Synthesis, Characterization and Study Biological Activity of New Para-methoxy Benzene Sulfonamide Derivatives and some Amino Acid

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Abstract

The synthesis of para- methoxy sulphonamides [3a- 3G] was obtained by reacting p-methoxy benzene sulphonyl chloride with primary amine functionalities of amine group [1a- 1G] in alkaline medium at temperature below 0℃ , structures of all Newly synthesized compound were analysed by FT- IR, H and CNMR spectroscopy, Anti bacterial of the titled compounds were screened and the compounds exhibited potent anti bacterial properties.

Key words, p-methoxy benzene, sulphonamide elemental analysis,anti- bacterial

1. Introduction

Amino acids derivatives are an important group of peptidomimetics with variety of application in medicinal chemistry. Sulphonamides are widely used in medicinal chemistry because of their low cost, low toxicity and excellent biological activities [1]. Recently, many synthetic methods have been reported for the preparation of sulphonamides [2] and these has led to the synthesis of new sulphonamide derivatives as drugs for clinical uses. Some of these sulphonamide derivatives from substituted benzene sulphonyl chlorides and their derivatives have shown potent anti-microbial properties [3]. Apart from anti-microbial properties, sulphonamides have been found useful in the treatment of burnt using mefenide [4] asthma using N-pentyl-N-(4,5-dibromo-2-methoxyphenyl)benzene sulphonamide [5]. Other sulphonamide drugs used in clinical treatments are Indisulam used in the treatment of multiple tumour types, most prominently in colon and lung cancer [6], Sulfasalazine used in the treatment of rheumatic arthritis [7] Spironolactone used as birth control drug [8] and Zonisamide used as an anti-convulsant sulphonamide [9] that Avery important role in human

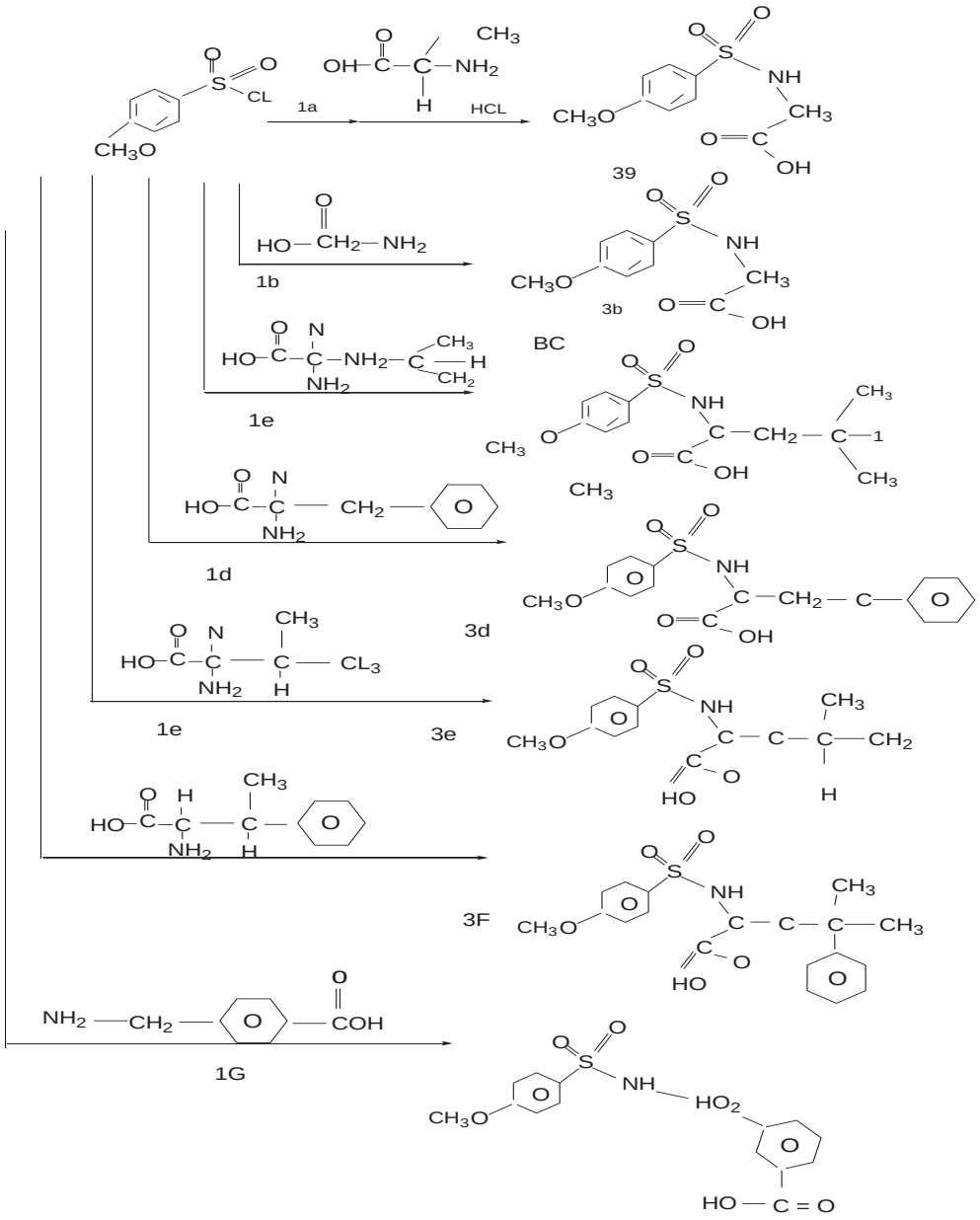
immune status[10]. Due to all edgiest, complications and resistant of sulphonamide drugs which have been a common clinical problem that has been un abated [11][12]. This research was to synthesize new sulphonamide drugs that is more effective and toxics free with amino acid which help to support human immune state.

