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Synthesis of new heterocyclic 3-piperidinyl-1,3,4-oxadiazole derivatives as potential drug candidate for the treatment of alzheimer's disease

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Abstract: A series of new *N*-substituted derivatives of 3-[(5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]propanamide (**7a-q**) was synthesized to evaluate new drug candidates for Alzheimer's disease. 4-Chlorobenzenesulfonyl chloride (**a**) and ethyl piperidin-3-carboxylate (**b**) were converted into 5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-thiol (**3**) through a series of three steps. A series of electrophiles, *N*-alkyl/aralkyl/aryl-3-bromopropanamide (**6a-q**), was synthesized by gearing up 3-bromopropionyl chloride (**5**) with different alkyl/aralkyl/aryl amines (**4a-q**). Target compounds were synthesized by reacting compound **3** with different electrophiles, **6a-q**, under basic conditions in an aprotic polar solvent. The synthesized compounds were subjected to spectral analysis, EI-MS, IR, ^{1}H-NMR and ^{13}C-NMR, for structural elucidation. The compounds were screened for enzyme inhibition activity against acetyl cholinesterase (AChE) enzyme. The validity of synthesized compounds as new drug candidates was also evaluated through hemolytic activity.

Subject: Biological evaluation of 1,3,4-oxadiazole hybrids

Keywords: 1,3,4-oxadiazoles; acetyl cholinesterase (AChE) enzyme; propanamides; piperidine

ABOUT THE AUTHORS

Aziz-ur-Rehman is working as Associate Professor in Government College University, Lahore, Pakistan. He has published more than two hundreds research papers in well known journals. He is an HEC (Pakistan) approved Ph.D. supervisor. Our group has been working on Organo-Pharmaceutical Research for seven years at Government College University, Lahore, Pakistan. The current project was designed and practically performed by our group. The spectral analysis of all the synthesized compounds was conducted by Syed Adnan Ali Shah. The biological activity and statistical analysis of all the synthesized compounds were conducted by Muhammad Ashraf.

PUBLIC INTEREST STATEMENT

The increased level of resistance of disease causing microorganisms for the available drugs is an alarming issue in the whole world. This issue has been resolved up to a great extent by the current synthesized compounds which could be a solid effort in this contest.

1. Introduction

Oxadiazoles have been the centre of interest for chemists due to their versatile therapeutic potential for two decades. The heterocyclic 1,3,4-oxadiazoles and their derivatives are widely used as anti-tuberculosis, antimicrobial and antimalarial (Holla et al., 1996; Shafi et al., 1995; Tan et al., 2006); analgesic, anticonvulsant, antidepressant and anti-HIV (Aziz-ur-Rehman et al., 2013; Goswami et al., 1984); anticancer and anti-inflammatory (Matsumoto et al., 1998; Omar et al., 1996); anti-mycobacterial (Sharma et al., 2008; Wagle et al., 2008), antibacterial (Khalid et al., 2016) and anti-enzymatic (Aziz-ur-Rehman et al., 2013) activities. Another heterocyclic core, piperidine is known to possess anti-cancer, analgesics, anti-HIV, antidepressants, anti-bacterial, anti-histaminic and anti-fungicidal activities (Castro et al., 2014; Khobare et al., 2015; Vitnik et al., 2016). Sulfonamides are widely used as drugs due to their anti inflammatory, antimicrobial, anti diuretic and anti thyroid potential (Aziz-ur-Rehman et al., 2013; El-Sayed et al., 2011; Ordonez et al., 2011; Zoumpoulakis et al., 2012).

Cholinesterases belong to a class of enzymes which include acetyl cholinesterase (AChE) and butyryl cholinesterase (BChE) enzymes. This class consists of serine hydrolase enzymes. Alzheimer's disease results in the loss of identification and poor memory. Loss of memory is the result of decline in neurotransmission in synaptic membrane. AChE cause hydrolysis of acetylcholine (ACh) into choline and acetate which inhibits the cholinergic neurotransmission in human brain and results in Alzheimer's disease. AChE performs main function to keep brain healthy by regulating the level of ACh in brain. Acetyl cholinesterase inhibiting agents are required to maintain the level of acetylcholine in synaptic cleft to keep cholinergic neurotransmission smooth. Alzheimer's disease, Parkinson's disease and senile dementia can be treated by these inhibitors (Zhao et al., 2013). Therefore the search of new AChE inhibitors may lead to new potent drug candidates for the mentioned diseases.

Hemolysis is related to the breakdown of red blood cells (RBCs) and the ability of compounds to break RBCs is evaluated through hemolytic activity. Hemolytic activity describes the toxicity level of different substances. In drug development programs it is an important factor to study the biologically active compounds that the specified compounds are either toxic or nontoxic and what's the level of their toxicity.

In the presented research work, an effort was made to synthesize clinically active compounds by gearing up 1,3,4-oxadiazole, piperidine and sulfonamide linkages of great therapeutic potential in a single moiety. Presented manuscript is a continuation of our previous work (Gul et al., 2013, Abbasi et al., 2013, Nafeesa et al., 2015, Nafeesa et al., 2017) where differently *S*-substituted 1,3,4-oxadiazoles were synthesized and evaluated for biological activities. The previous work by our group on cholinesterase enzyme inhibition potential revealed that 2,5-disubstituted-1,3,4-oxadiazole derivatives exhibited good inhibition potential for the AChE enzyme (Gul et al., 2013, Abbasi et al., 2013). A series of derivatives of 1,3,4-oxadiazole have been synthesized with structural modification and subjected to AChE inhibitory activity to inaugurate more potent inhibitors. The structural modification has a key role in affecting the bioactivities of compounds (Modi et al., 2012). The synthesized new series of *N*-substituted derivatives of 3-[(5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]propanamide (**7a-q**) was also analyzed for hemolytic potential to evaluate their level of toxicity.

2. Results and discussion

In the presented research work, a series of *N*-substituted derivatives of 3-[(5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]propanamide (**7a-q**) has been synthesized by following multistep protocol sketched in Scheme 1. The varying substituents are listed in Table 1.

The heterocyclic 1,3,4-oxadiazole, 5-[1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl]-1,3,4-oxadiazol-2-thiol (**3**) was synthesized by three step protocol. The first step involved the reaction of ethyl nipecotate (**b**) and 4-chlorobenzene sulfonyl chloride (**a**) in basic aqueous media to synthesize ethyl 1-(4-chlorophenylsulfonyl)piperidin-3-carboxylate (**1**). This product was collected at neutral pH for maximum yield. The second step involved refluxing of **1** with

