SYNTHESIS, CHARACTERIZATION AND ANTI-INFLAMMATORY ACTIVITY OF NEW SERIES OF 1, 3, 4 OXADIAZOLE DERIVATIVES

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ABSTRACT

After refluxing the mixture of Ethyl (2,4,6-trichlorophenoxy) acetate (1) hydrazine hydrate and absolute ethanol (50 ml) in round bottom flask formed a solid mass of 2,4,6-Trichlorophenoxy acetic acid hydrazide (2). Now Compound 2 and benzoic acid was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 20 hours. It formed a solid mass of 5-(2,4,6-Trichlorophenoxymethyl)-2-substituted phenyl 1,3,4-oxadiazole (3a-q). The structure of these compounds have been established by IR (KBr), $^1$H NMR (CDCl$_3$) and mass spectroscopy. Compounds (3a-q) have been screened for their anti-inflammatory activities.

KEY WORDS: 1,3,4 oxadiazole, Anti-inflammatory, Standard drug.

INTRODUCTION

Heterocyclic compounds have so far been synthesized mainly due to the wide range of biological activities. Much attention has paid to the synthesis of heterocyclic compounds bearing nitrogen like oxadiazoles due to their higher pharmacological activity. Oxadiazoles are five-membered heterocyclic compounds with two nitrogen and one oxygen atom. Oxadiazoles and its derivatives are reported to be good therapeutic agents. The synthesis of novel Oxadiazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades for biological and agricultural reasons. Oxadiazoles play important role in medicinal chemistry also. Different classes of Oxadiazole compounds possess an extensive spectrum of pharmacological activities. They are known to have various activities such as antibacterial and antifungal $^{[1,2]}$, antimicrobial $^{[3,4,5,6]}$, anti-inflammatory $^{[5,7,8,9]}$, analgesic $^{[9]}$, anticancer $^{[10]}$, anti-convulsant $^{[11]}$ and anti-hepatitis B viral...
activities\textsuperscript{[12]} etc. For these reasons the chemistry of 1,3,4-oxadiazoles have been the subject of many investigations.

**MATERIALS AND METHODS**

**Experimental Section**

**Ethyl (2,4,6-trichlorophenoxy) acetate (1)**

To a solution of 2,4,6-trichlorophenol (0.5 mole) in dry acetone (150 ml), ethylchloroacetate (0.60 mole) was added followed by anhydrous $\text{K}_2\text{CO}_3$ (1.0 mole). Refluxed the solution for 20 hours. After then remove the solvent. Water was used to treat the mixture. Benzene was used for extraction. Then we collect the organic layer which was dried on anhydrous $\text{Na}_2\text{SO}_4$, filtered and evaporated to give liquid ester product Ethyl (2,4,6-trichlorophenoxy) acetate (1).

Yield of (1): 68\%, m.p.: oily in nature, $R_f$: 0.85, Molecular formula: $\text{C}_{10}\text{H}_9\text{Cl}_3\text{O}_3$, Molecular Weight : 283.54.

**2,4,6-Trichlorophenoxyacetic acid hydrazide (2)**

In a round bottom flask, a mixture of (1) (0.01 mole), hydrazine hydrate (0.20 mole) and absolute ethanol (50 ml) was added. Now the flask was attached with a condenser having calcium chloride guard tube. Refluxed the mixture for 24 hours on water bath. Concentrate, cool the mixture and poured into crushed ice. The solid mass was separated out after keeping the mixture for 4-5 hours at room temperature. Now this solid mass (2) was filtered, dried, and recrystallized from ethanol. Yield of (2): 82 \%, m.p. : 112 °C, $R_f$ : 0.70, Molecular formula: $\text{C}_8\text{H}_7\text{N}_2\text{O}_2\text{Cl}_3$, Molecular Weight : 269.52.