2. Materials and methods

General procedure as described by Furnissat all[11] for synthesis of p-methoxy benzenes suphoamid [3a-3G]. Na_2CO_3 (2.785g, 26.25 mL) was added to a solution of amino acid [1a-1G] (12.5 mL) in H_2O (15mL) at -5℃ to 10℃ followed by additional of p-methoxy benzenes sulphonyl chloride [2] (2.86 g, 15 mmL) in three protons over a period of 1h, the slurry was warmed to room temperature and allowed to stir for 4 h, upon completion of the reaction which was monitored with TLC using $CHCL_3$/ CH_3OH solvent system(9:1) the reaction mixture was acidified with 20% concentrated HCL solution to (PH=2), after which crystallization occurred and the product was obtained via suction filtration. The filtration crude product was washed with tartaric acid of PH 2.2 buffer and dried in a vacuum over at 60℃ for 12 h to obtain p-methoxy- benzenes sulphoamides (3a-3G) in goes yield (78-80) preparation of the inoculums the standard clinical isolated organisms of *staphylococcus aurous*, *pseudomonas*, *streptococcus*, Klebsilla, Escherichia coli and protest were obtained from FMC owerri and the analysis was carried at. The strain of the organisms were propagated on nutrient agar plates and Maintained at 4℃ the isolates were sub-caltured in nutrient broth at 37 ℃ for 8h prior to anti-bacterial testing. Antibacterial sensitivity testing of compound Agar well diffusion technique as described by A density et al [12] was used to determine the anti-bacterial activity of synthesized compounds sensitivity test agar plates were inoculated with 0.1 ml of overnight culture of each bacteria strain (equivalent to 10^8 CFU /ml^{-1}).

The inoculated agar uniformed wells was bored in the inoculated nutrient agar with a micropipette, 200ml of 10mg /ml of each test compound solution was delivered into each well, Ciprofloxacin which is used as the positive standard was also test and the plates were left on the bench for 30minutes to allow the compound to diffuse into the agar, thereafter, the plates were incubated at 37℃ for 42h after in citation the plates were observed for in habitation zones around the wells, the diameters of the zones were measured with meter rule.

3. Results and Discussion



Scheme (1): derivatives of p-methoxy benzene sulphonamide of amino acids

The synthesis of p-methoxy benzene sulphonamide derivatives of amino acids was obtained by reacting p-methoxy benzene sulphonylchloride with primary amine functionalities of [1a-1G] in alkaline. At mediumat temperature below 0℃ to produce p-methoxy benzene sulphonamides [3a-3G] (scheme) the carboxylic and (- COOH) of the amino acid was converted to the sodium salt of the acid through electrophilic substitution of the H^+ with Na^+ from the base (Na_2CO_3). The formation of the amino acids and enhanced the solubility of the amino acids in aqueous medium.

