RESEARCH ARTICLE

Design, Synthesis and Characterization of Benzoxazepine Thiourea New Derivatives

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ABSTRACT

The thiosemicarbazide reacted with aromatic heterocyclic aldehyde like pyridine-3-carbaldehyde, 1*H*-pyrrole-2-carbaldehyde, furan-2-carbaldehyde in the presence of ethanol with a glacial acetic acids to produce the imine group known as Schiff bases. Which were treated with phthalic anhydride in the presence of dry toluene to produced benzoxazepinethiourea 1-[3-(furan-2-yl)-1,5-dioxo-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVA, 1-[1,5-dioxo-3-(1*H*-pyrrol-2-yl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVB, 1-[1,5-dioxo-3-(pyridin-3-ylmethyl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea inferior vena cava (IVC), as seven-member heterocyclic ring. The synthesised benzoxazepinethiourea derivatives IVC identified by on fourier-transform infrared (FTIR), mass spectral, moreover C,H,N, elemental analysis the structures of synthesized and benzoxazepinethiourea have determined. TLC was used to validate the purity of the compounds.

Keywords: Benzoxazepinethiourea, Characterization, Design, Schiff bases.

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INTRODUCTION

1,3- benzoxazepinethiourea is a seven-member heterocyclic ring containing oxygen atom in position one and nitrogen atom in position three, and the other five carbon atoms.

It is made by adding a two-membered imine group (Schiff bases) to a five-membered anhydride ring such as succinic phthalic, nitrophthalic and maleic anhydrides produce unsaturated seven-member heterocyclic.[1]

Pharmacological functions of some oxazepine and their derivatives are showed antihistamines, anti-cancer, antiviral, analgesic, antifungal, anticonvulsant, antithrombotic, antidepressant, antimicrobial, sedatives, and hypnotics activity.[2]

Furthermore, It has antimicrobial, anti-inflammatory, anti-tubercular, anti-cancer, and anti-psychotic depression properties.[3]

In addition, It is used to treat symptoms of depression, behavioral depression associated with schizophrenia, and other nervous system disorders. It is also used to suppress anxiety and tension states, relieve muscle spasms, and manage acute distress during alcohol withdrawal.[4]

This study aims to synthesize a new derivative of benzoxazepinethiourea via Schiff base with new different aromatic heterocyclic aldehyde and characterized by spectral methods, which are expected to enhance in the biological activity.

EXPERIMENTAL SECTION

Oxazepine and its new derivatives were examined in melting points equipment UK and the MS Model: 5973 Agilent Technology (HP) of Mass spectra. fourier-transform infrared (FTIR) spectra examined in KBr pallet in the 200–4000 cm^{-1} region on an infrared Shimadzu spectrophotometer, C, H, N Elemental equipment analysis were performed on an analyzer of flashing thermo.

Step I: Synthesis of Schiff Bases

In 60 mL ethanol, same moles of thiosemicarbazide (0.01 mole) with various aromatic heterocyclic aldehydes like pyridine-3-carbaldehyde, 1*H*-pyrrole-2-carbaldehyde, furan-2-carbaldehyde (0.01 mole) is dissolved. The mixture refluxed for 8 hours by using some drops of acetic acid glacially as a catalytic agent. After the reaction was over, the mixture was drained onto crushed ice. At temperature of room, the differentiated stock were dried after purified. Re-crystallization from ethanol was used to purify the oil. TLC was used to determine the purity of the compound. The colour was yellow, the yield was 84%, and the melting point range was 140–146 C.as showed in Scheme 1.[1,5-8]

Step II: Synthesis of Oxazepine and its New Derivatives

1-[3-(furan-2-yl)-1,5-dioxo-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVA, 1-[1,5-dioxo-3-(1*H*-pyrrol-2-yl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVB,

