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Synthesis and characterization of some sulfonamide dervatives

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Abstract

A new Sulfonamide derivatives have been synthesized by the series of reaction that treatment of tosyl methyl with 4-amino benzoate to give compound (1), followed by the reaction of the different anhydride to give imides derivatives (3,4). the compound (5)was synthesized by the reaction of compound (2) with phenyl phenacyl bromide ,and followed synthesis of beta lactm derivatives by treatment of derivatives Schiff bases (8-10) with chloro acetyl chloride. All new derivatives were characterized by physical properties (melting points,coulor) and Spectroscopic methods as (IR and ^{1}H NMR).

Keywords: sulfonamide, imides derivatives, β –lactam, schiff bases

INTRODUCTION

Sulfonamide compounds, known as chemotherapeutic agents, sulfonamide are broadly used of biological activities sush as antibacterial agents [1], anticancer [2] , anti-inflammatory [3], anti-diabetic [4] anti -epileptic [5] and antifungal agents .[6] N-Aryl and N-alkyl cyclic imides have been attracted more attention of organic and medicinal chemists due to the different applications in biological, synthetic, and polymer chemistry .[7,8]

Schiff bases containing imino group (-RC = N-) has the apparent number of applications in many fields including medicine, life sciences and chemical sciences

including analytical and inorganic chemistry. [9,10] Moreover, 2-azetidinone (β-lactam) ring is a basic characteristic of a large number of biologically active compounds. Besides antibiotic activity, and ring system displays a wide variety of pharmacological activities. [11,12] Given the biological importance of the sulfonate nucleus it was thought to synthesize and design a new sulfonamide derivatives with the purpose of the investigation in the future, anti-bacterial and anti-fungal activities possible.

RESULTS AND DISCUSSIONS

The [scheme 1 and 2] the identification of synthetic sequence used in our laboratories to prepare sulfonamide compounds (1-11) . The compound (1) ethyl 4-((tosylmethyl)amino)benzoate was synthesized by the react toluene -4- sulfonyl chloride with 4-amino ethyl benzoate.The formation of sulfonamide (1) was indicated by presence in their IR spectra of NH at 3207 cm^{-1}, abands at1365, 1159cm^{-1}due to stretching vibration of SO_2 and carbonyl group (C=O) of ester at 1710 cm^{-1} . ^1H NMR of compound(1): 1.23 (t,3H,COO$\underline{CH_2}CH_3$),4.01 (q,2H,COO$CH_2\underline{CH_3}$) , 7.55-6.28 ppm which belonged to aromatic protons. [13]

When compound (1) reacts with thiourea gave derivative(2). The IR spectrum showed appearance doublet bands of NH_2 at 3383,3261 cm^{-1} . The ^1H NMR of compound (2) exhibited signals at 9.5(s, 1H, NH CO),5.9 (s,2H,NH_2), 4.2(s, 1H, NHCH),7.73- 6.54 ppm which due to aromatic protons.

Reaction between compound(2) and Phthalic anhydride or naphthalic anhydride afforded the imides derivatives (3,4)in good yield. The spectrum of compound(3) showed the disappearance of doublet band of NH_2 and the appearance of the (C=O) bands at1765,1774 cm^{-1}.

The ^1H NMR of compound (3)showed singlet at10.74ppm related to NHCO ,multiplet signal at 8.04 -6.59 ppm due to twleve aromatic protons, singlet signal at 4.5 ppm for NH , at 2.24ppm assigned to protons of methyl group .[14]

Cyclization of derivative (2) with p- phenylphencylbromide in the presence of ethanol afforded compound (5). IR absorption bands of triazole compound exhibited the disappearancs of absorption bands due to NH_2 with the appearance of the (C=N) of oxazolineat 1606 cm^{-1}.

The ^1H NMR of compound (5) exhibited singlet signal at 8.52 due to NH,doublet and triplet signals at 4.0 ,4.3 ppm assigned to oxazoline protons .