hydrazine to acquire the corresponding carbohydrazide. The synthesized carbohydrazide, **2**, was refluxed with carbon disulfide in alcoholic media in presence of potassium hydroxide to synthesize the heterocyclic 1,3,4-oxadiazole, **3**. The product was filtered out from the solution with pH = 5-6. Low acidic pH was mandatory for maximum yield. The structure of compound **3** was characterized by IR spectrum with characteristic absorption band at 1591 cm^{-1} for *C*=N stretching and 1230, 1072 cm^{-1} for C-O-C stretching indicating the oxadiazole ring formation. Characteristic absorption of S-H group obtained at 2252 cm^{-1}. Parallel to this a series of *N*-alkyl/aralkyl/aryl-3-bromopropanamides (**6a-q**) was synthesized by the reaction of alkyl/aralkyl/aryl amines (**4a-q**) with 3-bromopropionyl chloride (**5**) in basic aq. medium. Target compounds were synthesized by gearing up compound **3** with these *N*-alkyl/aralkyl/aryl-3-bromopropanamides (**6a-q**) in aprotic solvent. IR spectra of these compounds revealed characteristic signals at 3340 for N-H stretching and 1660 for C=O stretching due to acid amide group with disappearance of S-H stretching. The ^{1}H-NMR spectra recorded in $CDCl_3$ at 300 or 400 MHz gave δ (ppm) around 7.70-7.64 and 7.52-7.47 as two doublets characteristic for *p*-chlorophenyl sulfonyl moiety with integration of two protons each. The characteristic two triplets of propanamide appeared at δ (ppm) 3.44-3.57 and 2.69-3.00 due to adjacent thiol and carbonyl groups respectively. The ^{13}C-NMR spectra recorded in $CDCl_3$ at 100 MHz presented signals at δ (ppm) 160.0-170.0 for two quaternary carbons of 1,3,4-oxadiazole ring at second and fifth positions. The quaternary carbon of carbonyl of amide appeared the most downfield in the spectra, that is, above δ 170.0 ppm. The quaternary carbons of *p*-chlorophenyl sulfonyl moiety appeared at δ 130.0-140.0 ppm. The methine carbons of the same moiety appeared at δ 125.0-130.0 ppm. The methine carbon of piperidine ring directly attached to oxadiazole appeared relatively download at δ (ppm) 30.0-40.0 but methylene carbons of this ring appeared at δ 20.0-30.0 ppm. The mass spectra of the synthesized compounds presented definite fragmentation pattern indicated through different *m/z* peaks. An isotopic peak was observed due to presence of ^{37}Cl for each compound. The fragmentation of 1,3,4-oxadiazole ring resulted into two radical cations at *m/z* 300 and 284 and one cation at *m/z* 286. The removal of a radical through cleavage of piperidine-oxadiazole bond resulted into a cation at *m/z* 258. The cation of *p*-chlorophenyl sulfonyl moiety appeared at *m/z* 175 which further produced cation at *m/z* 111 after removal of SO_2 group. The varying part presented two definite peaks for *N*-substitutedcarbonyl moiety and *N*-substituted moiety as cationic fragments. Similarly piperidine ring and other varying

substituents revealed characteristic signals at their corresponding δ values explicated in experimental section.

2.1. AChE inhibition studies

All the derivatives were screened for enzyme inhibitory potential analysis against AChE enzyme. The enzyme inhibition results of the synthesized compounds have been presented as % inhibition and 50% inhibitory concentration (IC_{50}) values in Table 2. Gul et al. synthesized fifteen acetamide derivatives of 5-(4-nitrophenyl)-1,3,4-oxadiazole-2-thiol and found them too weak inhibitors of AChE enzyme except one compound (Gul et al., 2013). Abbasi et al. synthesized fourteen *S*-substituted derivatives of 5-(2-nitrostyryl)-1,3,4-oxadiazole-2-thiol but all the derivatives remained least active inhibitors of AChE enzyme than the parent molecule (Abbasi et al., 2013). The active compounds among these series suggested that further structural modification at second and fifth positions of 1,3,4-oxadiazole ring may lead to the inauguration of new potent molecules (Modi et al., 2012). All the derivatives showed excellent to moderate inhibition activity against cholinesterase enzyme. Eserine was used as reference standard for AChE inhibition activity. Among the compounds **7c-h** bearing dimethylphenyl groups, two compounds, **7g** and **7h**, showed better inhibitory potential against AChE with IC_{50} values of 7.21±0.04 µM and 5.76±0.02 µM, respectively, with reference to Eserine, the reference standard, having IC_{50} value of 0.04±0.0.0001 µM. The better activity may be attributed to the presence of 3,4-dimethylphenyl and 3,5-dimethylphenyl groups due to collective electron donating inductive effect of two methyl groups. Both of these compounds bear one methyl group at *meta* position in common. Among the compounds bearing mono-substituted phenyl groups like **7b**, **7k**, **7l**, **7p** and **7q**, only two compounds, **7l** and **7p** exhibited excellent AChE inhibitory activity with IC_{50} values of 3.64±0.01 µM and 7.62±0.03 µM respectively as compared to the reference standard. The better activity of these compounds might be due to electron donating inductive and mesomeric effect of 4-ethylphenyl and 2-ethoxyphenyl groups respectively. Thus the position and size of substituents has a considerable effect on the bioactivity of the synthesized compounds (Modi et al., 2012). Three compounds **7o**, **7f** and **7d** were the least active ones against AChE.

2.2. Hemolytic activity studies

All derivatives were analyzed for their hemolytic activity with reference of positive control Triton-X and negative control Phosphate Buffer Saline (PBS). The highest hemolytic activity

was exhibited by the compounds **7q**, **7b** and **7h** with % lysis values of 20.2, 19.5 and 19.0 respectively, but very much less than positive control Triton-X. The lowest hemolysis was revealed by compound **7m**, **7p** and **7n** with % lysis values of 6.4, 6.5 and 7.3 respectively but appreciably higher than that of negative control PBS. The most active compounds against AChE, **7l** and **7p** presented the least hemolytic activity of 9.8 and 6.5 respectively but the other two compounds **7g** and **7h** showed higher value of hemolytic activity.

3. Conclusion

A new series of potent molecules as new drug candidates against Alzheimer's disease was synthesized and systematically characterized by EI-MS, IR, ^{1}H-NMR and ^{13}C-NMR. The screening of synthesized molecules for anti-enzymatic activity depicted their excellent to moderate behavior. The most active compounds **7l**, **7p**, **7f** and **7c** bearing low % of hemolytic activity may be subjected to *in vivo* study for the treatment of Alzheimer's diseases. Some new derivatives with slight modifications may be synthesized in search of potential drug candidates. This may open more information for structure/activity relationship and rational design of potent novel drug molecules.

4. Materials and methods

4.1. Material

Thin layer chromatography was performed to assure the purity of all synthesized compounds. Ethyl acetate and *n*-hexane were used in different proportions as mobile phase. TLC was performed on pre-coated silica gel G-25-UV_{254} plates. UV lamp at 254 nm was used to visualize the spots on TLC. Different chemicals and analytical solvents were purchased from local suppliers. Griffin and George melting point apparatus was used to take melting points by open capillary method. IR spectra were recorded by KBr pellet method on Jasco-320-A spectrophotometer. Mass spectra (EIMS) were recorded on JMS-HX-110 spectrometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at 400, 300 and 100 MHz frequencies on Bruker spectrometers. Deuterated chloroform ($CDCl_3$) was used as solvent while TMS was the reference standard. Chemical shift values were presented in ppm unit.

4.2. Synthesis of ethyl 1-[(4-chlorophenyl)sulfonyl]piperidin-3-carboxylate (1)

Ethyl 1-[(4-chlorophenyl)sulfonyl]piperidin-3-carboxylate (**1**) was synthesized by the reaction of 4-chlorobenzene sulfonyl chloride (**a**; 0.05 mol) and ethyl piperidin-3-carboxylate (**b**; 0.05 mol) on stirring in aqueous medium for 4 hours. Dynamic pH was maintained at 9-10 by addition of 5% solution of Na_2CO_3. Reaction completion was assured by thin layer chromatography. *n*-Hexane and EtOAc (70:30) mixture was used to develop TLC and visualized in UV light. On completion reaction mixture was neutralized and product was collected by solvent extraction method. The solvent was evaporated to acquire pure product.

4.3. Synthesis of 1-[(4-chlorophenyl)sulfonyl]piperidin-3-carbohydrazide (2)

Compound **1** (0.05 mol) was converted into 1-[(4-chlorophenyl)sulfonyl]piperidin-3-carbohydrazide (**2**) on reflux for 3 hours with hydrated hydrazine (80 %) in methanol. TLC was developed to confirm the completion of reaction. On completion of reaction, excess methanol was distilled off and reaction contents were cooled to room temperature. Cold distilled water was added to reaction mixture and product was quenched by simple filtration. Precipitates were thoroughly washed and dried.

4.4. Synthesis of 5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-thiol (3)

5-(1-(4-Chlorophenylsulfonyl)-3-piperidinyl)-1,3,4-oxadiazol-2-thiol (**3**) was synthesized from compound **2** (0.06 mol) on reflux with CS_2 (0.12 mol) in ethanol in the presence of solid KOH (0.06 mol). Reaction mixture was refluxed for 5 hours. To assure the reaction completion, TLC was developed in EtOAc and *n*-hexane. On reaction completion, excess ethanol was distilled off and cold distilled water was added to reaction mixture. Finally dil. HCl was used to acidify the reaction contents for pH of 4-5 to get maximum yield. Precipitates obtained were filtered and thoroughly washed with water.

