fig. 5: The FT-IR spectrum of compound (C4)

Table (2): IR and ^{1}H-NMR spectral data for compounds (C1 – C5)

Comp. No	Characteristic IR bands Cm^{-1}							H^1-NMR\ ppm (DMSO\ 300 MHz)
	NH	CH arom	CH aliph	C=O	C=N	C=C arom	other	
C1		3030	2980-2887	1664	1627	1599-1525	3348-3329 (NH_2)	
C2	3340	3064	2926-2872	1724-1683	1635	1599-1516		d(7.89-7.91) near $N(CH_3)_2$, d(7.76-7.79) far $N(CH_3)_2$, m (7.34-7.65) benzo[b] thiophene ring. s (6.53) (=CH) , s (5.83) ($N-CH_2$) q (5.14) (OCH_2), s(4.44) (NH), s(2.96) aliphatic $[N(CH_3)_2]$, t (0.9) aliphatic(CH_3) proton.
C3	3290-3189	3024	2990-2835	1681-1668	1626	1589-1510	(3385-3350) for (NH_2)	
C4	3265-3235	3057	2935-2870	1688-1660	1618	1593-1516	(3169) (N=CH),(858) for (C-Br)	
C5	3363-3224	3055	2947-2868	1680-1662	1626	1591-1514	(3171) (N=CH), (777) for (C-Cl)	

Determination of antibacterial activity:

The effect of (C1-C5) on different microorganisms was studied and compared between them .However ,the results can seen in Table (3) ,(4),(5),(6),which they show that the concentrations (10000,5000,1000,500) µg /ml exhibit very effective inhibition towards the three types of bacteria , *Pseudomonas aeruginosa* and *E.coli* ,gram negative bacteria and *S. aureus* ,gram positive bacteria. In experiment, we found Broad-spectrum antimicrobial activity toward *S.aureus* a maximum of 1-2 cm in (C1- C5) compounds , *E.coli* and *P. aeruginos*a and about 1-2 cm in (C1- C5) compounds.

Table(3) The effect of(C1-C5) (10000) µg/ml represented by inhibition zone (mm) against different bacterial species.

Comp.No	Bacterial species		
	S. aureus	*E.coli*	*P. aeruginosa*
C1	+++	+++	++
C2	++	++	++
C3	++	++	++
C4	+++	+++	+++
C4	++	++	+++

Table(4) The effect of(C1-C5) (5000) µg/ml represented by inhibition zone (mm) against different bacterial species.

Comp.No	Bacterial species		
	S. aureus	*E.coli*	*P. aeruginosa*
C1	+++	+++	++
C2	+++	+++	+++
C3	++	++	++
C4	++	+++	++
C5	+++	+++	+++

Table(5) The effect of(C1-C5) (1000) µg/ml represented by inhibition zone (mm) against different bacterial species.

Comp.No	Bacterial species		
	S. aureus	*E.coli*	*P. aeruginosa*
C1	+++	+++	++
C2	+++	+++	+++
C3	++	++	++
C4	++	+++	++
C5	+++	+++	+++

Table(6) The effect of(C1-C5) (500) µg/ml represented by inhibition zone (mm) against different bacterial species.

Comp.No	Bacterial species		
	S. aureus	*E.coli*	*P. aeruginosa*
C1	+++	+++	++
C2	+++	+++	+++
C3	+++	+++	+++
C4	++	+++	++
C5	+++	+++	+++

(-) No inhibition zone
(+) Inhibition zone between (7-10) mm.
(++) Inhibition zone between (10-15) mm .
(+++) Inhibition zone between (15-20) mm .

References:

[1] Liu, X. H.; Tan, C. X. and Weng, J. Q. 2011. Phase transfer-catalyzed, One-pot synthesis of some novel n-pyrimidinyl -n'- nicotinyl thiourea derivatives. Phosphorus, Sulfur Silicon Relat.Elem,186(3):552–557.

[2] Su, N. N.; Li, Y.; Yu, S. J. ; Zhang, X.; Liu, X. H. and Zhao, W. G. 2013.Microwave-assisted synthesis of some novel 1,2,3-triazoles by click chemistry, and their biological activity. Res. Chem. Intermed, 39(2): 759–766.

[3] Liu, X. H.; Pan, L.; Tan, C. X.; Weng, J. Q.; Wang, B. L. and Li, Z. M. 2011. Synth- esis, crystal structure, bioactivity and DFT calculation of new oxime ester derivatives containing cyclopropane moiety. Pestic. Biochem. Physiol, 101(3):143–147.

