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Synthesis and identification of Five Membered Rings Heterocyclic Compounds Derived from Trimethoprim

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Abstract

This study includes the preparation and identification of five membered rings Hetrocyclic Compounds derived from Trimethoprim by reaction Schiffs, bases(1a-h)(prepared by reaction some aromatic aldehyde with Trimethoprim using Microwave technique) with Hydroxy acidic acid (Glycolic acid), the prepared compounds were identified by I.R spectroscopy and some of them by NMR spectroscopy and C.H.N.S micro analysis. [DOI: 10.22401/ANJS.00.1.01]

Keywords: Synthesis Four Membered Rings, Heterocyclic, Trimethoprim.

1. Introduction

Heterocyclic Compounds are compounds that contain in their chemical composition a heterogeneous atom of one or more atoms other than carbon atoms from atoms containing heterogeneous rings (N,O,S,P,Si, and As) [1]. Nitrogen, oxygen and sulfur are the most heterogeneous atoms know and dispersed as atoms within these rings, also, heterogeneous ring compounds may be saturated or aromatic in nature depending on their chemical composition [2,3]. These compounds are widespread in nature and are essential for life in multiple forms, such as natural products such as nucleic acids, anthocyanins, flavones and alkaloids in plants, In addition, some vitamins contain heterogeneous ring compounds and proteins containing amidazole and indole rings [4-6], The research carried out by the researchers is the preparation of heterogeneous ring compounds by breaking the (CH = N) bond in Schiff's Bases and Anil compounds and attacking them by other compounds to form new heterogeneous rings. [7]

2. Experimental

Melting points were determined in open glass capillaries and were found uncorrected. The purity of the compounds was checked by TLC. IR spectra were recorded in KBr on Shimadzu infrared Spectrophotometer Fourier Transform FT- IR 8400S. ^{1}H NMR spectra were recorded on a Bruker Ultrashield 400MHZ instrument in DMSO as solvent and TMS as an internal standard. Elemental analysis was carried out on a Eurovectro, EA 3000A, Italy. All reagents were purchased from (Aldrich, Scharlau, Alfa Aesar, Solarbio) and used without further purification.

2.1 Synthesis of Schiffs' bases 2,4-bis (substituted amino)-5-(3,4,5-trimethoxy benzyl) Pyrimidine (1a-h)

A series of Schiff bases were prepared from the reaction of trimethoprim (TMP) (1 mole), with different aldehydes (2 moles), in presence of a few drops of (ethanol absolute and glacial acetic acid). A mixture was transfered to a round bottom flask, and was irradiated in microwave system for (2.5-5) min then the mixture was left to dry for (10-15) day and the formed crystals were filtered and washed with little cold ethanol and dried, the physical and analytical data for the prepared derivatives are shown in Table **(**1**).**

2.2 Synthesis of 2,4-bis(2-(substituted) oxazolidin-3-yl-4-one)5-(3,4,5-trimethoxybenzyl)Pyrimidine (2a-h)

Schiff bases (1a-1l) (0.005 mol) and Glycolic acid (0.76gm, 0.01 mol) was dissolved in 1:4 dioxane (25ml) with constant stirring. The content was transferred to round bottom flask and heated under reflux for 5 hours. The mixture was allowed to cool at room temperature. The solid product was

filtered, washed with ice cold water, dried and re-crystallized from ethanol. [8]. The physical properties data for the prepared derivatives are shown in Table (2**).**

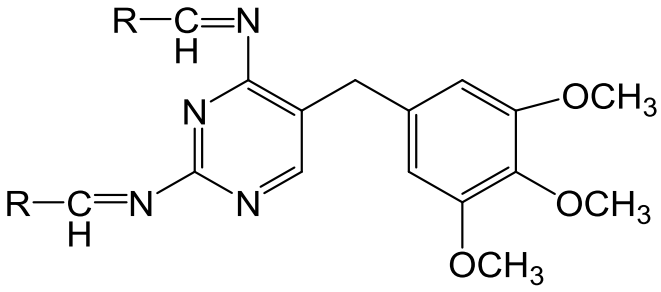
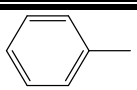
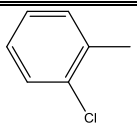
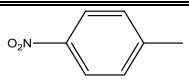
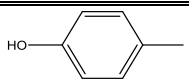
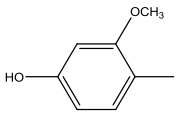
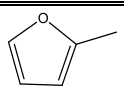
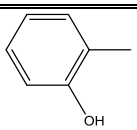
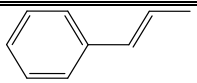


Table (1)
Physical properties of 2,4-bis(substituted amino)-5-(3,4,5-trimethoxy benzyl) pyrimidine (1a-h).