The nucleophilic attack of the electrophilic suphut of the p- methoxy benzene sulphonyl chloride[2] by the amino group the amino acids[1a-1G] from ammonium ion. The abstraction of the ammonium proton by leaving group chloride ion led to the amide which under wet acidification with 20 molar HCl to afford the expected p-methoxy benzene sulphoamide [3a-3G] structures of the synthesized compound were established by IR, NMR (H^1, C^{13}) and elemental analysis, the assignment C1-C7 are for carbons of p-methoxy benzene sulphonyl carbons C1-C6 are for the carbons of aminoacids lalkoic acids and the melting points ranges fron 78℃ - 126℃ , the FTIR (cm^{-1}) showed- so signals at the range of 1140.83-1162 NH- signals at 3320- 3489 and c=0 signals at 1702-1708 the NMR spectral (H) showed – OH chemical shift at δ 7.88 – δ12.56 with [3b] having the highest value of δ 12,56 because of the lower Number of protons at the alpha carbon of the carboxyl carbon and this reduced the pull of electron from – OH.

Table-1: Result of anti- bacterial susceptibility of p- methoxy benzene sulphonamides with 200ml of 10mg/ml of each compounding mm

Comp	Staph	Proteus	E-coil	K & Ep	Stre
3a	17	16	20	14	17
3b	16	15	18	16	17
3c	16	17	19	16	17
3d	18	19	20	17	20
3e	16	25	16	15	19
3f	18	20	20	18	19
3G	17	18	18	18	20
Cpx	24	22	26	28	22

Cpx= ciproftoxcin (stand and drug)

Table-2: The FT-IR spectrum of compounds 1a- 3G

Comp	szo	NH	-OH	C=O	Ar	CH_3
3a	1162.15	3275.24	3426.26	1706.09	1520.92	1433.16
3b	1140.83	3270.75	3361.07	1708.02	1530.57	1530.57
3c	1155.4	3270.78	3361.07	1707.06	1529.6	1529.6
3d	1161.1	3220.57	3421.8	1702.24	1546.94	1415.8
3e	1150.58	3318.7	3418.94	1704.17	1543.1	1430.26
3f	1142	3278	3362	1706	1539	1440
3G	1150	3280	3350	1705	1544	1448