**Synthesis of 5-(2,4,6-trichlorophenoxymethyl)-2-substituted phenyl 1,3,4-oxadiazole (3a-q):** 5-(2,4,6-Trichlorophenoxymethyl)-2-(phenyl)-1,3,4-oxadiazole (3a): Compound (2) (0.001 mole) and benzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 20 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3a): 67 \%, m.p.: 146 °C, $R_f$ : 0.90, Molecular formula: $\text{C}_{15}\text{H}_9\text{N}_2\text{O}_2\text{Cl}_3$, Molecular weight: 355.61. %N: Found: 7.59\%; Caled: 7.87\%.
IR (KBr): 2996 (C-H), 1665 (C=N), 1564 (C=C), 799 (C-Cl). \(^1\)H NMR (CDCl\(_3\)): 5.18 (s, 2H, OCH\(_2\)), 7.21-7.58 (m, 6H, ArH).

5-(2,4,6-Trichlorophenoxymethyl)-2-(2'-chlorophenyl)-1,3,4-oxadiazole (3b)

Compound 2 (0.001 mole) and 2-chlorobenzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 23 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3b): 76 %, m.p.: 178 °C, R\(_f\): 0.87, Molecular formula: C\(_{15}\)H\(_8\)N\(_2\)O\(_2\)Cl\(_4\), Molecular weight: 390.05. %N: Found: 6.93%; Calcd: 7.18%.

5-(2,4,6-Trichlorophenoxymethyl)-2-(4'-chlorophenyl)-1,3,4-oxadiazole (3c)

Compound 2 (0.001 mole) and 4-chlorobenzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 25 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3c): 80 %, m.p.: 122 °C, R\(_f\): 0.88, Molecular formula: C\(_{15}\)H\(_8\)N\(_2\)O\(_2\)Cl\(_4\), Molecular weight: 390.05. %N: Found: 7.30%; Calcd: 6.59%.

5-(2,4,6-Trichlorophenoxymethyl)-2-(2',4'-dichlorophenyl)-1,3,4-oxadiazole (3d)

Compound 2 (0.001 mole) and 2,4-dichlorobenzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 22 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3d): 70 %, m.p.: 170 °C, R\(_f\): 0.93, Molecular formula: C\(_{15}\)H\(_7\)N\(_2\)O\(_2\)Cl\(_5\), Molecular weight: 424.50. %N: Found: 6.38%; Calcd: 6.59%.

\(^1\)H NMR (CDCl\(_3\)): 5.35 (s, 2H, OCH\(_2\)), 7.26-7.96 (m, 5H, ArH).
5-(2,4,6-Trichlorophenoxymethyl)-2-(2′,4′-dichlorophenoxymethyl)-1,3,4-oxadiazole (3e)
Compound 2 (0.001 mole) and 2,4-dichlorophenoxy acetic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 26 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3e): 74 %, m.p.: 128 °C, Rf : 0.87, Molecular formula: C_{16}H_{9}N_{2}O_{2}Cl_{5}, Molecular weight: 454.52. %N: Found: 6.04%; Calcd: 6.16%.

IR (KBr): 3016 (C-H), 1675 (C=N), 1576 (C=C), 796 (C-Cl).

^1H NMR (CDCl₃): 5.21 (s, 2H, OCH₂ of dichlorophenoxy), 5.35 (s, 2H, OCH₂ of trichlorophenoxy), 7.06-7.41 (m, 5H, ArH).

5-(2,4,6-Trichlorophenoxymethyl)-2-(4′-aminophenyl)-1,3,4-oxadiazole (3f)
Compound 2 (0.001 mole) and 4-amonobenzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 28 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3f): 78 %, m.p.: 108 °C, Rf : 0.83, Molecular formula: C_{15}H_{10}N_{3}O_{2}Cl_{3}, Molecular weight: 370.62. %N: Found: 11.41%; Calcd: 11.33%.

IR (KBr): 3379 (NH₂), 2977 (C-H), 1664 (C=N), 1581 (C=C), 798 (C-Cl).