Comp. No.	*R*	*Color*	*Reaction Time min.*	*M.P C°*	*Yield %*
1a		Milky	5.	75-78	82
1b		Yellow Greenish	4	66-69	90
1c		Orange	3	65-67	91
1d		Yellow	4.5	101-103	85
1e		White Green	4	70-73	78
1f		Dark Brown	3	107- 109	86
1g		Orange	3.5	142-145	75
1h		Dark Yellow	2.5	78-80	88

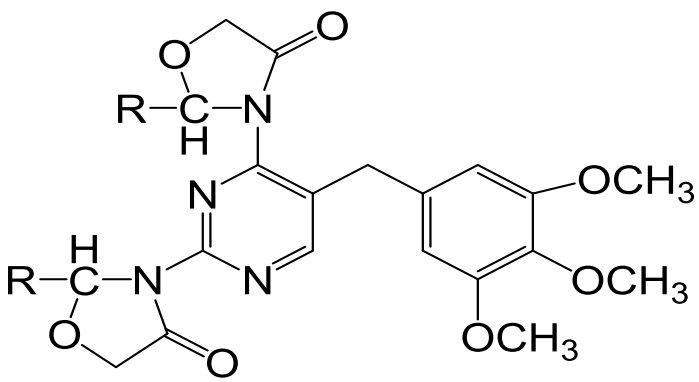
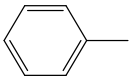
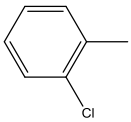
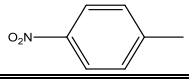
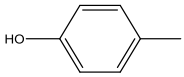
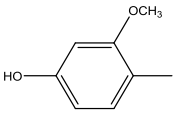
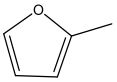
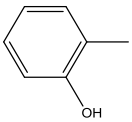
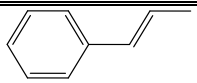


Table (2)
Analytical data 2,4-bis(2-(substituted) oxazolidin-3-yl-4-one) 5-(3,4,5-trimethoxybenzyl) pyrimidine (2a-h).

Comp. No.	*R*	*Color*	*M.P C°*	*Yield %*
2a		White	190-193	75
2b		White	170-172	78
2c		Milky	115-118	83
2d		Dark yellow	170-173	72
2e		Milky	oily	65
2f		Light brown	185 dec	83
2g		light yellow	178-180	79
2h		Light yellow	120-123	85

3. Results and Discussion:

Schiff bases (1a-h) were prepared by mixing of trimethoprim (1) with substituted aromatic aldehydes, the reactions were performed under microwave irradiation. The compounds (1a-h) when reacted with Glycolic acid in 1,4-dioxane gave 3,3'-(5-(3,4,5-trimethoxybenzyl) pyrimidine-2,4-diyl) bis (2-(substituted) oxazolidin-4-one (2a-h). The reactions pathway is shown in Scheme (1). The Schiff bases (1a-h) were then characterized by the elemental analysis, IR spectral studies and ^{1}H-NMR spectral studies. The IR spectra of the Schiff bases are recorded using the KBr disc and showed the prominent band at (1560-1670) cm^{-1} for the azomethine group and the disappearance of band to a group (NH_2) which was shown at (3300-3500) cm^{-1}. The ^{1}H-NMR spectral data of Schiff base (1c) are shown in Table (3) and Fig. (1). These Schiff bases on cyclo-condensation reaction with Glycolic acid afforded oxazolidin-4-one (2a-h) and the structures of compounds (2a-h) have been confirmed by IR spectral studies, some by elemental and ^{1}H-NMR spectral studies, the IR spectrum showed a band at (1654-1690) cm-1 for C=O β-lactam and 1435 (C-O-C oxazolidine) and the ^{1}H-NMR spectral data of oxazolidin-4-one Compound (2a) are shown in Table (3) and Fig. (2) [9,10].

Table (3)
FT-IR, ^{1}H-NMR spectral data for some synthesized compounds.