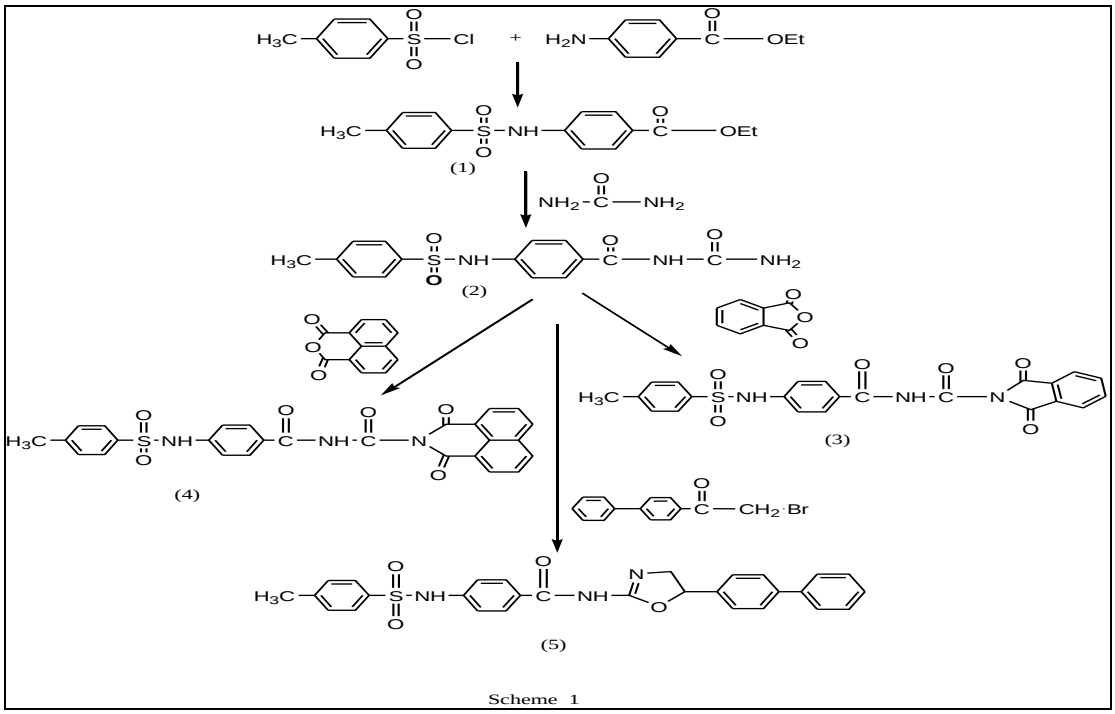
Condensation of compound (2) with p-chloro isothiocyante in ethanol afforded compound (6). IR spectrum of (6)shows a bands at 3217 cm^{-1}, 1687cm^{-1} related to NH and C=O respectively.^1H-NMR spectrum of this derivative shows singlet signals at 9.87ppm5.89ppm,4.5ppm for NHCO,NHCS, $NHSO_2$ respectively.

From another hand, the cyclo addition of compound (6) with malonic acid afforded the derivative (7). IR spectrum of(7)shows a bands at 3207 cm^{-1} for NH ,1728 and 1722 due to cyclic carbonyl .^1H NMR spectrum of compound(7) exhibited singlet