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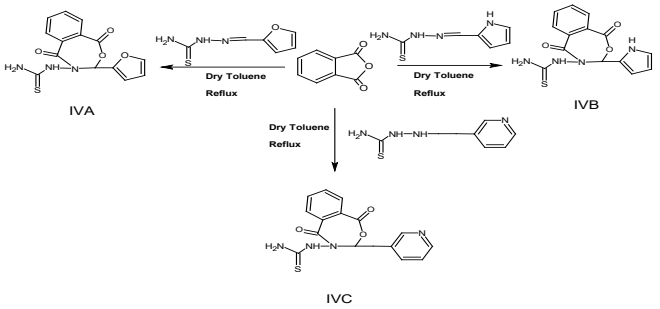
Table 1: Physical properties, Yield, melting point, and Molecular weight of synthesized oxazepine IVC, IVB, IVA

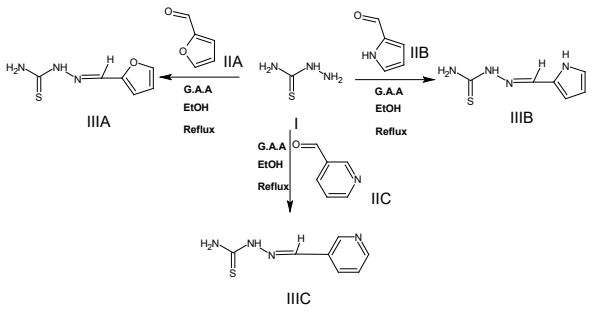
Symbol	*Molecular formula*	*M. W(gm/mole)*	*Color*	*Melting points / °C*	*Yield (%)*
IVA	$C1_4H_{11}N_3O_4S$	317	Deep yellow	140–142	72
IVB	$C1_4H_{12}N_4O_3S$	316	Deep yellow	144–146	75
IVB	$C1_6H_{14}N_4O_3S$	342	Brown	142–144	71

Table 2: Elemental analysis C H N of the synthesized oxazepineIVC, IVB,IVA compounds symbol

		C (%)	*H (%)*	*N (%)*
IVA	Theoretical Data	52.99	3.49	20.17
			3.36	20.03
IVB	practicalData	52.83	3.82	17.71
	TheoreticalData		3.77	17.59
IVC	practicalData	53.16	4.12	16.36
	TheoreticalData	53.04	4.01	16.27
	practicalData	56.13		56.03



Scheme 1: Synthesis of schiff bases



Scheme 2: Synthesis of benzoxazepinethio urea derivatives IVA, IVB, IVC

1-[1,5-dioxo-3-(pyridin-3-ylmethyl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVC synthesized by the following method which In 50 mL of dry toluene,[9-11] same moles (0.02 mole) of Imine group with 0.02 mole of phthalic anhydride The effect was an 8-hour reflux blend. The mixture left to cool to room temperature after the reaction finished. At room temperature, the differentiated stock was purified and dried. Re-crystallization from dioxin filtered the sample.[12-14] The TLC was used to determine the purity of the compound as showed in Scheme 2. The physical occurrence obtained the such as color melting point, molecular formula and finally yield were showed Table I.[5,16,17]

RESULTS AND DISCUSSION

IR, mass spectra of the synthesized oxazepine derivative 1-[3-(furan-2-yl)-1,5-dioxo-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVA, 1-[1,5-dioxo-3-(1*H*-pyrrol-2-yl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVB, 1-[1,5-dioxo-3-(pyridin-3-ylmethyl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVC.

IR, mass spectra of the synthesized oxazepine IVC also support its composition,as described below. Table 1 and 2 display the molecular formula and melting points, as well as instrumena of (C,H,N) for analyses of elemental The final product of benzoxazepinethiourea are obtained a good accordance determined to the suggested design structural formula.

The Mass spectra of 1-[3-(furan-2-yl)-1,5-dioxo-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVA showed molecular ion peaks at 317, 250,234,175,105,77,67 in mass spectral data confirmed the composition of synthesized oxazepine. Correspondence to the $C_{14}H_{11}N_3O_4S$, $C_{10}H_8N_3O_3S$, $C_{10}H_6N_2O_3S$, $C_9H_5NO_3$, C_7H_5O, C_6H_5, C_4H_3O Formula.