Table-3: The ^{1}HNMR and C^{13} NMR spectrum of compounds

Comp	^{1}HNMR	C^{13} NMR
3a	1.13-1.15 (3Hd, J 2.96 CH_3) 2.28(3Hs, J 3.27, Ar- CH3) 3.72- 3.76 (Hs , J1.03, CH) 4,35 (-NH- Dwarf) 8.02 -8– 8.04 (- OH-J.100) 7.15 (1HD, J0.30 Ar-H) 7.45 (1Hd J, 0.24 , Ar-h)	**C^{13} NMR** 129.91 C_6 , 21.38C_7, 178.78 C_1 , 51.36C_2, 18.86 C_3 145.41C_1, 143.92 C_2 ,126.29C_3, 138.88 C_4 , 125.98C_5,
3b	2.37 (3Hs, J 6.75, Ar- CH_3) 3.56- 3.54 (2Hs, J 10.34, CH_2) 4.33 (- NH, J 0.81, NH) 7.36 (1Hd, J 4.53, Ar-H) 7.36 (1Hd, Ar-H) 7.70 (1Hd, J 4.3 Ar-H)	C_{13} 72.93C_1, 138.52 C_2 ,129.74C_3, 58.04 C_4 , 129.68C_5, 21.37C_7, 174.30 C_1, 142.78C_2, 38.42 C_3 , 72.60C_4, 126.78, 126.83, 128 ph
3C	2.31(1Hs, J 3.16 ,Ar-CH_3) 2.299 (ph-H , J1.10) 4.32(NH, J0.70) 5.73(2Hd, J1.17- CH_2) J1.17- CH_2) 7.11- 7.23 (1 Hd, J7.69, AR) 7.29 (1Hd- Ar-H) 7.48- 7.57(1 Hd x2) J2.24 ,AR-H) 2.78- 2.99 (ph-H, J 1.10) 4.32 (NH, J,0.70)	C_{13} 172.93C_1, 138.53 C_2 ,129.74C_3, 58.04 C_4 , 129.68C_5, 137.36C_6, 21.37C_7, 174.30 C_1, 142.78C_2, 38.42 C_3 , 72.60C_4, 126.78, 126.83, 128.54 ph C_{13} 172.93C_1, 138.53 C_2 ,129.74C_3, 58.04 C_4 , 129.68C_5, 137.36C_6, 21.37C_7, 174.30 C_1, 142.78C_2, 38.42 C_3 , 72.60C_4, 126.78, 126.83, 128.54 ph
3D	5.73 (2Hd, J 1.17m –CH_2) 7.11- 7.23 (1Hd, J 7.69m Ar-H) 7.29 (1Hd , Ar-H) 7.48- 7.57 (1H:dx) J 2.29- Ar-H) 7.98 (OH- dw arf peak , J 100)	C_{13} 172.64C_1, 142.82 C_2 ,129.74C_3, 72.61 C_4 , 127.82C_5, 138.81C_6, 21.40C_7, 173.55 C_1, 61.66C_2, 30.85 C_3 , 19.31C_5
3e	0.77-0.83 (3Hd, J 5.91- CH_3X_2) 1.89-1.93(3Hs, J1.05 , Ar-H) 2.36 (Hm ,2.30- CH) 4.52 (1 Hd, J2.13- CH)	C_{13} 170.50C_1, 140.80 C_2 ,129.70C_3, 72.50 C_4 , 127.50C_5, 135.81C_6, 22.43C_7, 172.50 C_1, 62.60C_2, 32.85 C_3 , 19.20C_5
3G	2.31 (1Hs, J3.15, Ar-CH_3) 7.28 (1Hd, Ar-H), 7.90 (-oH) 2.70- 2.90 (Ph-h, J 1.20) 4.30 (NH- J 0.70- CH_2)	C_{13} 172.90C_1, 135.53 C_2 ,129.70C_3, 58.50 C_4 , 129.68C_5, 137.30C_6, 21.70 C_7, 175.30 C_1, 140 C_2, 35.42 C_3 , 72.5C_4, 126.70, 126.80, 128.50 ph
3f	1.80-1.90 (3Hm s, J 1.0m Ar-H) 2.30 (Hm , J2.30-CH) 3.50 (1Hd, J2.10-Ch) 4.40 (-NH) 7.80- 7.90 (OH-) 7.60- 7.67 (1Hdm J1.90- Ar-H)	C_{13} 172.64C_1, 142.82 C_2 ,129.74C_3, 72.61 C_4 , 127.82C_5, 138.81C_6, 21.40C_7, 173.55 C_1, 61.66C_2, 30.85 C_3 , 19.31C_5