^1H NMR (DMSO-d₆): 4.59 (s, 2H, OCH₂), 5.08 (s, 2H, NH₂), 7.67-7.87 (m, 6H, ArH).

5-(2,4,6-Trichlorophenoxymethyl)-2-(2′-aminophenyl)-1,3,4-oxadiazole (3g)
Compound 2 (0.001 mole) and anthranilic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 24 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3g): 59 %, m.p.: 146°C, Rf : 0.86, Molecular formula: C_{15}H_{10}N_{3}O_{2}Cl_{3}, Molecular weight: 370.62. %N: Found: 11.19%; Calcd: 11.33%.

IR (KBr): 3362 (NH₂), 3010 (C-H), 1655 (C=N), 1600 (C=C), 768 (C-Cl).
5-(2,4,6-Trichlorophenoxy methyl)-2-(4'-nitrophenyl)-1,3,4-oxadiazole (3h)

Compound 2 (0.001 mole) and 4-nitrobenzoic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 28 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3h): 64 %, m.p.: 188˚C, Rf : 0.86, Molecular formula: C_{15}H_{8}N_{3}O_{4}Cl_{3}, Molecular weight: 400.60. %N: Found: 10.26%; Calcd: 10.48%.

\[ \text{IR (KBr): } 2973 (\text{C-H}), 1650 (\text{C=N}), 1586 (\text{C=C}), 1340 (\text{NO}_2-\text{Aromatic}), 788 (\text{C-Cl}). \]

\[ ^1\text{H NMR (CDCl}_3\text{): } 5.36 (s, 2H, OCH}_2, 7.36-8.40 (m, 6H, ArH). \]

\[ \text{Mass (m/z): } 400(\text{M}^+), 249, 150, 122. \]

5-(2,4,6-Trichlorophenoxy methyl)-2-(2'-acetoxyphenyl)-1,3,4-oxadiazole (3i): Compound 2 (0.001 mole) and acetylsalicylic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 25 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3i): 61 %, m.p. 168˚C, Rf : 0.44, Molecular formula: C_{17}H_{11}N_{2}O_{4}Cl_{3}, Molecular weight: 413.64. %N: Found: 6.56%; Calcd: 6.77%.

\[ \text{IR (KBr): } 3011 (\text{C-H}), 1715 (\text{OCOCH}_3), 1680 (\text{C=N}), 1593 (\text{C=C}), 796 (\text{C-Cl}). \]

5-(2,4,6-Trichlorophenoxy methyl)-2-[1-(4'-isobutylphenyl)ethyl]-1,3,4-oxadiazole (3j)

Compound 2 (0.001 mole) and 2-(4-isobutylphenyl) propionic acid (ibuprofen) (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 24 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3j): 81 %, m.p.: 108˚C, Rf : 0.85, Molecular formula: C_{21}H_{21}N_{2}O_{2}Cl_{3}, Molecular weight: 439. 77. %N: Found: 6.52%; Calcd: 6.37%.

\[ \text{IR (KBr): } 2970 (\text{C-H}), 1675 (\text{C=N}), 1563 (\text{C=C}), 797 (\text{C-Cl}). \]
**5-(2,4,6-Trichlorophenoxy)methyl)-2-[1-(2'-fluoro-4'-biphenyl) ethyl]-1,3,4-oxadiazole (3k):** Compound 2 (0.001 mole) and 2-(2-fluoro-4-biphenyl) propionic acid (flurbiprofen) (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 28 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3k): 67 %, m.p.: 160˚C, Rf: 0.80, Molecular formula: C_{23}H_{16}N_{2}O_{2}Cl_{3}F, Molecular weight: 477.75. %N: Found: 5.69%; Calcd: 5.86%.