	Spectra data		*% Analysis*		
	IR-Spectra(cm-1 KBr-pellets)	***^{1}HNMR – Spectra (DMSO) (δ ppm)***	***C (found)***	***H (found)***	***N (found)***
1a	2835cm^{-1} (C-HAlph.) 3045 (νC-HAr.) 1461cm^{-1} (ν C=CAr.), 1610 (νC=N)cm^{-1}				
1b	2937cm^{-1} (C-HAlph.) 3065 (νC-HAr.) 1472cm^{-1} (ν C=CAr.), 1611 (νC=N)cm^{-1}, 724(νC-Cl)				
1c	2915cm^{-1} (C-HAlph.) 3065 (νC-HAr.) 1473cm^{-1} (ν C=CAr.), 1590 (νC=N)cm^{-1}, 1521(NO_2) cm^{-1}	2.5 DMSO 3.33(d,2H,CH_2) 3.52(s,3H,OCH_3) 3.63(s,6H,2OCH_3) 6.27(s,2H,aro) (7,52-7.63) (m,8H,Ar.) 8.63(s,2H,imine.) 9.08 (s,1H,in pyri. cyclic)	(60.43) 60.22	(4.35) 4.48	(15.10) 15.23
1d	2855cm^{-1} (C-HAlph.) 3025 (νC-HAr.) 1462cm^{-1} (ν C=CAr.), 1560 (νC=N)cm^{-1}, 3496 (OH) cm^{-1}				
1e	2870cm^{-1} (C-HAlph.) 3019 (νC-HAr.) 1471cm^{-1} (ν C=CAr.),1590 (νC=N)cm^{-1}, 3310 (OH) cm^{-1}, 1269 (O-C-O) cm^{-1}				
1f	2835cm^{-1} (C-HAlph.) 3007 (νC-HAr.) 1458cm^{-1} (ν C=CAr.),1640 (νC=N)cm^{-1}, 1236 (O-C-O) cm^{-1}				
1g	2870cm^{-1} (C-HAlph.) 3093 (νC-HAr.) 1490cm^{-1} (ν C=CAr), 1615 (νC=N)cm^{-1}, 3331 (OH) cm^{-1}				
1h	2833cm^{-1} (C-HAlph.) 3040 (νC-HAr.) 1450cm^{-1} (ν C=CAr), 1672 (νC=N)cm^{-1}1577 (C=C Alph.) cm^{-1}				
2a	2841cm^{-1} (C-HAlph.) 3100 (νC-HAr.) 1442cm^{-1} (ν C=CAr.),1654 (νC=O)cm^{-1}, 1249(νC-N)cm^{-1}	2.50 DMSO 3.60(s,2H,CH_2) 3.70 (s,3H, OCH_3) 3.83(s,6H,2OCH_3) 4.62(s,4H,CH_2-O) 6.36(s,2H,Ar.) 6.50(s,2H,CH-N.) (7,36-7.64) (m,10H,Ar.) 8.08(s,1H,)			
2b	2830cm^{-1} (C-HAlph.) 3075 (νC-HAr.) 1417cm^{-1} (ν C=CAr.), 1663 (νC=O)cm^{-1}, 1255(νC-N)cm^{-1}				
2c	2841cm^{-1} (C-HAlph.) 3093 (νC-HAr.) 1411cm^{-1} (ν C=CAr.), 1681 (νC=O)cm^{-1}, 1228(νC-N)cm^{-1}, 1553(NO_2)cm^{-1}				

2d	2850cm^{-1} (C-HAlph.) 3077 (νC-HAr.) 1404cm^{-1} (ν C=CAr.),1660 (νC=O)cm^{-1}, 1271 (νC-N)cm^{-1}, 3515(OH)cm^{-1}				
2e	2860cm^{-1} (C-HAlph.) 3024 (νC-HAr.) 1413cm^{-1} (ν C=CAr.),1679 (νC=O)cm^{-1} , 1226 (νC-N)cm^{-1}, 3260(OH)cm^{-1}				
2f	2881cm^{-1} (C-HAlph.) 3015 (νC-HAr.) 1412cm^{-1} (ν C=CAr.),1683 (νC=O)cm^{-1}, 1237 (νC-N)cm^{-1}, 1230(C-O-C)cm^{-1}		(59.78) 59.62	(4.66) 4.79	(9.96) 10.08
2g	2833cm^{-1} (C-HAlph.) 3019 (νC-HAr.) 1416cm^{-1} (ν C=CAr.), 1675 (νC=O)cm^{-1}, 1251 (νC-N)cm^{-1}, 3305(OH)cm^{-1}				
2h	2850cm^{-1} (C-HAlph.) 3015 (νC-HAr.) 1415cm^{-1} (ν C=CAr.), 1690 (νC=O)cm^{-1}, 1246 (νC-N)cm^{-1}, 1566(C=CAlph.)cm^{-1}				