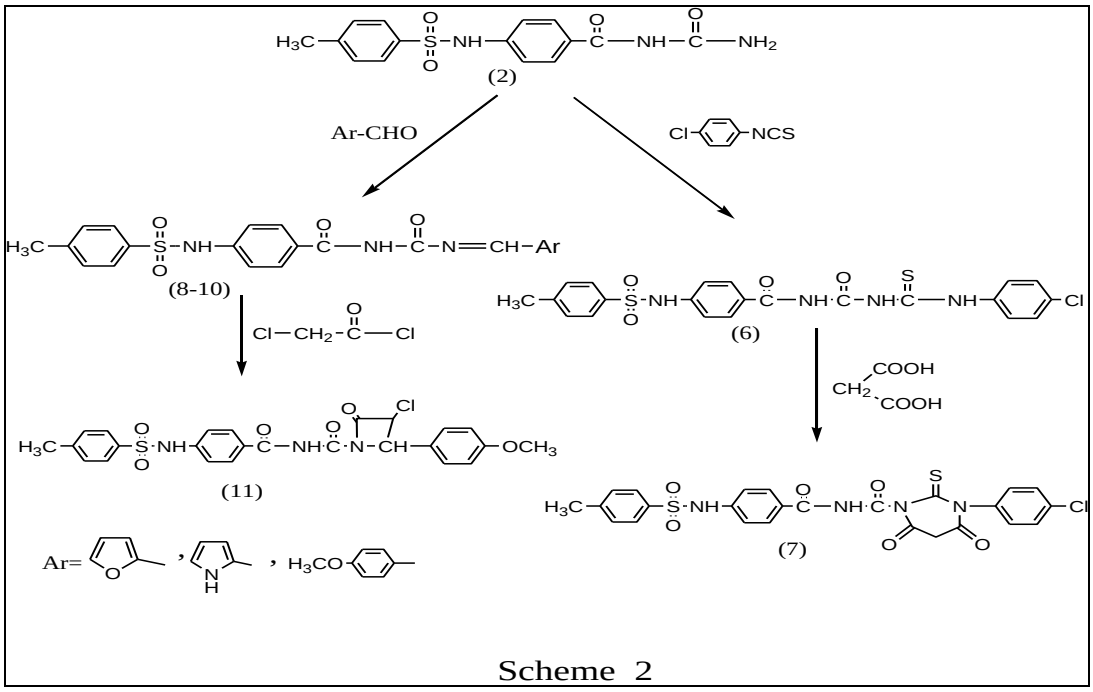
signals at 9.68 ppm which was assigned to NHCO ,4.5 ppm was attributed to N-H proton, while amultiplet signals at 7.87-6.42 ppm belong to aromatic protons.

Condensation of compound (2) with different substituted aromatic aldehydes in absolute ethanol gave arylidine derivatives(8-10). The formation of these azomethines was indicated by the presence in the IR spectra of (CH=N) stretching bands at 1604-1599 cm^{-1}combined with the disappearance of $NH_2$and C=O stretching bands. The ^1H NMR of compound (8) showed singlet signals at10.1ppm was attributed to NHCO ,4.5 ppm was assigned to NH . a multiplet signals at 8.54-648 ppm which belonged to aromatic protons and (N=CH).

Treatment of compound(10) with triethylamine and chloro acetyl chloride gave azetidinyl derivative (11). The structure of compound (11) established by IR spectral data which was showed the disappearance band of (CH=N) in the region 1604cm^{-1} combined with the appearance of absorption band at1728 cm^{-1} (C=O β lactam). The ^1H NMR of compound (5)showed doublet signals at 5.73 -5.32ppm due to azetidinyl ring proton, a multiplet signals at 8.35 -6.54 (m,12H, Ar-H) due to aromatic protons.



Scheme 1



Scheme 2

EXPERIMENTAL

MATERIALS AND PHYSICAL MEASUREMENTS

Melting points were determined in open capillary tubes on a Gallenkamp melting point apparatus and are uncorrected. FTIR measurements were recorded on Shimadzu model FT-IR-8400S.The UV-Visible spectra were measured in ethanol using Shimadzu UV-Vis. 160 a spectrophotometer.^{1}H-NMR spectra were obtained with a Bruker spectrophotometer model Ultra Shield at 300 MHz in DMSO-d6 solution with the TMS as internal standard. In this study were reagents grade and they are available from Sigma-Aldrich and Fluka companies. Purity of the compounds was checked on silica coated Merck-TLC plates using, chloroform, benzene and acetone as mobile phase.