**IR (KBr):** 3014 (C-H), 1663 (C=N), 1560 (C=C), 1074 (C-F), 765 (C-Cl).

**1H NMR (CDCl₃):** 1.60 (d, 3H, CH₃), 3.78-3.86 (q, 1H, CH), 4.61 (s, 2H, OCH₂), 7.18-7.53 (m, 10H, ArH).

**Mass (m/z):** 477(M⁺), 249, 227, 199, 185.

**5-(2,4,6-Trichlorophenoxy)methyl)-2-[1-(6'-methoxynaphth-2'-yl) ethyl]-1,3,4-oxadiazole (3l):** Compound 2 (0.001 mole) and 2-(6-methoxynaphth-2-yl) propionic acid (naproxen) (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 24 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3l): 60 %, m.p. 206˚C, Rf: 0.78 , Molecular formula: C_{22}H_{17}N_{2}O_{3}Cl_{3}, Molecular weight: 463.75. %N: Found: 5.78%; Calcd: 6.04%.

**IR (KBr):** 2984 (C-H), 1670 (C=N), 1580 (C=C), 765 (C-Cl).

**1H NMR (CDCl₃):** 1.58 (d, 3H, CH₃), 3.80-3.84 (q, 1H, CH), 3.87 (s, 3H, OCH₃), 4.62 (s, 2H, OCH₂), 7.10-7.43 (m, 6H, naphthyl), 7.68 (s, 2H, chlorophenyl).

**5-(2,4,6-Trichlorophenoxy)methyl)-2-(naphth-2'-ylmethyl)-1,3,4-oxadiazole (3m):**

Compound 2 (0.001 mole) and naphthylacetic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 27 hours. The mixture was concentrated,
cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3m): 52 %, m.p.: 258, Rf: 0.82, Molecular formula: C_{20}H_{13}N_{2}O_{2}Cl_{3}, Molecular weight: 419.69. %N: Found: 6.41%; Calcd: 6.67%.

**IR (KBr):** 2998 (C-H), 1674 (C=N), 1577 (C=C), 781 (C-Cl).

5-(2,4,6-Trichlorophenoxymethyl)-2-[2-(2’,6’-dichloroanilino) benzyl]-1,3,4-oxadiazole (3n): Compound 2 (0.001 mole) and 2-(2,6-dichloroanilino) phenyl acetic acid (diclofenac) (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 26 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3n): 65 %, m.p. 192°C Rf: 0.77, Molecular formula: C_{22}H_{14}N_{3}O_{2}Cl_{5}, Molecular weight: 529.64. %N: Found: 7.72%; Calcd: 7.93%.

**IR (KBr):** 3388 (NH), 2993 (C-H), 1654 (C=N), 1568 (C=C), 753 (C-Cl).

5-(2,4,6-Trichlorophenoxymethyl)-2-(2’-hydroxyphenyl)-1,3,4-oxadiazole (3o): Compound 2 (0.001 mole) and salicylic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 24 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3o): 38 %, m.p. 152°C Rf: 0.63, Molecular formula: C_{15}H_{9}N_{2}O_{3}Cl_{3}, Molecular weight: 371.60. %N: Found: 7.33%; Calcd: 7.53%.

**IR (KBr):** 3566 (OH), 3012 (C-H), 1662 (C=N), 1584 (C=C), 758 (C-Cl).

5-(2,4,6-Trichlorophenoxymethyl)-2-(4’-hydroxyphenyl)-1,3,4-oxadiazole (3p)
Compound 2 (0.001 mole) and 4-hydroxyphenyl acetic acid (0.001 mole) was dissolved in phosphorus oxychloride and refluxed on a heating mantle for 28 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.
Yield of (3p): 44 %, m.p. 158°C, Rf: 0.61, Molecular formula: C_{16}H_{11}N_{2}O_{3}Cl_{3}, Molecular weight: 385.63. %N: Found: 7.13%; Calcd: 7.26%.