The Mass spectra of 1-[1,5-dioxo-3-(1*H*-pyrrol-2-yl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea IVB showed molecular ion peaks at 316, 250,234,175,105,77,64 in mass spectral data confirmed the composition of synthesized oxazepine. Correspondence to the $C_{14}H_{12}N_4O_3S$, $C_{10}H_8N_3O_3S$, $C_{10}H_6N_2O_3S$, $C_9H_5NO_3$, C_7H_5O, C_6H_5 C_4H_4N Formula.

Eventually; FTIR spectra (KBr, cm-1) (Figure 1) of 1-[1,5-dioxo-3-(pyridin-3-ylmethyl)-1,5-dihydro-2,4-benzoxazepin-4(3*H*)-yl]thiourea **IVC** showed 3417 (N-H), 3065 (C-H)Aromatic and 2935 (C-H)Ali, 1670 (C= O)1473 respectively.

The mass spectra and IVC showed molecular ion peaks at 328, 264,205,175,105,77 in mass spectral data confirmed the composition of synthesized oxazepine. C15H12N4O3S, $C_{11}H_{10}N_3O_3S$, $C_{10}H_9N_2O_3$, $C_9H_5NO_3$, C_7H_5O, C_6H_5 Formula (Figure 2).

Result: From the all physiochemical data tabulated in Tables 1 and 2 included C,H,N, elemental analysis, melting point and

IR, mass spectra approve the formation of a seven-membrane ring of oxazepine more over FTIR, mass spectra showed good support to formation the target compound by calculated the molecular weight through the mass spectra.

CONCLUSION

In the present study, benzoxazepinethioureawas synthesized and characterizedby different physical features like melting point and color, by a different spectral technique likeIR,massspectra,also instrumentally by elemental analyses C, H, N. The IR spectra showedthree important bands on 3417, 3065, 2935 which were corresponding to (N-H), (C-H) aromaticand (C-H) aliphatic.that is good support to the formation of benzoxazepinethioureashowedion peak at 328 which is suitable to the molecular weight of synthesized benzoxazepinethiourea derivatives IVC.Elemental analyses C, H, N, showed goodagreement between the theoretical and practical value.Melting pointshowed identification with benzoxazepine derivatives furthermore according to the published articles

According to all and the physical and chemical measurements, we can charecterizedthe structure of the synthesizedbenzoxazepinethiourea1-[3-(furan-2-yl)-1,5-dioxo-1,5-dihydro- 2,4-benz oxazepin-4(3H)-yl]thiourea IVA, 1-[1,5-dioxo-3-(1H-pyrrol-2-yl)-1,5-dihydro-2,4-benzoxazepin-4(3H)-yl]thiourea IVB, 1-[1,5-dioxo-3-(pyridin-3-ylmethyl)-1,5-dihydro-2,4-benzoxazepin-4(3H)-yl]thiourea IVC