Synthesis of 4-Methyl-N-(4-propionyl-phenyl)-benzenesulfonamide) (1)

A mixture of Toluene -4- Sulfonyl chloride (tosyl chloride) (0.01 mole, 1.9g) and 4-amino ethyl benzoate(0.01 mole,1.49g) with (0.01 mole , 1.01gm) Triethyl amine in dry benzene (25 ml) was refluxed for 6 h. The excess of solvent was evaporated and the product was filtered off ,recrystallized from ethanol. Yield: 88% , M.P: 251-253 °C , FT-IR (KBr, ν, cm^{-1}): 3207 (NH), 1710(C=O), 1365, 1159 (SO2). ^{1}H NMR (300 MHz, DMSO-d6, δ, ppm): 7.55-6.28 (m, 8H, Ar-H), 4.5 (s, 1H, NH), 2.24 (s, 3H, CH3), 1.23 (t,3H,COOCH2CH3),4.01 (q,2H,COOCH2CH3) ; Anal. % calc./found for $C_{16}H_{17}NO_4S$ (Mw.319): C, 60.18/ 59.92 ; H, 5.32/ 5.21; N,4.38/ 4.11; S, 10.03/ 10.27.

Synthesis of 4-Methyl-N-(4-ureidocarbonyl-phenyl)-benzenesulfonamide (2)

A mixture of compound (1) (0.01mol ,3.34gm) or (0.01mol , 0.6 gm)thiourea in 25 ml absolute ethanol were refluxed for 5 hrs. After cooling and filtering, the white precipitate were obtained to give compound(2).

Yield: 70% , M.P: 195-97 °C , FT-IR (KBr, νcm⁻¹): , 3383- 3261 (NH_2), 3213(NH),1687(C=O), 1336, 1157 (SO_2). ¹H NMR (300 MHz, DMSO-d6, δ, ppm): 9.5(s,1H,NHCO) , 7.73-6.54(m, 8H, Ar-H),5.9 (s,2H,NH_2), 4.2 (s, 1H, NH), 2.34 (s, 3H, CH_3); Anal. % calc./found for $C_{15}H_{15}N_3O_4$ (m.w.333): C, 54.05/53.89 ; H, 4.50/4.3 8; N,12.61/ 12.45 ; S,9.60/ 9.47.

General procedure for the synthesis of imides derivatives(3,4) :

Phthalic anhydride or naphthalic anhydride (0.01 mole) in 30 ml acetic acid was added to compound (2) (0.01mole 3.34gm) and the reaction was refluxed for 7hrs. then the mixture was poured on crushed ice, the formed solid product was filtered off and recrystallized from petroleum ether (40-60 ^oC).

N-(1,3-Dioxo-1,3-dihydro-isoindole-2-carbonyl)-4-(toluene-4-sulfonylamino)-benzamide (3)

Yield: 66% , M.P: 231-233 °C , FT-IR (KBr, ν, cm⁻¹): 3207 (NH),1765-1745(C=O,cyclic), 1687(C=O), 1334, 1159 (SO2). ¹H NMR (300 MHz, DMSO-d_6, δ, ppm): 10.74(s,1H,NHCO), 8.04-6.59(m, 12H, Ar-H), 4.5 (s, 1H, NH), 2.24 (s, 3H, CH3); Anal. % calc./found for $C_{23}H_{17}N_3O_6S$ (M.w.463): C, 59.61/59.44; H, 3.67/ 3.54; N,9.07/9.28; S,6.91/6.78.

N-(1,3-Dioxo-1H,3H-benzo[de]isoquinoline-2-carbonyl)-4-(toluene-4-sulfonylamino)-benzamide (4)

Yield: 66% , M.P: 253--255 °C , FT-IR (KBr, ν, cm⁻¹): 3215 (NH),1770-1734(C=O,cyclic), 1685(C=O), 1338, 1155 (SO2). ¹H NMR (300 MHz, DMSO-d6, δ, ppm): 10.76(s,1H,NHCO), 8.55-7.20 (m, 14H, Ar-H), 4.23 (s, 1H, NH), 2.33 (s, 3H, CH3) ; Anal. % calc./found for $C_{27}H_{19}N_3O_6S$ (M.w.513) C, 63.15/62.96 ; H, 3.70/3.56, N 8.18/8.01; S,6.23/ 6.08.