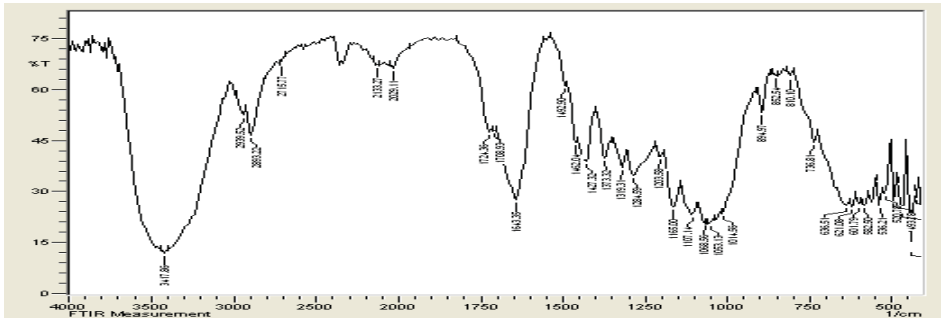


Fig.1: The FT-IR spectrum of compound a3

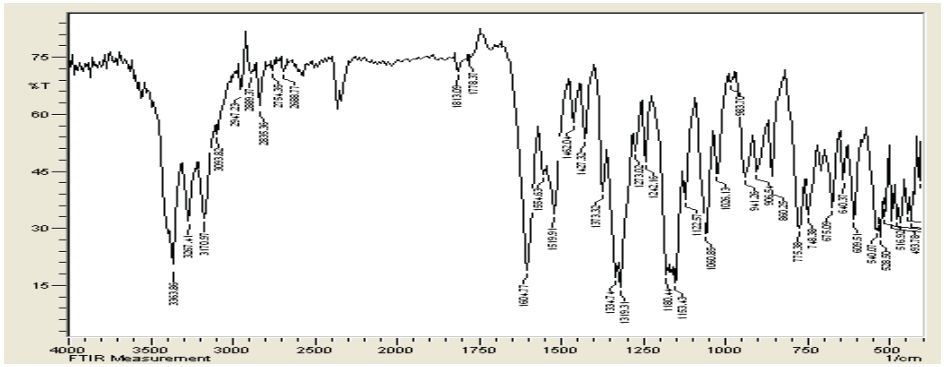


Fig.2: The FT-IR spectrum of compound b3

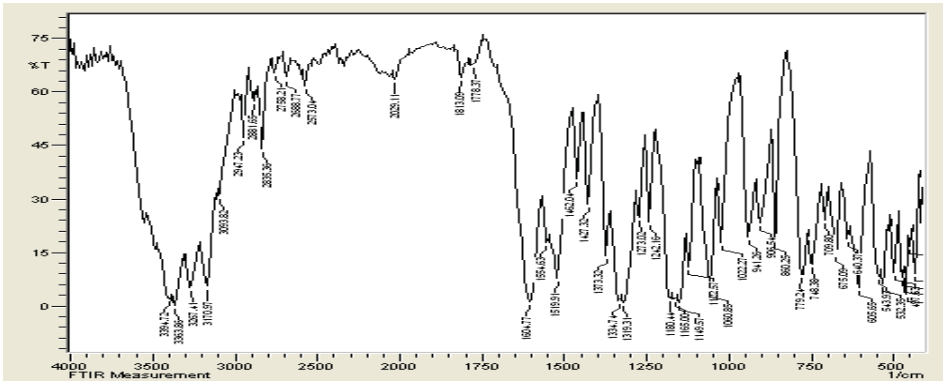


Fig.3: The FT-IR spectrum of compound c3

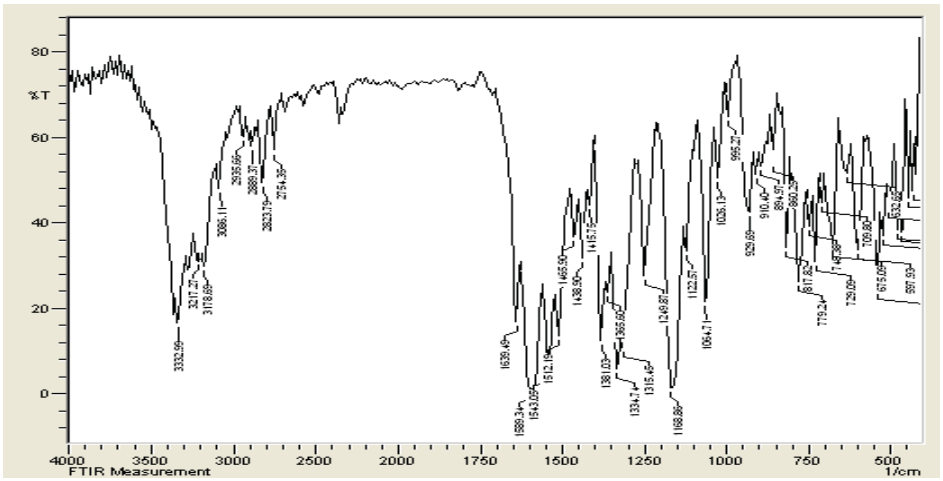


Fig.4: The FT-IR spectrum of compound d3

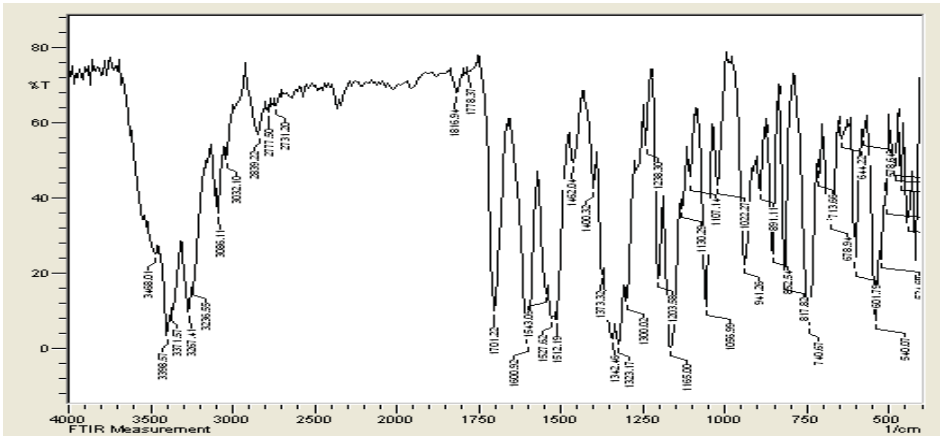


Fig.5: The FT-IR spectrum of compound e3

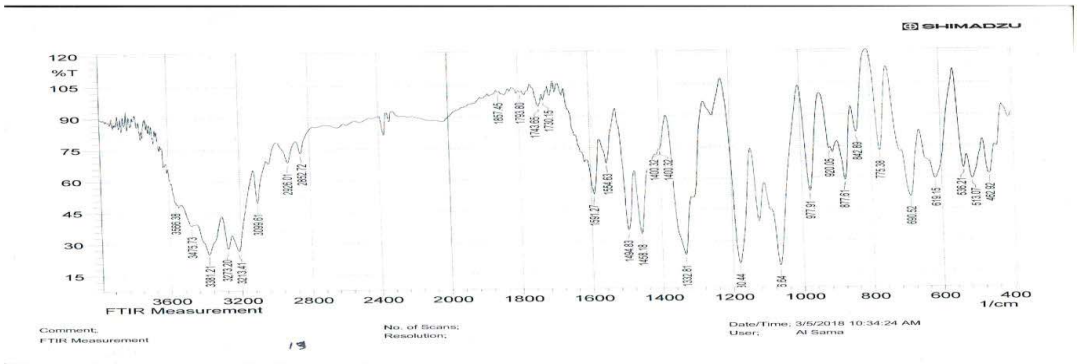


Fig.6: The FT-IR spectrum of compound f3

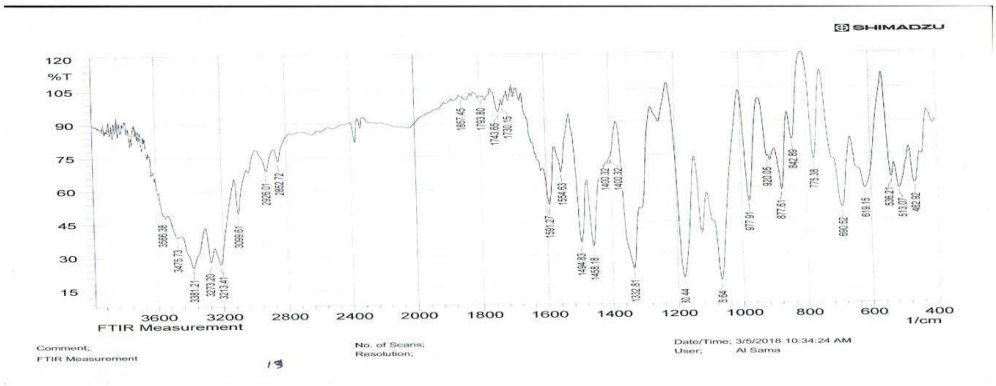


Fig.7: The FT-IR spectrum of compound g3