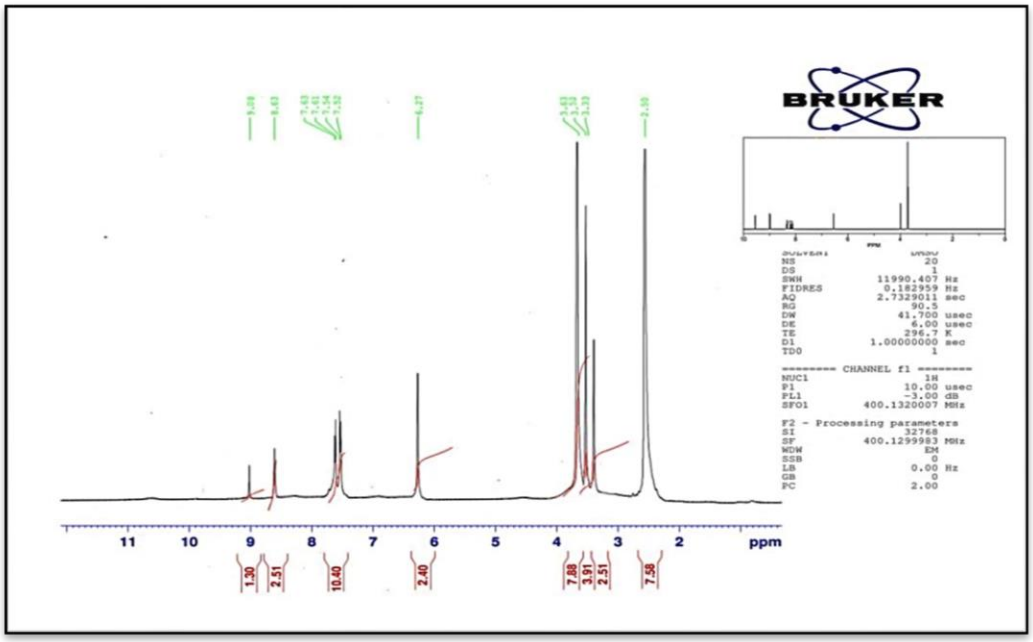


Fig.(1) ^{1}H-NMR spectrum for compound (1c).