Synthesis of N-(5-Biphenyl-4-yl-4,5-dihydro-oxazol-2-yl)-4-(toluene-4-sulfonylamino)-benzamide (5)

To stirring of compound (2) (0.01mole,3.34g) in ethanol(20ml),(p-phenylphencylbromide(0.01mle,2.74g)was added,then the mixture was refluxed for12h .The product was collected and recrystaslized from chloroform. Yield: 68% , M.P: 271-273 °C , FT-IR (KBr, ν, cm⁻¹): 3215(NH),1689(C=O), 1606(C=N),1387, 1155 (SO_2),1290 (C-O) . ¹H NMR (300 MHz, DMSO-d6, δ, ppm): 10.77

(s,1H,NHCO) , 7.82-6.83 (m, 17H, Ar-H),4.0(d,2H,CH_2),4.3(t,1H,CH), 4.20 (s, 1H, NH), 2.33 (s, 3H, CH_3) ; Anal. % calc./found for $C_{29}H_{25}N_3O_4S$ (M.w.511): C, 68.10/68.29; H, 4.89/4.73; N,8.21/8.08 ;S,6.26/6.15 .

Synthesis of N-(((4-chlorophenyl)carbamothioyl)carbamoyl)-4-((tosylmethyl)amino)benzamide (6)

A mixture of compound(2)(0.01mol , 3.34gm) and 4-chlorophenylisothiocyanate (0.01mol,1.69gm) in absolute ethanol(20mL) was refluxed for 7hr,then cooled. The formed precipitate was filtered off and recrystallized from ethanol.

Yield: 69% , M.P: 234-236°C , FT-IR (KBr, ν, cm^{-1}): 3217 cm^{-1} (NH),1687(C=O), 1334, 1155 (SO2). ^{1}H NMR (300 MHz, DMSO-d6, δ, ppm):9.87 (s,1H,NHCO),5.89 (s,1H,NH), 7.89-6.43 (m, 12H, Ar-H), 4.5 (s, 1H, $NHSO_2$) 2.34 (s, 3H, CH3) ;Anal. % calc./found for $C_{22}H_{19}N_4O_4S_2Cl$ (m.w.502.5): C, 52.53/52.69; H, 3.78/3.55; N,11.14 /11.32;S,12.73 /12.52.

Synthesis of 3-(4-Chloro-phenyl)-4,6-dioxo-2-thioxo-tetrahydro-pyrimidine-1-carboxylic acid 4-(toluene-4-sulfonylamino)-benzoylamide (7)

The compound (6) (0.01mol ,5.02gm) was refluxed with malonic acid (0.01mol,1.05) in dry benzene (25mL) for 8 hr. The solution was concentrated and the solid formed filtered off and recrystallized from benzene. Yield: 66% , M.P: 270-272 °C , FT-IR (KBr, ν, cm^{-1}): 3207 (NH),1728 ,1722(C=O,cyclic), 1687(C=O), 1334, 1159 (SO2), 1033 (C=S). ^{1}H NMR (300 MHz, DMSO-d6, δ, ppm):9.68(s,1H,NHCO), 7.87-6.42 (m, 12H, Ar-H), 4.5 (s, 1H, NH), 2.34 (s, 3H, CH3) Anal. % calc./found for $C_{25}H_{19}N_4O_6S_2Cl$ (m.w.570.5): C, 52.58/52.35; H, 3.33/3.15; N,9.81 /9.78 ;S,11.21 /11.09.

General procedure for the synthesis of Schiff bases (8-10):

A mixture of compound (2) (0.02 mol ,6.68gm) and(0.02mol)of the different aldehyde was refluxed in absolute ethanol (20 mL) for 7 h. The mixture was cooled and the product obtained recrystallized from of ethanol.