REFERENCES

1. Alsafee, Bassam Abdulhussein Hasan, et al. Synthesis and characterization of Cu (II) and Fe (II) metal complexes of oxazepine derivative via Schiff base [Fe (HPOHBOT) Cl2] and [Cu (HPOHBOT) Cl_2]. African Journal of Pharmacy and Pharmacology, 2016;(10)35:728-736.
2. Abbas, Abbas Khudhair; Jber, Nasreen Raheem. Synthesis and Estimation of Biological Activity of New Oxazepine Derivatives. International Journal of Pharmaceutical Research, 2020;(12).2:3750-3758
3. Sallal, Z.; Ghanem, H. Synthesis of New 1, 3-Oxazepine Derivatives Containing Azo Group. Journal of Kufa for Chemical Science, 2011;(2):11-23.
4. Hamak KF, Eissa HH. Synthesis, characterization, biological evaluation and anti corrosion activity of some heterocyclic compounds oxazepine derivatives from Schiff bases. Organic Chemistry: Current Research. 2013 May 1;2(3):1.
5. Hasan BA, Abdulridha MM. Preparation and Characterisation of Sometransation Metal Complexes of New [Butanal (5-Ethyl-1, 3, 4-Oxadia-Zol-2-Yl) Hydrazone]. The Swedish Journal of Scientific Research, 2014;(1)5:23-36.
6. Alsafee BA. Preparation and characterisation of some transition metal complexes of new 4-[(5-ethyl-1, 3, 4-oxadiazol-2-yl) sulfanyl] aniline. The Swedish Journal of Scientific Research. 2014;1(6):11-23.
7. Alsafee, Bassam Abdulhussein Hasan. Preparation and characterization of some transition metal complexes of 4-amino-N-(5-sulfanyl-1, 3, 4-thiadiazol-2-yl) benzenesulfonamide. International Journal of Scientific & Engineering Research, 2015 (6)1:37-45.
8. Abdulridha, Maitham M, Hassan, Bassam A, Hamed, Fadil M. Synthesis and antibacterial evaluation of 1, 3, 4-thiadiazole containing 1, 3, 4-oxadiazole bearing schiff bases. International journal of pharmaceutical research, 2018(4)10:380-388.
9. Alsafee, Bassam Abdulhussein Hasan. Synthesis, Identification and Antibactrial Activity of Some New Heterocyclic Compounds Contaning 1, 3, 4-Thiadiazole and 1, 3, 4-Oxadiazole Bearing Schiff Base. Iraqi National Journal Of Chemistry, 2017(17).2:103-116.
10. Hassan, Bassam A.; Hamed, Fadil Mohsen; ALYASEEN, Firas F. Phytochemical screened, characterization and antibacterial activity of hesperetin and hesperidin extracted and isolated from dried oranges peels. International Journal of Research in Pharmaceutical Sciences, 2018;(9)4:1362-1367.
11. Bassam, A.; Hassan, Hameedi N. Nasera; Maitham, M. Abdulridha. Synthesis and antimicrobial evaluation of fused heterocyclic compound [1, 2, 4] triazolo [4, 3-b][1, 2, 4, 5] tetra zine. International Journal of Research in Pharmaceutical Sciences, 2019(10) 2: 1254-1258.
12. Shalaal, Semma H., Et Al. Maceration Techniques Extraction of Thymus Vulgaris and Laurel (Laurus Nobilis) Leaves with Antibacterial Study. Plant Archives, 2019(19)2: 4041-4044.
13. Bassam A Hassan,Maitham M Abdulridha,Fadil M Hameddesign and Antibacterial Activity of 3,6-Diphenyl-1,5,6,7,8,8 Ahexahydro[1,2,4] Triazolo[4,3-B][1,2,4,5] Tetrazine As Fused Heterocyclic Compounds. Biochem. Cell. Arch. 2020;(20)1: 1499-1502.
14. HAMED, Fadil M., et al. Phytochemical and antimicrobial study of acetone extracts of menthe and olive leaves. The Journal of Research on the Lepidoptera, 2019(50)2:51-56.
15. Mohammed A, Khalid F, Waleed F. Synthesis, Characterization and Kinetic Studies of Some Oxazepine and Oxazepane Derivatives. Journal of university of Anbar for Pure science. 2007;1(3).
16. Abdulridha, Maitham M., et al. Phytochemical And Antibacterial Activity Of The Pegnum Harmala Seeds And Its Alkaloids. Plant Archives, 2019(19)1:1439-1444.
17. Alyaseen, Firas F., et al. Extraction, Isolation and Chemical Identification of Piperine Alkaloid from Black Pepper Seeds and Its Antibacterial Activity. Plant Archives, 2018(18)2:2171-2176.