4.5. General procedure for synthesis of N-alkyl/aralkyl/aryl-3-bromopropanamides (6a-q)

N-Alkyl/aralkyl/aryl amines (**4a-q**; 0.03 mol) and 3-bromopropionyl chloride (**5**; 0.03 mol) were stirred in basic aqueous medium to obtain *N*-alkyl/aralkyl/aryl-3-bromopropanamides (**6a-q**). Sodium carbonate (5% aq. soln.) was used to control pH at 9-11. Vigorous stirring for 1 hour resulted into the formation of product. Precipitates formed were simply filtered and liquid products were obtained by solvent extraction. Complete use of the reactants was confirmed by TLC.

4.6. General procedure for synthesis of N-alkyl/aralkyl/aryl-3-[(5-{1-[(4-chlorophenyl) sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]propanamide (7a-q)

Compound **3** (0.2 g, 0.55 mmol) and equimolar *N*-alkyl/aralkyl/aryl-3-bromopropanamides (**6a-q**) were stirred in *N,N*-dimethylformamide (DMF) to acquire the target compounds. Compound **3** was dissolved in 10 mL DMF followed by LiH (0.55 mmol) and stirred for 0.5 hour. The synthesized electrophiles, **6a-q**, were added and the reaction mixture was further stirred for 3-4 hours. The products were acquired through filtration, washed by distilled water and dried.

4.7. Cholinesterase enzyme inhibition assay

The Acetyl cholinesterase activity was performed according to the reported method (Ellman et al., 1961).

4.8. Hemolytic activity

Hemolytic activity of the compounds was determined according to the reported method (Powell et al., 2000; Sharma et al., 2001).

4.9. Statistical analysis

All the measurements were obtained in triplicate and statistical analysis was performed by Microsoft Excel 2010. Results are presented as mean ± sem. Confidence level of ANOVA results is about 90%. IC_{50} (concentration with 50% inhibition) for enzyme inhibition was computed with suitable dilutions for each sample and results were calculated using EZ-Fit software (Perrella Scientific Inc, Amherst, USA).

4.10. Spectral data of synthesized compounds

4.10.1. 5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazole-2-thiol ***(3)***

White amorphous solid; Yield: 85%; M.P. 145-146 °C; Molecular formula: $C_{13}H_{14}ClN_3O_3S_2$; Molecular Mass: 359 $gmol^{-1}$; IR (KBr, cm^{-1}) ν_{max}: 3033 (Ar-H), 2252 (S-H stretching), 1591 (C=N stretching), 1524 (Ar C=C stretching), 1327 (-SO_2 stretching), 1230, 1072 (C-O-C stretching); ^{1}H-NMR ($CDCl_3$, 300 MHz, δ/ppm): 7.70 (d, J = 8.4 Hz, 2H, H-2" & H-6"), 7.52 (d, J = 8.7 Hz, 2H, H-3" & H-5"), 3.90 (dd, J = 11.7, 3.6 Hz, 1H, H_e-2'), 3.65 (br.d, J = 11.7 Hz, 1H, H_a-2'), 3.10-3.02 (m, 1H, H-3'), 2.65 (br.t, J = 9.9 Hz, 1H, H_e-6'), 2.49 (td, J = 11.4, 3.0 Hz, 1H, H_a-6'), 2.10-2.06 (m, 1H, H_e-5'), 1.90-1.82 (m, 1H, H_e-4'), 1.81-1.70 (m, 1H, H_a-5'), 1.69-1.58

(m, 1H, H_a-4'); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 178.4, 163.6 (quaternary C of oxadiazole), 139.7, 134.6 (Aromatic quaternary C), 129.5 (Aromatic C of =CH), 128.9 (Aromatic C of =CH), 47.5, 46.1 (aliphatic C of CH_2), 33.7 (Aliphatic C of CH), 26.5, 23.5 (aliphatic C of CH_2); EIMS (*m/z*): 361 $[M+2]^+$, 359 $[M]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 111 $[C_6H_4Cl]^+$.

4.10.2. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-phenylpropanamide ***(7a)***

Dirty green crystalline solid; Yield: 75%; M.P. 71-73 °C; Mol. formula: $C_{22}H_{23}ClN_4O_4S_2$; Mol. Mass: 507 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1347 (-SO_2 str.), 1514 (Ar C=C str.), 1571 (C=N str.), 3043 (Ar-H), 1233, 1075 (C-O-C stretching), 3345 (N-H stretching), 1665 (C=O stretching); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.84 (br.s, 1H, -NH), 7.68 (d, *J* = 8.0 Hz, 2H, H-2″ & H-6″), 7.50 (d, *J* = 7.6 Hz, 4H, H-3″, H-5″, H-2‴ & H-6‴), 7.28 (t, *J* = 7.6 Hz, 2H, H-3‴ & H-5‴), 7.08 (t, *J* = 7.2 Hz, 1H, H-4‴), 3.75 (br.d, *J* = 10.0 Hz, 1H, H_e-2′), 3.52 (t, *J* = 6.4 Hz, 2H, H-3‴), 3.44 (br.d, *J* = 10.0 Hz, 1H, H_a-2′), 3.22-3.19 (m, 1H, H-3′), 2.94 (t, *J* = 6.4 Hz, 2H, H-2‴), 2.91-2.89 (m, 1H, H_e-6′), 2.68-2.65 (m, 1H, H_a-6′), 2.05-1.73 (m, 4H, H-4′ & H-5′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 171.4, 163.7, 163.6 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.3, 140.2 (Aromatic quaternary C), 130.1, 129.6, 129.4, 124.1, 119.9 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2); EIMS (*m/z*): 509 $[M+2]^+$, 507 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_7H_6NO]^+$, 111 $[C_6H_4Cl]^+$, 92 $[C_6H_6N]^+$.

4.10.3. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(3-methylphenyl)propanamide ***(7b)***

Light grey amorphous solid; Yield: 72%; M.P. 79-81 °C; Mol. formula: $C_{23}H_{25}ClN_4O_4S_2$; Mol. Mass: 521 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1349 (-SO_2 str.), 1512 (Ar C=C str.), 1572 (C=N str.), 1237, 1077 (C-O-C stretching), 3341 (N-H stretching), 1663 (C=O stretching), 3045 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.81 (br.s, 1H, -NH), 7.68 (d, *J* = 8.0 Hz, 2H, H-2″ & H-6″), 7.50 (d, *J* = 7.6 Hz, 2H, H-3″ & H-5″), 7.36 (s, 1H, H-2‴), 7.27 (d, *J* = 7.6 Hz, 1H, H-6‴), 7.16 (t, *J* = 7.6 Hz, 1H, H-5‴), 6.90 (d, *J* = 7.2 Hz, 1H, H-4‴), 3.76 (br.d, *J* = 10.8 Hz, 1H, H_e-2′), 3.51 (t, *J* = 6.0 Hz, 2H, H-3‴), 3.50-3.47 (m, 1H, H_a-2′), 3.22-3.18 (m, 1H, H-3′), 2.92 (t, *J* = 6.0

Hz, 2H, H-2‴), 2.90-2.88 (m, 1H, H_e-6′), 2.68-2.65 (m, 1H, H_a-6′), 2.30 (s, 3H, CH_3-3‴′), 2.07-2.04 (m, 1H, H_e-5′), 1.95-1.91 (m, 1H, H_e-4′), 1.72-1.68 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 170.4, 164.1, 163.9 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 139.0, 136.8 (Aromatic quaternary C), 130.1, 129.6, 127.5, 124.6, 121.4, 118.0 (Aromatic C of =CH), 50.6, 47.4, 40.7 (aliphatic C of CH_2), 40.4 (Aliphatic C of CH), 28.2, 25.6, 24.4 (aliphatic C of CH_2), 20.9 (C of CH_3); EIMS (*m/z*): 523 $[M+2]^+$, 521 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 162 $[C_{10}H_{12}NO]^+$, 134 $[C_8H_8NO]^+$, 111 $[C_6H_4Cl]^+$, 106 $[C_7H_8N]^+$.