**IR (KBr):** 3603 (OH), 2991 (C-H), 1652 (C=N), 1578 (C=C), 748 (C-Cl).

5-(2,4,6-Trichlorophenoxymethyl)-2-mercapto-1,3,4-oxadiazole (3q): A mixture of hydrazide 2 (0.005 mole), potassium hydroxide (0.005 mole) and carbon disulphide (5 ml) in ethanol (50 ml) was refluxed on water bath for 18 hours. The mixture was concentrated, cooled and poured into crushed ice. The solid mass separated out, filtered, dried and recrystallized from methanol.

Yield of (3q): 56 %, m.p.: 160 °C, Rf : 0.87, Molecular formula: C_{9}H_{5}N_{2}O_{2}SCl_{3}, Molecular weight: 311.57. %N: Found: 8.83%; Calcd: 8.98%.

**IR (KBr):** 3049 (C-H), 1632 (C=N), 1586 (C=C), 1160 (C=S), 734 (C-Cl).

**1H NMR (CDCl_{3}):** 5.17 (s, 2H, OCH_{2}), 7.50 (s, 2H, ArH), 10.84 (bs, 1H, SH).

RESULT AND DISCUSSION

2,4,6-Trichlorophenoxyacetic acid hydrazide (2): The IR spectrum of the compound (2) showed peaks at 3359 cm^{-1}, NH stretching; 3072 cm^{-1}, CH stretching; 1669 cm^{-1}, C=O stretching; 1580 cm^{-1}, C=C stretching of aromatic rings and 757 cm^{-1}, C-Cl stretching vibrations. Its NMR spectrum which showed a singlet at δ 3.99 for OCH\textsubscript{2} protons, a singlet at δ 4.58 was also observed for NH\textsubscript{2} protons. In the aromatic region a singlet at δ
7.35 was noticed and point out the existence of 3 & 5 aromatic protons. A broad singlet at δ 8.06 was noticed and point out the existence of CONH proton.

5-(2,4,6-Trichlorophenoxymethyl)-2-(aryl)-1,3,4-oxadiazoles (3a-p): The IR spectrum of the compounds (3a-p) showed peaks at 3016-2970 cm⁻¹, CH stretching; 1680-1650 cm⁻¹, C=N stretching; 1600-1560 cm⁻¹, C=C stretching of aromatic rings and 800-740 cm⁻¹, C-Cl stretching vibrations.