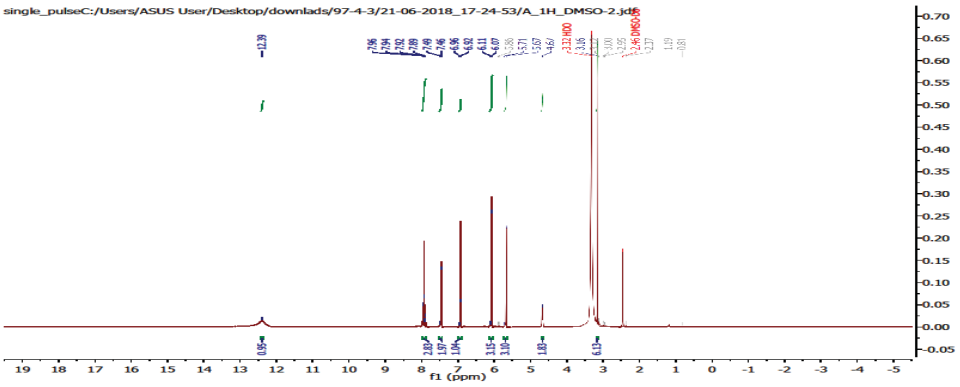


Fig.8: The HNMR spectrum of compound a3

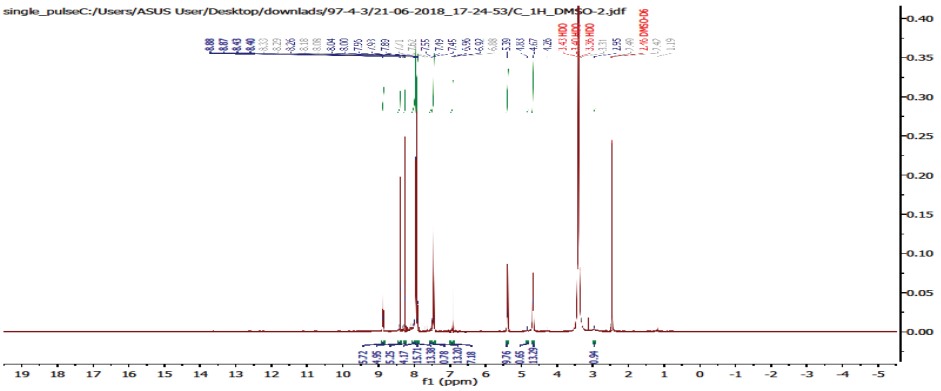


Fig.9: The HNMR spectrum of compound b3

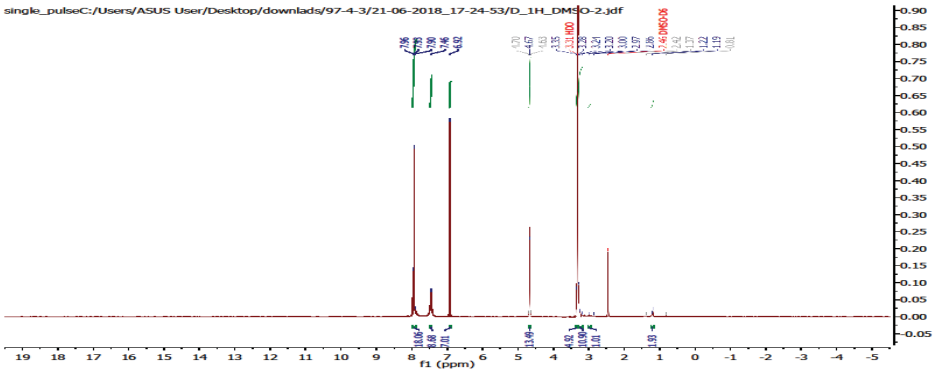


Fig.10: The HNMR spectrum of compound c3

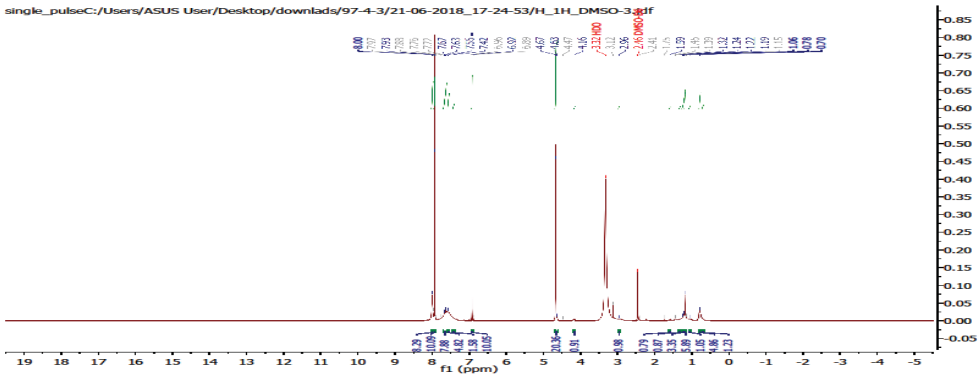


Fig.11: The HNMR spectrum of compound d3

The carbon–13 (C^{13}) synthesis compounds while the carbonyl carbon C1 ’were observed at chemical shief δ 172.71 − δ178.76 . The combination of IR, NMR and the elemental analysis data confirmed the synthesized of the compound [3a- 3G]. The anti-bacterial screeing carried out with 200ml of 10 mg/ml of each synthesized compound showed active in hibition properties on the growth of staphylococcus aurous, pseudomonas aeruginosa, streptococcus, klebsiella pneumonia, Escherichia coli and proteus mirabillis (table). Bnzene sulphonamide derivatives of aminoacid [3a-3G] have been successfailly synthesized by the Nucleophilic attack of on the eletro philic sulphonyl cohloride [2]. The synthesised compounds exhibited potent antibiotics properties since they showed zine of inhibition with 200ml of 100mg/mml of each tested or ganism.

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