4.10.4. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2,3-dimethylphenyl)propanamide ***(7c)***

Light pink amorphous solid; Yield: 70%; M.P. 81-83 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1345 (-SO_2 str.), 1515 (Ar C=C str.), 1568 (C=N str.), 1231, 1073 (C-O-C stretching), 3348 (N-H stretching), 1669 (C=O stretching), 3046 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.67 (d, *J* = 8.4 Hz, 2H, H-2″ & H-6″), 7.49 (d, *J* = 8.0 Hz, 2H, H-3″ & H-5″), 7.41 (d, *J* = 7.6 Hz, 1H, H-6‴′), 7.37 (br.s, 1H, -NH), 7.07 (t, *J* = 7.2 Hz, 1H, H-5‴′), 7.00 (d, *J* = 7.2 Hz, 1H, H-4‴′), 3.84 (br.d, *J* = 10.8 Hz, 1H, H_e-2′), 3.55 (t, *J* = 6.4 Hz, 2H, H-3‴), 3.54-3.53 (m, 1H, H_a-2′), 3.22-3.18 (m, 1H, H-3′), 2.97 (t, *J* = 6.4 Hz, 2H, H-2‴), 2.83 (br.t, *J* = 10.0 Hz, 1H, H_e-6′), 2.59 (br.t, *J* = 8.8 Hz, 1H, H_a-6′), 2.27 (s, 3H, CH_3-3‴′), 2.12 (s, 3H, CH_3-2‴′), 2.11-2.09 (m, 1H, H_e-5′), 1.93-1.91 (m, 1H, H_e-4′), 1.80-1.67 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.9, 163.7, 163.8 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 138.6, 135.9, 128.5 (Aromatic quaternary C), 130.1, 129.6, 127.5, 126.3, 122.0 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 19.9, 14.8 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.5. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2,4-dimethylphenyl)propanamide ***(7d)***

Light grey amorphous solid; Yield: 76%; M.P. 78-80 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1341 (-SO_2 str.), 1519 (Ar C=C str.), 1564 (C=N str.), 1238, 1076 (C-O-C stretching), 3347 (N-H stretching), 1664 (C=O stretching), 3049 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.67 (d, J = 8.0 Hz, 2H, H-2″ & H-6″), 7.54 (d, J = 8.4 Hz, 1H, H-6‴′), 7.49 (d, J = 8.4 Hz, 2H, H-3″ & H-5″), 6.99-6.97 (m, 2H, H-3‴′ & H-5‴′), 3.84 (br.d, J = 10.8 Hz, 1H, H_e-2′), 3.54 (t, J = 6.4 Hz, 2H, H-3‴), 3.53-3.51 (m, 1H, H_a-2′), 3.23-3.19 (m, 1H, H-3′), 2.96 (t, J = 6.4 Hz, 2H, H-2‴), 2.81 (br.t, J = 9.6 Hz, 1H, H_e-6′), 2.58 (br.t, J = 9.2 Hz, 1H, H_a-6′), 2.26 (s, 3H, CH_3-2‴′), 2.19 (s, 3H, CH_3-4‴′), 2.10-2.07 (m, 1H, H_e-5′), 1.92-1.89 (m, 1H, H_e-4′), 1.75-1.68 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.9, 163.6, 163.5 (Carbonyl C & quaternary C of oxadiazole), 142.6, 140.2, 137.2, 134.1, 131.5 (Aromatic quaternary C), 130.1, 129.6, 127.3, 126.1, 123.2 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 20.7, 17.5 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.6. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2,5-dimethylphenyl)propanamide ***(7e)***

Grey amorphous solid; Yield: 77%; M.P. 89-91 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1345 (-SO_2 str.), 1511 (Ar C=C str.), 1560 (C=N str.), 1241, 1076 (C-O-C stretching), 3346 (N-H stretching), 1659 (C=O stretching), 3057 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.67 (d, J = 8.4 Hz, 2H, H-2″ & H-6″), 7.58 (s, 1H, -NH), 7.49 (d, J = 8.4 Hz, 2H, H-3″ & H-5″), 7.29 (s, 1H, H-6‴′), 7.03 (d, J = 7.6 Hz, 1H, H-4‴′), 6.87 (d, J = 7.6 Hz, 1H, H-3‴′), 3.84 (br.d, J = 10.8 Hz, 1H, H_e-2′), 3.54 (t, J = 5.6 Hz, 2H, H-3‴), 3.54-3.52 (m, 1H, H_a-2′), 3.21-3.18 (m, 1H, H-3′), 2.96 (t, J = 6.0 Hz, 2H, H-2‴), 2.81 (br.t, J = 10.0 Hz, 1H, H_e-6′), 2.57 (br.t, J = 9.2 Hz, 1H, H_a-6′), 2.28 (s, 3H, CH_3-2‴′), 2.18 (s, 3H, CH_3-5‴′), 2.10-2.07 (m, 1H, H_e-5′), 1.92-1.89 (m, 1H, H_e-4′), 1.80-1.60 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.8, 163.7, 163.5 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 135.9, 133.8, 132.5 (Aromatic quaternary C), 130.4, 129.9, 126.7, 123.3, 122.0 (Aromatic C of =CH), 50.6, 47.3, 40.7 (aliphatic C of CH_2), 40.3 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 22.8, 17.8 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$,

300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^{+}$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^{+}$, 175 $[C_6H_4ClO_2S]^{+}$, 176 $[C_{11}H_{14}NO]^{+}$, 148 $[C_9H_{10}NO]^{+}$, 120 $[C_8H_{10}N]^{+}$, 111 $[C_6H_4Cl]^{+}$.

4.10.7. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2,6-dimethylphenyl)propanamide ***(7f)***

White amorphous solid; Yield: 74%; M.P. 84-86 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1346 (-SO_2 str.), 1512 (Ar C=C str.), 1561 (C=N str.), 1243, 1069 (C-O-C stretching), 3338 (N-H stretching), 1658 (C=O stretching), 3053 (Ar-H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ/ppm): 7.68 (d, J = 8.5 Hz, 2H, H-2″ & H-6″), 7.51 (d, J = 8.5 Hz, 2H, H-3″ & H-5″), 7.32 (s, 1H, -NH), 7.10-7.06 (m, 3H, H-3‴ to H-5‴), 3.83 (br.d, J = 9.4 Hz, 1H, H_e-2′), 3.57 (t, J = 6.8 Hz, 2H, H-3‴), 3.52 (br.d, J = 11.5 Hz, 1H, H_a-2′), 3.24-3.21 (m, 1H, H-3′), 3.00 (t, J = 6.8 Hz, 2H, H-2‴), 2.88 (br.t, J = 9.9 Hz, 1H, H_e-6′), 2.63 (br.t, J = 9.9 Hz, 1H, H_a-6′), 2.22 (s, 6H, CH_3-2‴ & CH_3-6‴), 2.11-2.09 (m, 1H, H_e-5′), 1.96-1.94 (m, 1H, H_e-4′), 1.80-1.70 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 174.3, 164.6, 163.2 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.4, 137.4, 132.7 (Aromatic quaternary C), 130.1, 129.6, 127.5, 125.8 (Aromatic C of =CH), 50.6, 47.1, 40.6 (aliphatic C of CH_2), 40.2 (Aliphatic C of CH), 28.6, 25.4, 24.2 (aliphatic C of CH_2), 18.5 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^{+}$, 535 $[M]^{+}$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^{+}$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^{+}$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^{+}$, 175 $[C_6H_4ClO_2S]^{+}$, 176 $[C_{11}H_{14}NO]^{+}$, 148 $[C_9H_{10}NO]^{+}$, 120 $[C_8H_{10}N]^{+}$, 111 $[C_6H_4Cl]^{+}$.