N-[4-(3-Furan-2-ylmethylene-ureidocarbonyl)-phenyl]-4-methyl-benzenesulfonamide (8)

Yield: 67% ; M.p: 268-270 °C; FTIR (KBr, ν, cm^{-1}): 3275((NH),1693 (C=O), 1599(C=N), 1329,1153 (SO_2) . ^{1}H- NMR (300 MHz, DMSO-d6, δ, ppm): 10.1 (s,1H,NHCO), 8.54-6.48 (m, 12 H, Ar-H,CH=N), 4.5 (s, 1H, NH), 2.34 (s,3H, CH_3); Anal. % calc./found for $C_{20}H_{17}N_3O_5S$ (M.w.411): C, 58.39 /52.17; H, 4.13 /3.96; N,10.21/10.08 ;S,7.78 /7.51.

4-Methyl-N-{4-[3-(1H-pyrrol-2-ylmethylene)-ureidocarbonyl]-phenyl}-benzenesulfonamide (9)

Yield: 54% ; M.p: 222-224 °C ; FTIR (KBr, ν, cm^{-1}):3271(NH, pyrrol),3217(NH)1691 (C=O), 1600 (C=N), 1506 ,1159(SO_2) . ^{1}H- NMR (300 MHz, DMSO-d6, δ, ppm): 9.60 (s,1H,NHCO), 8.37 -6.42 (m,12 H, Ar-H,CH=N),5.1(s,1H,NH of pyrrol 4.5 (s, 1H, NH), 2.34 (s, 3H, CH_3); Anal. % calc./found for $C_{20}H_18N_4O_4S$ (m.w.510): C, 58.53/58.34; H, 4.39 /4.14; N,13.65/13.49;S,7.80 /7.65.

N-{4-[3-(4-Methoxy-benzylidene)-ureidocarbonyl]-phenyl}-4-methyl-benzenesulfonamide (10) .

Yield: 83% ; M.p: 192-194 °C; FTIR (KBr, ν, cm^{-1}): 3217(NH),1689 (C=O), 1604 (C=N), 1336 ,1155 (SO_2) . ^{1}H- NMR (300 MHz, DMSO-d6, δ, ppm): 10.77(s,1H,NHCO), 7.82-6.77 (m,13 H, Ar-H,CH=N), 4.2 (s, 1H, NH), 3.75 (s, 3H,O- CH_3) ,2.32 (s, 3H, CH 3) Anal. % calc./found for $C_{23}H_{21}N_3O_5S$ (M.w.451): C, 61.19/61.39; H, 4.65 /4.46; N,9.31 /9.08 ;S,7.09 /6.95 .

Synthesis of N-[3-Chloro-2-(4-methoxy-phenyl)-4-oxo-azetidine-1-carbonyl]-4-(toluene-4-sulfonylamino)-benzamide(11)

To a stirred solution of compound **10** (0.01mol ,4.51gm) triethyl amine (0.02 mol 2.02) in dry dioxin (15mL) chloroacetylchloride (0.02mol , 2.22gm) was added dropwise in(0-5°C) the recation mixture was then stirred for 6 hours, then pourd into ice-water . The solid was filtered and recrystallized from chloroform.Yield: 66%.

M.p.: 243-245 °C. FT-IR (KBr, ν, cm^{-1}): 3213(NH),1728 (C=O, β-Lactom), 1681 (C=O amide). ^{1}H- NMR (300 MHz, DMSO- d_6 , δ, ppm): 9.53(s, 1H, NH), 8.35-6.54 (m, 12H, Ar-H), 5.73 (d, 1H ,N-CH) ,5.32(d,1H, CH-Cl),2. 75 (s,3H,OCH_3), 2.34 (s, 3H, CH 3) Anal. % calc./found for $C_{25}H_{22}N_3O_6SCl$ (M.w.527.5): C, 56.87/68.29; H, 4. 17/4.34; N,7.96 /8.17 ;S,6.06 /6.18

CONCLUSIONS

New imides, oxazol ,pyrimidine ,schiff bases and azetidine compounds with a sulfonamido moiety,Compound 1-11] were successfully synthesized through simple methods. The structures of compounds synthesized FTIR,^{1}H-NMR, and C.H.N analysis.