[4] Liu, X. H.; Pan, L.; Ma, Y.; Weng, J. Q.; Tan, C. X.; Li, Y. H.; Shi, Y. X.; Li, B. J.; Li, Z. M. and Zhang, Y. G. 2011. Design, synthesis, biological activities, and 3D-QSAR of new N,N'-diacylhydrazines containing2-(2,4-dichlorophenoxy) propane moiety. Chem. Biol. Drug Des, 78(4): 689–694.

[5] Chen, P. Q.; Tan, C. X.; Weng, J. Q. and Liu, X. H. 2012. Synthesis, Structure and DFT calculation of chlorimuron-ethyl. Asian. J. Chem, 24(6):2808–2810.

[6] Liu, X. H.; Weng, J. Q. and Tan, C. X. 2013. Synthesis, crystal structure, and fungicidal activity of 5-(4-cyclopropyl-5-((3-fluorobenzyl)thio)-4H-1,2,4-triazol-3-yl)-4-methyl-1,2,3-thiadiazole. J. Chem, 2013:doi:10.1155/2013/306361.

[7] Tong, J. Y.; Shi, Y. X.; Liu, X. H.; Sun, N. B. and Li, B. J. 2012. Synthesis and fungicidal activity of 1,2,4-triazole derivatives containing 2-fluorophenyl moiety. Chin. J. Org. Chem,32(12):2373–2377.

[8] Weng, J. Q.; Wang, L. and Liu, X. H. 2012. Synthesis, Crystal structure and herbicidal activity of a 1,2,4-triazol-5(4H)-one derivative. J. Chem. Soc. Pakistan, 34(9):1248–1252.

[9] Liu, X. H.; Zhao, W. G.; Wang, B. L. and Li, Z. M. 2012. Synthesis, Bioactivity and DFT structure-activity relationship study of novel 1,2,3-thiadiazole derivatives. Res. Chem. Intermed,38(8):1999–2008.

[10] Marino , G. 1971. Electrophilic substitutions of five-membered rings, Adv. Heterocycl. Chem, 13: 235-314.

[11] Iddon , B. and Scrowston , R. M. 1970. Recent Advances in the Chemistry of Benzo[b]thiophenes, Adv. Heterocycl. Chem., 11:177-183.

[12] Gilchrist, T. L. 1992. Heterocyclic Chemistry, Longman publications, London,2nded,319.

[13] AL. Abodi, A. K.; Majed, N.; Kadhem, S. A. and Al-Bayati, R. H. 2012. Synthesis and Characterization of New 1,3-Oxazol-5-(4H)-one Derivatives, Am . J. Org. Chem, 2(6): 143-150.

[14] Turan-Zitouni, G.; Kaplancikli, Z. A.; Erol, K. and Kiliç, F. S. 1999. Synthesis and analgesic activity of some triazoles and triazolothiadiazines, Farmaco,54(4): 218–223.

[15] Pandey, V. K., Gupta, V. D., Mrinalini Upadhyay, Mridula Upadhyay, V. K. Singh and Meenal Tandon. 2005. Synthesis, characterization and Biological activity of 1,3,4-substituted 2-azatidinones. Indian. J. Chem, 44B(1):158-162.

[16] Hadi , M. A. , Mohammad , L. A. and Hussein, A. A,. 2014. Preparation and Characterization of Some Transition Metal Complexes with (N, S, O) New Schiff Base Ligand, Baghdad. Science. Journal ,11(1):158-164.

تحضيرودراسة الفعالية البايولوجية لبعض مشتقات الايميدازول الجديدة

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الخلاصة:
يتضمن البحث تحضيرمشتقات الاستر بواسطة تفاعل مشتقات الاميدازول (C1) مع خلات كلوريد الاثيل في الايثانول وهيدروكسيدالصوديوم ليعطي (C2).في حين المركب(C3) حضر بواسطة تفاعل مشتق الاستر(C2) مع الهيدرازين المائي في الايثانول . المركب (C3) تفاعل مع الديهايدات اروماتية مختلفة في الايثانول المطلق اعطى قواعد شيف (C4,C5).تم تشيخص المركبات بواسطة اطياف تحت الحمراء وفوق البنفسجية والرنين النووي المغناطيسي و تم دراسة الفعالية البايولوجية للمركبات المحضرة كمضادات للبكتيريا .

الكلمات المفتاحية: اسيتوهايدرازايد ، قواعد شيف ، ايميدازول