4.10.8. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(3,4-dimethylphenyl)propanamide ***(7g)***

White amorphous solid; Yield: 70%; M.P. 78-80 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1342 (-SO_2 str.), 1513 (Ar C=C str.), 1563 (C=N str.), 1241, 1076 (C-O-C stretching), 3342 (N-H stretching), 1657 (C=O stretching), 3055 (Ar-H); ^{1}H-NMR ($CDCl_3$, 600 MHz, δ/ppm): 7.70 (d, J = 8.5 Hz, 2H, H-2″ & H-6″), 7.59 (s, 1H, H-2‴), 7.52 (d, J = 8.5 Hz, 2H, H-3″ & H-5″), 7.31 (s, 1H, -NH), 7.21 (dd, J = 7.9, 1.8 Hz, 1H, H-6‴), 7.05 (d, J = 8.1 Hz, 1H, H-5‴), 3.80 (br.d, J = 10.2 Hz, 1H, H_e-2′), 3.55 (t, J = 6.9 Hz, 2H, H-3‴), 3.51-3.49 (m, 1H, H_a-2′), 3.24-3.20 (m, 1H, H-3′), 2.94 (t, J = 6.8 Hz, 2H, H-2‴), 2.90 (br.t, J = 8.8 Hz, 1H, H_e-6′), 2.65 (br.t, J = 9.4 Hz, 1H, H_a-6′), 2.22 (s, 3H, CH_3-4‴), 2.21 (s, 3H, CH_3-3‴), 2.09-2.07 (m, 1H, H_e-5′), 1.96-1.94 (m, 1H, H_e-4′), 1.79-1.72 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$,

100 MHz, *δ*/ppm): 171.4, 163.9, 163.7 (Carbonyl C & quaternary C of oxadiazole), 142.7, 141.1, 140.2, 137.3, 128.7 (Aromatic quaternary C), 130.3, 129.8, 123.3, 122.0, 121.4 (Aromatic C of =CH), 50.6, 47.2, 40.7 (aliphatic C of CH_2), 40.3 (Aliphatic C of CH), 28.4, 25.4, 24.3 (aliphatic C of CH_2), 19.8, 18.6 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.9. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(3,5-dimethylphenyl)propanamide ***(7h)***

Light grey amorphous solid; Yield: 73%; M.P. 108-110 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1353 (-SO_2 str.), 1521 (Ar C=C str.), 1562 (C=N str.), 1245, 1076 (C-O-C stretching), 3345 (N-H stretching), 1662 (C=O stretching), 3056 (Ar-H); ^{1}H-NMR ($CDCl_3$, 300 MHz, *δ*/ppm): 7.69 (d, *J* = 8.4 Hz, 2H, H-2″ & H-6″), 7.61 (s, 1H, -NH), 7.50 (d, *J* = 8.4 Hz, 2H, H-3″ & H-5″), 7.12 (s, 2H, H-2‴ & H-6‴), 6.73 (s, 1H, H-4‴), 3.78 (br.d, *J* = 11.1 Hz, 1H, H_e-2′), 3.51 (t, *J* = 6.6 Hz, 2H, H-3‴), 3.48-3.46 (m, 1H, H_a-2′), 3.22-3.16 (m, 1H, H-3′), 2.91 (t, *J* = 6.6 Hz, 2H, H-2‴), 2.88-2.85 (m, 1H, H_e-6′), 2.64 (br.t, *J* = 9.3 Hz, 1H, H_a-6′), 2.25 (s, 6H, CH_3-3‴ & CH_3-5‴), 2.06-2.04 (m, 1H, H_e-5′), 1.95-1.92 (m, 1H, H_e-4′), 1.79-1.72 (m, 2H, H_a-5′ & H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, *δ*/ppm): 171.4, 164.1, 163.9 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 136.5 (Aromatic quaternary C), 130.1, 129.6, 125.4, 124.5 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 21.3 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.10. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(tetrahydro-2-furanylmethyl)propanamide ***(7i)***

Yellow sticky mass; Yield: 71%; Mol. formula: $C_{21}H_{27}ClN_4O_5S_2$; Mol. Mass: 515 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1357 (-SO_2 str.), 1527 (Ar C=C str.), 1567 (C=N str.), 1227, 1070 (C-O-C stretching), 3343 (N-H stretching), 1667 (C=O stretching), 3057 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, *δ*/ppm): 7.69 (d, *J* = 8.4 Hz, 2H, H-2″ & H-6″), 7.50 (d, *J* = 8.4 Hz, 2H, H-3″ & H-5″), 5.98 (s, 1H, -NH), 3.93-3.90 (m, 2H, H-2‴ & H_e-2′), 3.82 (q, *J* = 7.2 Hz, 1H, H_e-5‴), 3.70 (q, *J* =

8.0 Hz, 1H, H_a-5‴′), 3.63-3.55 (m, 2H, H_a-2′ & H_a-6‴′), 3.47 (t, *J* = 6.8 Hz, 1H, H-3‴), 3.18-3.10 (m, 2H, H-3′ & H_b-6‴′), 2.74 (t, *J* = 6.8 Hz, 2H, H-2‴), 2.73 (t, *J* = 10.8 Hz, 1H, H_e-6′), 2.50 (br.t, *J* = 10.8 Hz, 1H, H_a-6′), 2.12-2.09 (m, 1H, H_e-5′), 1.98-1.83 (m, 3H, H_e-4′ & H-3‴′), 1.78-1.73 (m, 1H, H_a-5′), 1.67-1.62 (m, 2H, H-4‴′), 1.54-1.49 (m, 1H, H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, *δ*/ppm): 171.7, 163.9, 163.3 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2 (Aromatic quaternary C), 130.3, 129.6 (Aromatic C of =CH), 76.2 (aliphatic tertiary C), 67.8, 50.8, 47.5, 44.3 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 39.8, 30.9, 28.3, 25.8, 25.4, 24.5 (aliphatic C of CH_2); EIMS (*m/z*): 517 $[M+2]^+$, 515 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 156 $[C_8H_{14}NO_2]^+$, 128 $[C_6H_{10}NO_2]^+$, 111 $[C_6H_4Cl]^+$, 100 $[C_5H_{10}NO]^+$.

4.10.11. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-phenethylpropanamide ***(7j)***

Dirty green sticky mass; Yield: 74%; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1350 (-SO_2 str.), 1513 (Ar C=C str.), 1565 (C=N str.), 1238, 1076 (C-O-C stretching), 3344 (N-H stretching), 1666 (C=O stretching), 3059 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, *δ*/ppm): 7.67 (d, *J* = 8.8 Hz, 2H, H-2″ & H-6″), 7.50 (d, *J* = 8.4 Hz, 2H, H-3″ & H-5″), 7.27 (t, *J* = 7.2 Hz, 2H, H-3‴′ & H-5‴′), 7.19 (t, *J* = 7.2 Hz, 1H, H-4‴′), 7.16 (d, *J* = 7.2 Hz, 2H, H-2‴′ & H-6‴′), 3.83 (dd, *J* = 11.2, 2.4 Hz, 1H, H_e-2′), 3.54-3.52 (m, 1H, H_a-2′), 3.51 (t, *J* = 6.8 Hz, 2H, H-3‴), 3.43 (t, *J* = 6.8 Hz, 2H, H-8‴′), 3.20-3.15 (m, 1H, H-3′), 2.80 (t, *J* = 6.8 Hz, 2H, H-7‴′), 2.78-2.76 (m, 1H, H_e-6′), 2.69 (t, *J* = 6.8 Hz, 2H, H-2‴), 2.56 (dt, *J* = 11.6, 2.8 Hz, 1H, H_a-6′), 2.10-2.06 (m, 1H, H_e-5′), 1.92-1.89 (m, 1H, H_e-4′), 1.76-1.72 (m, 1H, H_a-5′), 1.69-1.64 (m, 1H, H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, *δ*/ppm): 172.0, 163.8, 162.9 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 134.8 (Aromatic quaternary C), 130.8, 129.9, 128.7, 128.6, 127.9 (Aromatic C of =CH), 51.2, 47.9 (aliphatic C of CH_2), 40.7 (Aliphatic C of CH), 39..9, 39.8, 35.8, 28.5, 25.4, 24.6 (aliphatic C of CH_2); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.12. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2-ethylphenyl)propanamide ***(7k)***