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REFERENCES

1. Nassir, N.; Yatimah , A.;, Zanariah, A.; , Raied , M. S.; Ekhlass, M. T.; Aidil, A. H. **Synthesis and Antibacterial Evaluation of Some Novel Imidazole and Benzimidazole Sulfonamides,** *Molecules* **2013**, *18*,11978-11995.

2. Oana M. D.; Florentina, L.; Cornelia, V.; Mihai, M.; Valentin, N.; Romona, F.; Dragos, P.; Lenuta, P . Synthesis and Biological Evaluation of New 2-Azetidinones with Sulfonamide Structures**.** Molecules 2013,18 ,4140-4157

3. Bano, S.; Javed, K.; Ahmad, S.; Rathish, I.G.; Singh, S.; Alam, M.S. **Synthesis and biological evaluation of some new 2-pyrazolines bearing benzene sulfonamide moiety as potential anti-inflammatory and anti-cancer agents**. *Eur. J. Med. Chem* .**2011**, *46*, 5763-5764

4. Muhammad , A.; Saima , N.; Aziz, u.; Rehman, S. R.; Khalid ,M. K.; Muhammad, A.; Rumana, N.; Umber, A.*T.* **Evaluation of Sulfonamide Derivatives of Dagenan Chloride as Lipoxygenase and α Glucosidase Inhibitors**. *J. Pharm. Res. 2015, 14(1),* 47-54 .

5. Ajeet, A. K.; Mishra, A. K. **Recent Advances in Development of Sulfonamide Derivatives and Their Pharmacological Effects.** Am. J. Pharm. Sci. 2015, 3(1), 18-24.

6. Muzammi ,T. P.; Khetani, D.B. **Synthesis and Characterization of Schiff base m-nitro aniline and their complexes**. Res. J. Chem. Sci . 2015 , 5(5), 52-55.

7. Thierry, V.; Alain, P.; Andre , L.; Richard ,N. G. **Re-examination of Microwave-Induced Synthesis of Phthalimides** *Tetrahedron* 2000,56, 5473–5478.

8. Jayakumar R.; Balaj ,R.; Nanjundan ,S. **Studies on copolymers of 2-(N-phthalimido)ethyl methacrylate with methyl methacrylate**. Eur. Polym. J. 2000 , 36 (8), 1659 -1666

9. Satyanarayana ,V. S. V.; Sreevani, P.; Amaravadi, S.; Vijayakumar ,V.; Satyanarayana, V. S. V.; Sreevani, P.; Sivakumar, A.; Vijayakumar, V. **Synthesis and antimicrobial activity of new Schiff bases containing coumarin moiety and their spectral characterization**. *Arkivoc* **2 008 ,17,** 221–233**.**

10- Enis, N. M.; Thahira ,B. S. A. R.; ,Edward R. T. T.; Abhimanyu ,V.; Karen, A. C.; Mohamed, I.M. T. , Haslina ,A. **Synthesis, Characterization and Biological Evaluation of Transition Metal Complexes Derived from N, S Bidentate Ligands**. *Int. J. Mol. Sci.* 2015, *16(5)*, 11034-11054

11- Pradeep, K. S.; Chandrakant, P. S.;. Anand, K. H. The Chemistryand Harmacolgical Potential of 2-azatidinones Incorporated with Halogen atoms and Cyano Groups. A REVIEW World J. Pharm. Pharm. Sci. 2016, 5(3), **433-455**

12- Aakash , D.; Pradeep ,K.; Balasubramanian , N.; Siong, M.; Kalavathy , R.; Rakeshkumar, M.; Vasudevan , M. **2-azetidinone derivatives: Synthesis, antimicrobial, anticancer evaluation and QSAR studies.** Acta. Pol. Pharm. Drug Research, 2016, 73(1) , 65-78.

13- Silverstein ,R.M, and Basslar ,G.C.,' **Spectroscopic identification of organic compound'**, 7thed Johin Willey and son, New York. 2005.

14- Williams ,D.H.; Felming ,**'Spectroscopic method in organic chemistry**, 1sted. New York . 1986