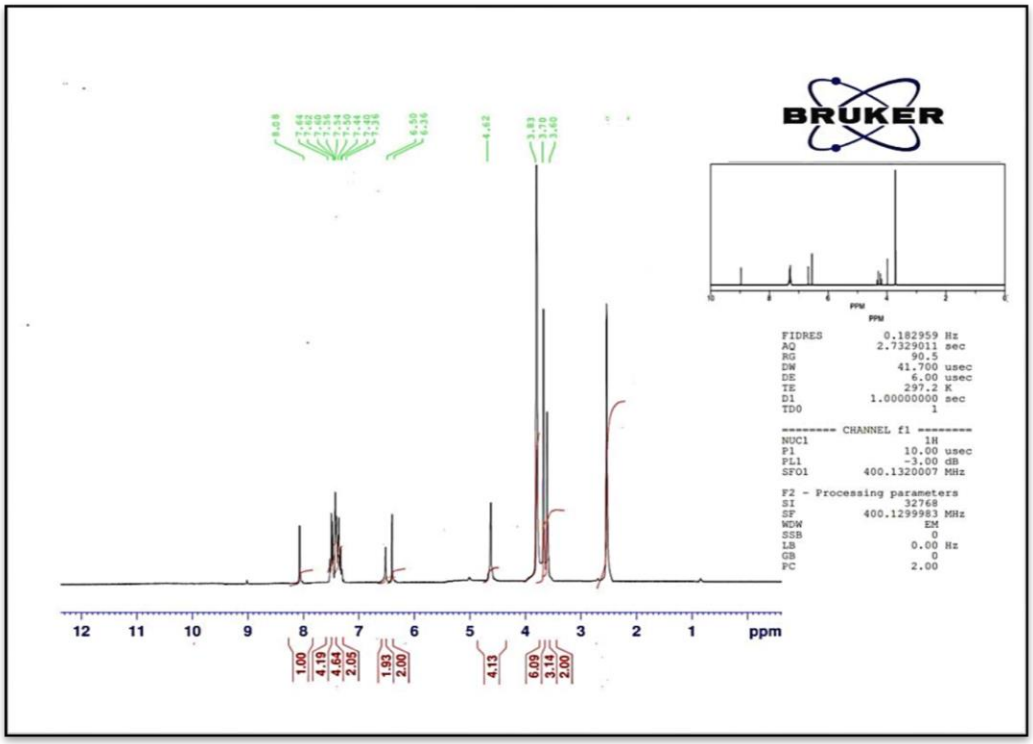
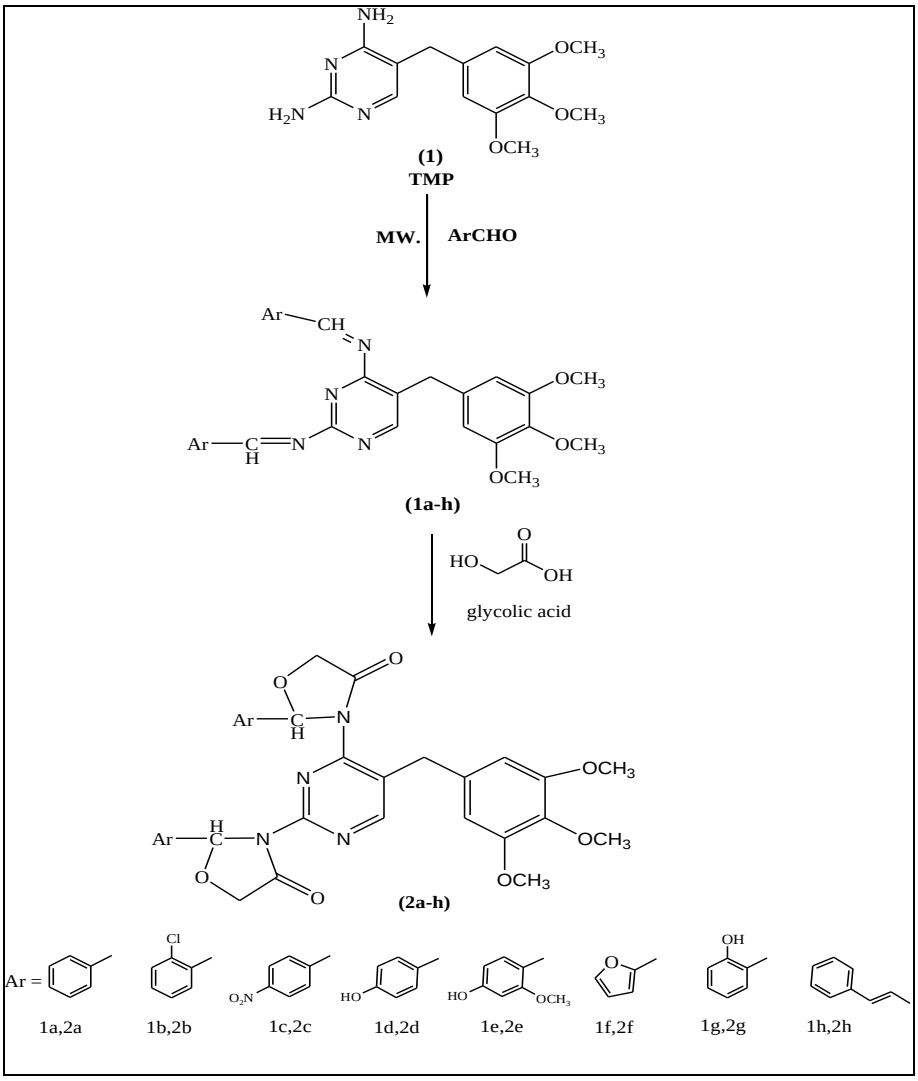


Fig.(2) ^{1}H-NMR spectrum for compound (2a).



Scheme (1)

Conclusion

A successful achievement of cycloaddition reaction of imines to glycolic acid to give oxazolidin-4-one ring is obtained. The expected plausible reaction mechanism was suggested according to the spectral data of FT-IR and ^{1}HNMR which is consistent with formation of charged linear intermediate in the transition state which then collapses via internal cyclization reaction to produce the target molecule.

Acknowledgment:

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