Brown crystalline solid; Yield: 78%; M.P. 66-68 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1345 (-SO_2 str.), 1511 (Ar C=C str.), 1560 (C=N str.), 1225, 1068 (C-O-C stretching), 3337 (N-H stretching), 1657 (C=O stretching), 3057 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.71 (t, J = 8.0 Hz, 1H, H-6‴′), 7.67 (d, J = 8.4 Hz, 2H, H-2″ & H-6″), 7.49 (d, J = 8.4 Hz, 2H, H-3″ & H-5″), 7.40 (s, 1H, -NH), 7.18 (t, J = 6.4 Hz, 2H, H-4‴′ & H-5‴′), 7.12 (d, J = 7.2 Hz, 1H, H-3‴′), 3.84 (br.d, J = 10.0 Hz, 1H, H_e-2′), 3.54 (t, J = 6.4 Hz, 2H, H-3‴), 3.53-3.51 (m, 1H, H_a-2′), 3.21-3.19 (m, 1H, H-3′), 2.98 (t, J = 6.4 Hz, 2H, H-2‴), 2.81 (br.t, J = 8.8 Hz, 1H, H_e-6′), 2.58 (q, J = 7.6 Hz, 2H, $CH_3\underline{CH_2}$-2‴′), 2.56-2.55 (m, 1H, H_a-6′), 2.10-2.07 (m, 1H, H_e-5′), 1.92-1.89 (m, 1H, H_e-4′), 1.76-1.66 (m, 2H, H_a-4′ & H_a-5′), 1.18 (t, J = 7.2 Hz, 3H, $\underline{CH_3}CH_2$-2‴′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.9, 163.7, 163.5 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 135.9, 127.4 (Aromatic quaternary C), 130.1, 129.6, 128.8, 128.5, 124.5, 118.8 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5, 23.5 (aliphatic C of CH_2), 12.9 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.13. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(4-ethylphenyl)propanamide ***(7l)***

Light brown solid; Yield: 74%; M.P. 77-79 °C; Mol. formula: $C_{24}H_{27}ClN_4O_4S_2$; Mol. Mass: 535 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1346 (-SO_2 str.), 1512 (Ar C=C str.), 1561 (C=N str.), 1226, 1078 (C-O-C stretching), 3338 (N-H stretching), 1656 (C=O stretching), 3058 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.68 (d, J = 8.0 Hz, 2H, H-2″ & H-6″), 7.50 (d, J = 7.6 Hz, 2H, H-3″ & H-5″), 7.40 (d, J = 7.6 Hz, 2H, H-2‴′ & H-6‴′), 7.11 (d, J = 7.2 Hz, 2H, H-3‴′ & H-5‴′), 3.77 (br.d, J = 8.4 Hz, 1H, H_e-2′), 3.52 (t, J = 6.4 Hz, 2H, H-3‴), 3.51-3.49 (m, 1H, H_a-2′), 3.21-3.19 (m, 1H, H-3′), 2.93 (t, J = 6.4 Hz, 2H, H-2‴), 2.89-2.87 (m, 1H, H_e-6′), 2.63-2.60 (m, 1H, H_a-6′), 2.58 (q, J = 7.2 Hz, 2H, $CH_3\underline{CH_2}$-4‴′), 2.10-2.06 (m, 1H, H_e-5′), 1.94-1.93 (m, 1H, H_e-4′), 1.75-1.72 (m, 2H, H_a-4′ & H_a-5′), 1.18 (t, J = 7.6 Hz, 3H, $\underline{CH_3}CH_2$-4‴′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 171.4, 163.7, 163.5 (Carbonyl C & quaternary C of oxadiazole), 143.9, 142.7, 141.4, 140.2 (Aromatic quaternary C), 130.1, 129.6, 128.6, 119.6 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 28.0, 25.5, 24.5 (aliphatic C of CH_2),

15.8 (C of CH_3); EIMS (*m/z*): 537 $[M+2]^+$, 535 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 176 $[C_{11}H_{14}NO]^+$, 148 $[C_9H_{10}NO]^+$, 120 $[C_8H_{10}N]^+$, 111 $[C_6H_4Cl]^+$.

4.10.14. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2-ethyl-6-methylphenyl)propanamide ***(7m)***

White amorphous solid; Yield: 73%; M.P. 64-66 °C; Mol. formula: $C_{25}H_{29}ClN_4O_4S_2$; Mol. Mass: 549 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1341 (-SO_2 str.), 1507 (Ar C=C str.), 1556 (C=N str.), 1236, 1075 (C-O-C stretching), 3346 (N-H stretching), 1667 (C=O stretching), 3053 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.67 (d, J = 8.4 Hz, 2H, H-2″ & H-6″), 7.49 (d, J = 8.0 Hz, 2H, H-3″ & H-5″), 7.14-7.06 (m, 3H, H-3‴ to H-5‴), 3.81 (br.d, J = 10.4 Hz, 1H, H_e-2′), 3.57 (br.t, J = 6.4 Hz, 2H, H-3‴), 3.51 (br.d, J = 12.0 Hz, 1H, H_a-2′), 3.23-3.19 (m, 1H, H-3′), 2.99 (t, J = 6.4 Hz, 2H, H-2‴), 2.89 (br.t, J = 10.4 Hz, 1H, H_e-6′), 2.61 (br.t, J = 10.8 Hz, 1H, H_a-6′), 2.55 (q, J = 7.6 Hz, 2H, $CH_3\underline{CH_2}$-2⁗), 2.20 (s, 3H, CH_3-6⁗), 2.10-2.07 (m, 1H, H_e-5′), 1.94-1.92 (m, 1H, H_e-4′), 1.73-1.67 (m, 2H, H_a-4′ & H_a-5′), 1.14 (t, J = 7.2 Hz, 3H, $\underline{CH_3}CH_2$-2⁗); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 174.3, 163.7, 163.5 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.9, 140.2, 133.1, 131.8 (Aromatic quaternary C), 130.8, 130.1, 129.6, 128.5, 126.5 (Aromatic C of =CH), 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5, 23.9 (aliphatic C of CH_2), 18.9, 12.9 (C of CH_3); EIMS (*m/z*): 551 $[M+2]^+$, 549 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 190 $[C_{12}H_{16}NO]^+$, 162 $[C_{10}H_{12}NO]^+$, 134 $[C_9H_{12}N]^+$, 111 $[C_6H_4Cl]^+$.

4.7.15. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-benzyl propanamide ***(7n)***

Yellow sticky mass; Yield: 76%; Mol. formula: $C_{23}H_{25}ClN_4O_4S_2$; Mol. Mass: 521 $gmol^{-1}$; IR (KBr, ν_{max} cm^{-1}): 1344 (-SO_2 str.), 1510 (Ar C=C str.), 1559 (C=N str.), 1239, 1076 (C-O-C stretching), 3351 (N-H stretching), 1671 (C=O stretching), 3056 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.64 (d, J = 8.4 Hz, 2H, H-2″ & H-6″), 7.48 (d, J = 8.4 Hz, 2H, H-3″ & H-5″), 7.31-7.25 (m, 5H, H-2⁗ to H-6⁗), 4.41 (s, 2H, H-7⁗), 3.80 (br.d, J = 10.4 Hz, 1H, H_e-2′), 3.52 (br.d, J = 10.4 Hz, 1H, H_a-2′), 3.47 (br.t, J = 6.4 Hz, 2H, H-3‴), 3.18-3.14 (m, 1H, H-3′), 2.80-2.78 (m, 1H, H_e-6′), 2.77 (t, J = 6.8 Hz, 2H, H-2‴), 2.56 (dt, J = 10.0, 2.4 Hz, 1H, H_a-6′), 2.07-

2.04 (m, 1H, H_e-5′), 1.91-1.88 (m, 1H, H_e-4′), 1.73-1.70 (m, 1H, H_a-5′), 1.68-1.63 (m,1H, H_a-4′); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.0, 163.9, 163.4 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2, 138.6 (Aromatic quaternary C), 130.1, 129.6, 128.8, 128.6, 127.4 (Aromatic C of =CH), 50.8, 47.5, 42.6 (aliphatic C of CH_2), 40.6 (Aliphatic C of CH), 39.9, 28.3, 25.4, 24.5 (aliphatic C of CH_2); EIMS (*m/z*): 523 $[M+2]^+$, 521 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 162 $[C_{10}H_{12}NO]^+$, 134 $[C_8H_8NO]^+$, 111 $[C_6H_4Cl]^+$, 106 $[C_7H_8N]^+$.

4.7.16. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-cyclohexyl propanamide ***(7o)***

Light brown amorphous solid; Yield: 72%; M.P. 74-76 °C; Mol. formula: $C_{22}H_{29}ClN_4O_4S_2$; Mol. Mass: 513 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1340 (-SO_2 str.), 1514 (Ar C=C str.), 1555 (C=N str.), 1242, 1069 (C-O-C stretching), 3353 (N-H stretching), 1674 (C=O stretching), 3054 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.68 (d, *J* = 8.4 Hz, 2H, H-2″ & H-6″), 7.50 (d, *J* = 8.4 Hz, 2H, H-3″ & H-5″), 3.84 (br.d, *J* = 10.8 Hz, 1H, H_e-2′), 3.76-3.73 (m, 1H, H-1‴), 3.57-3.54 (m, 1H, H_a-2′), 3.45 (t, *J* = 6.6 Hz, 2H, H-3‴), 3.22-3.15 (m, 1H, H-3′), 2.79 (br.d, *J* = 10.2 Hz, 1H, H_e-6′), 2.70 (t, *J* = 6.6 Hz, 2H, H-2‴), 2.57 (br.t, *J* = 9.6 Hz, 1H, H_a-6′), 2.14-2.06 (m, 1H, H_e-5′), 1.95-1.86 (m, 3H, H_e-4′, H_e-3‴ & H_e-5‴), 1.76-1.71 (m, 1H, H_a-5′), 1.70-1.66 (m, 2H, H_a-3‴ & H_a-5‴), 1.60-1.51 (m, 3H, H_a-4′ & H-4‴), 1.37-1.28 (m, 2H, H_e-2‴ & H_e-6‴), 1.14-1.08 (m, 2H, H_a-2‴ & H_a-6‴); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 172.4, 164.1, 163.9 (Carbonyl C & quaternary C of oxadiazole), 142.7, 140.2 (Aromatic quaternary C), 130.1, 129.6 (Aromatic C of =CH), 50.8, 47.5 (aliphatic C of CH_2), 47.9, 40.5 (Aliphatic C of CH), 40.32, 32.4, 28.3, 26.3, 25.5, 25.4, 24.5 (aliphatic C of CH_2); EIMS (*m/z*): 515 $[M+2]^+$, 513 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 154 $[C_9H_{16}NO]^+$, 126 $[C_7H_{12}NO]^+$, 111 $[C_6H_4Cl]^+$, 98 $[C_6H_{12}N]^+$.

4.7.17. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(2-ethoxyphenyl)propanamide ***(7p)***

Grey amorphous solid; Yield: 78%; M.P. 81-83 °C; Mol. formula: $C_{24}H_{27}ClN_4O_5S_2$; Mol. Mass: 551 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1348 (-SO_2 str.), 1517 (Ar C=C str.), 1561 (C=N str.), 1225,

1077 (C-O-C stretching), 3335 (N-H stretching), 1656 (C=O stretching), 3053 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 8.31 (d, J = 7.6 Hz, 1H, H-6‴), 7.68 (d, J = 8.4 Hz, 2H, H-2″ & H-6″), 7.49 (d, J = 8.0 Hz, 2H, H-3″ & H-5″), 7.00 (t, J = 7.6 Hz, 1H, H-4‴), 6.91 (t, J = 7.6 Hz, 1H, H-5‴), 6.83 (d, J = 8.0 Hz, 1H, H-3‴), 4.08 (q, J = 6.8 Hz, 2H, $CH_3\underline{CH_2}O$-2‴), 3.86 (br.d, J = 10.8 Hz, 1H, H_e-2′), 3.67-3.64 (m, 1H, H_a-2′), 3.55 (t, J = 6.8 Hz, 2H, H-3‴), 3.23-3.18 (m, 1H, H-3′), 2.99 (t, J = 6.8 Hz, 2H, H-2‴), 2.66 (br.t, J = 10.8 Hz, 1H, H_e-6′), 2.45 (br.t, J = 10.4 Hz, 1H, H_a-6′), 2.17-2.09 (m, 1H, H_e-5′), 1.94-1.87 (m, 1H, H_e-4′), 1.84-1.78 (m, 1H, H_a-5′), 1.65-1.59 (m,1H, H_a-4′), 1.41 (t, J = 6.8 Hz, 3H, $\underline{CH_3}CH_2O$-2‴); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 170.5, 164.2, 163.8 (Carbonyl C & quaternary C of oxadiazole), 148.1, 142.7, 140.2, 126.7 (Aromatic quaternary C), 130.5, 129.9, 125.5, 122.7, 120.4, 113.6 (Aromatic C of =CH), 64.8, 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 14.9 (C of CH_3); EIMS (*m/z*): 553 $[M+2]^+$, 551 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 192 $[C_{11}H_{14}NO_2]^+$, 164 $[C_9H_{10}NO_2]^+$, 136 $[C_8H_{10}NO]^+$, 111 $[C_6H_4Cl]^+$.

4.7.18. 3-[(5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]-N-(4-ethoxyphenyl)propanamide ***(7q)***

Brick brown amorphous solid; Yield: 68%; M.P. 70-72 °C; Mol. formula: $C_{24}H_{27}ClN_4O_5S_2$; Mol. Mass: 551 gmol^{-1}; IR (KBr, ν_{max} cm^{-1}): 1347 (-SO_2 str.), 1516 (Ar C=C str.), 1563 (C=N str.), 1235, 1078 (C-O-C stretching), 3348 (N-H stretching), 1667 (C=O stretching), 3052 (Ar-H); ^{1}H-NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.68 (d, J = 6.0 Hz, 2H, H-2″ & H-6″), 7.50 (d, J = 7.2 Hz, 2H, H-3″ & H-5″), 7.39 (d, J = 6.4 Hz, 2H, H-2‴ & H-6‴), 6.81 (d, J = 6.8 Hz, 2H, H-3‴ & H-5‴), 3.98 (q, J = 7.2 Hz, 2H, $CH_3\underline{CH_2}O$-4‴), 3.69-3.65 (m, 1H, H_e-2′), 3.55-3.44 (m, 3H, H_a-2′ & H-3‴), 3.22-3.17 (m, 1H, H-3′), 2.98-2.88 (m, 3H, H-2‴ & H_e-6′), 2.69-2.62 (m, 1H, H_a-6′), 2.08-2.04 (m, 1H, H_e-5′), 1.89-1.83 (m, 1H, H_e-4′), 1.76-1.70 (m, 2H, H_a-4′ & H_a-5′), 1.37 (t, J = 6.8 Hz, 3H, $\underline{CH_3}CH_2O$-4‴); ^{13}C-NMR ($CDCl_3$, 100 MHz, δ/ppm): 171.4, 164.1, 163.7 (Carbonyl C & quaternary C of oxadiazole), 154.8, 142.7, 140.2, 136.1 (Aromatic quaternary C), 130.2, 129.7, 121.5, 115.7 (Aromatic C of =CH), 63.2, 50.8, 47.5, 40.9 (aliphatic C of CH_2), 40.5 (Aliphatic C of CH), 28.3, 25.5, 24.5 (aliphatic C of CH_2), 14.7 (C of CH_3); EIMS (*m/z*): 553 $[M+2]^+$, 551 $[M]^+$, 359 $[C_{13}H_{13}ClN_3O_3S_2]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 284

$[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 192 $[C_{11}H_{14}NO_2]^+$, 164 $[C_9H_{10}NO_2]^+$, 136 $[C_8H_{10}NO]^+$, 111 $[C_6H_4Cl]^+$.

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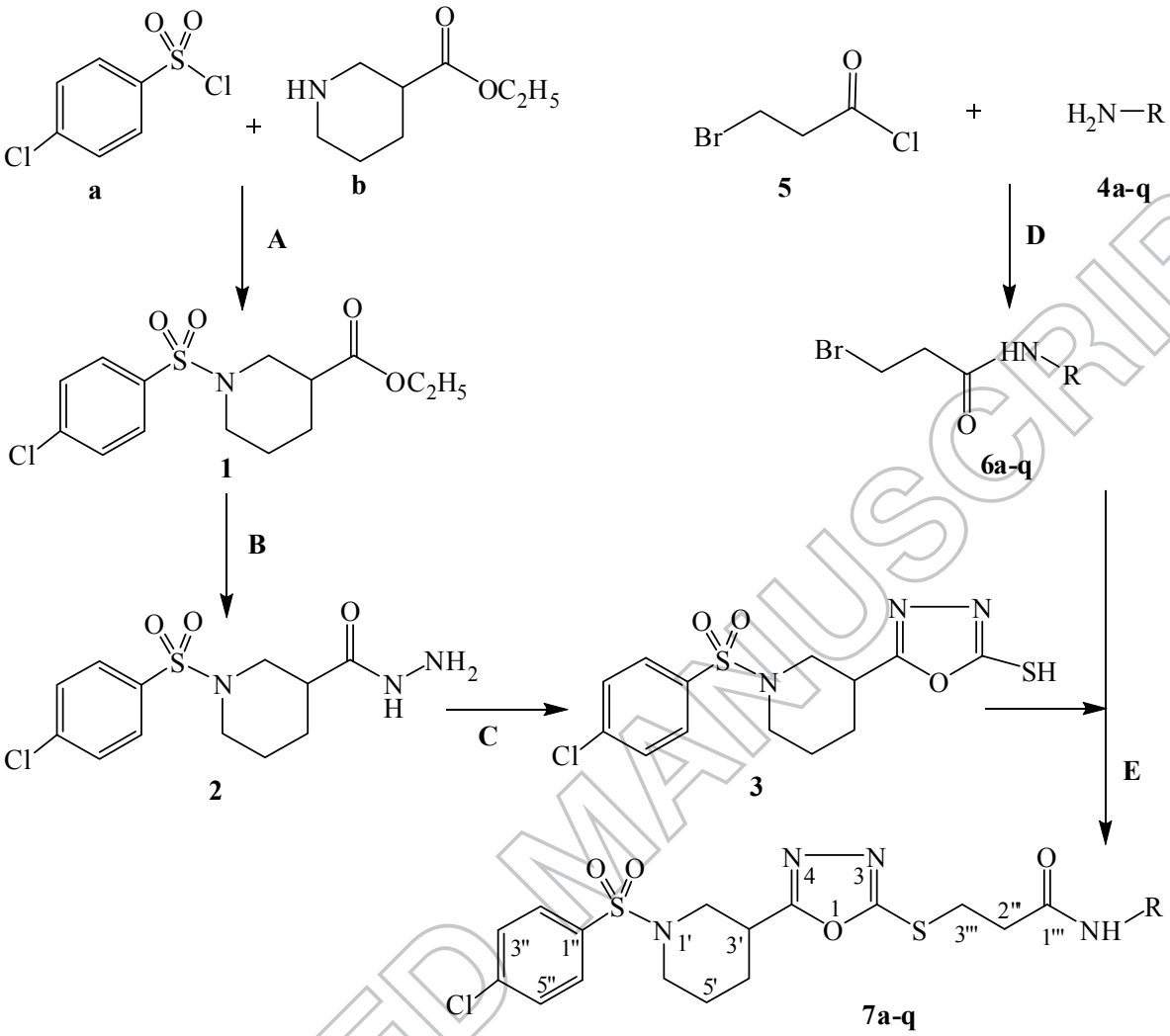


Scheme 1: Outline for the synthesis of *N*-substituted derivatives of 3-[(5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl)sulfanyl]propanamide (**7a-q**). **Reagents and conditions:** (A) 5% Na_2CO_3 soln./H_2O/pH=9-10/stirring for 4 hrs. (B) N_2H_4/MeOH/reflux for 3 hours. (C) CS_2/KOH/EtOH/refluxing for 5 hours. (D) 5% Na_2CO_3 soln./H_2O/pH=9-10/stirring for 1 hour. (E) DMF/LiH/stirring for 3-4 hours.

Table 1: Different alkyl/aralkyl/aryl substituents

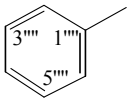
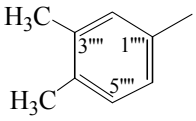
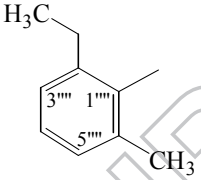
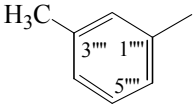
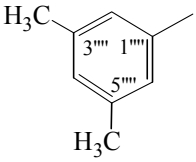
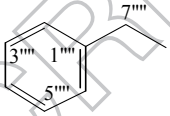
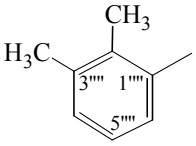
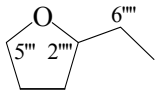
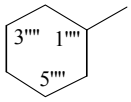
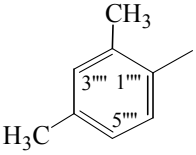
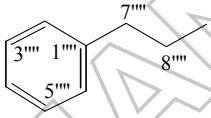
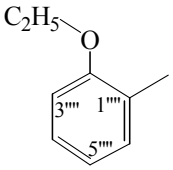
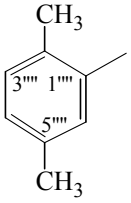
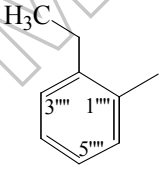
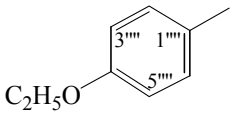
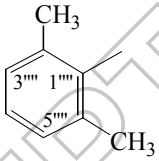
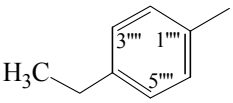
Comp.	R	Comp.	R	Comp.	R
7a		**7g**		**7m**	
7b		**7h**		**7n**	
7c		**7i**		**7o**	
7d		**7j**		**7p**	
7e		**7k**		**7q**	
7f		**7l**			

Table 2: Acetyl cholinesterase (AChE) enzyme inhibition and Hemolytic activity

Compd.	AChE		Hemolysis
	% Inhibition at 0.5 mM	IC_{50} (µM)	%
7a	94.35±0.86	45.86±0.17	9.7
7b	92.14±0.94	51.63±0.23	19.5
7c	91.24±0.63	58.24±0.19	10.6
7d	87.43±1.13	117.28±0.74	11.3
7e	91.64±0.75	64.35±0.43	8.6
7f	86.75±0.79	122.74±0.52	9.2
7g	95.62±0.09	7.21±0.04	13
7h	97.24±0.07	5.76±0.02	19
7i	-	-	-
7j	92.78±0.65	43.96±0.12	11.3
7k	97.34±0.15	21.74±0.09	9.2
7l	97.26±0.08	3.64±0.01	9.8
7m	96.15±0.24	32.74±0.08	6.4
7n	89.25±0.97	95.21±0.45	7.3
7o	85.76±0.97	176.83±0.45	8.1
7p	95.32±0.25	7.62±0.03	6.5
7q	91.24±0.32	34.15±0.07	20.2
Eserine	**91.27±1.17**	**0.04±0.0001**	**-**
Triton-X 100			**99.27**
PBS			**0.12**

NOTE: IC_{50} values (concentration for 50% inhibition) of compounds were recorded using EZ–Fit Enzyme kinetics software (Perella Scientific Inc. Amherst, USA). Results are presented as mean ± SEM.