The NMR and Mass spectrum of compounds (3a-q): Compound 3a showed a singlet at δ 5.18, δ 5.35 and point out the existence of OCH₂ protons, in the aromatic region a multiplet was observed at δ 7.21-7.58 for 7 aromatic protons. Compound 3d showed a singlet at δ 5.35 and point out the existence of OCH₂ protons. The presence of 5 aromatic protons was confirmed by the appearance of the multiplet at δ 7.26-7.96. Compound 3e showed two singlets centered at δ 5.21 and δ 5.35 indicating the presence of OCH₂ protons attached to the 2,4-dichlorophenyl and 2,4,6-trichlorophenyl rings respectively. In the aromatic region a multiplet at δ 7.06-7.41 was noticed and point out the existence of 5 aromatic protons. Its mass spectral data showed M⁺ at m/z 452, consistent with the expected molecular formula C₁₆H₉N₂O₂Cl₅. Further fragments were obtained at m/z 237, 209 and 195. Compound 3f showed a singlet at δ 4.59 indicating the presence of OCH₂ protons. The singlet for NH₂ protons was observed at δ 5.08. In the aromatic region a multiplet of 6 protons was observed at δ 7.67-7.87 indicating the presence of phenyl protons. Compound 3h showed a singlet at δ 5.36 for OCH₂ protons. A complex multiplet was observed at δ 7.36-8.40 indicating the presence of 6 aromatic protons. Its mass spectral data showed M⁺ at m/z 400, having molecular formula C₁₅H₈N₃O₄Cl₃. Further fragments were obtained at m/z 249, 150 and 122. The compound 3j was identified by its NMR spectral data, which showed a double doublet at δ 0.88 for six (CH₃)₂ protons. A doublet and a quartet were also observed at δ 1.56 and 3.69-3.74 for CH₃ and CH₃CH protons respectively. Moreover a doublet and a multiplet of CH₂ and CH protons of isobutyl group were observed at δ 2.45 and δ 1.84-1.89 respectively. The singlet of OCH₂ protons was also observed at δ 4.64, a complex multiplet of 6 phenyl protons was observed in the aromatic region at δ 7.11-7.61. Its mass spectral data showed M⁺ at m/z 439, having molecular formula C₂₁H₂₁N₂O₂Cl₃. Further fragments were obtained at m/z 395, 189 and 161. Compound 3k showed a doublet and a quartet for CH₃ and CH protons at δ 1.60 and 3.78-3.86 respectively. A singlet of OCH₂ protons was observed at δ 4.61, in the
aromatic region a complex multiplet of 10 protons was obtained at \( \delta \) 7.18-7.53 and point out the existence of phenyl protons. Its mass spectral data showed \( M^+ \) at \( m/z \) 477, having molecular formula \( C_{22}H_{16}N_2O_2Cl_3F \). Further peaks were observed at \( m/z \) 249, 227, 199 and 185. Compound 3l showed a doublet and a quartet at \( \delta \) 1.58 and 3.80-3.84 for the presence of \( \text{CH}_3 \) and \( \text{CH} \) protons respectively. A singlet for the mehoxy protons in the naphthyl ring was observed at \( \delta \) 3.87. The singlet of \( \text{OCH}_2 \) protons attached to the oxadiazole ring was also observed at \( \delta \) 4.62. A multiplet of 6 naphthyl protons was observed in the aromatic region at \( \delta \) 7.10-7.43, whereas the two protons of trichlorophenyl ring were obtained as a singlet at \( \delta \) 7.68.

5-(2,4,6-Trichlorophenoxymethyl)-2-mercapto-1,3,4-oxadiazole (3q): The IR spectrum of the compound (3q) showed peaks at 3049 cm\(^{-1}\), CH stretching; 1632 cm\(^{-1}\), C=N stretching; 1586 cm\(^{-1}\), C=C stretching of aromatic rings; 1160 cm\(^{-1}\), C=S stretching and 734 cm\(^{-1}\), C-Cl stretching vibrations.

NMR spectra of (3q) showed a singlet at \( \delta \) 5.17 for \( \text{OCH}_2 \) protons. The two trichlorophenyl protons were obtained as a singlet at \( \delta \) 7.50. Furthermore a broad singlet was observed at \( \delta \) 10.84 indicating the presence of SH protons. On the basis of these spectral data the following structure was assigned to the compounds.

**BIOLOGICAL ACTIVITY**

The synthesized 1,3,4-Oxadiazole derivatives were screened for their anti-inflammatory activity by carageenin-induced rat paw edema method of Winter et al\(^{180}\). The oxadiazole
derivatives of 2,4,6-trichlorophenol (3a-n & 3q) showed anti-inflammatory activity ranging from 49.99% to 72.72% at 70mg/Kg oral dose after 4 hours, whereas the standard drug Ibuprofen showed 86.35% inhibition of rat paw edema at the same oral dose. The results have shown in table-1.

The oxadiazole derivatives 3d (Ar = 2,4-dichlorophenoxy methyl) and 3j (Ar = 1-(4-isobutylphenyl)ethyl) showed maximum anti-inflammatory activity (72.72%), and when these groups were replaced by 4-aminophenyl (3f) and 4-nitrophenyl (3h) the activity was found to be minimum (51.51% and 49.99% respectively). A good anti-inflammatory activity was also observed when aryl group at 2-position of the oxadiazole nucleus was replaced by mercapto group. Rest of the compounds showed moderate to good activity.

Table-1: Anti-inflammatory Activity of 1,3,4-Oxadiazole Derivatives

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Mean Paw Volume ± SEM</th>
<th>% Inhibition ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibuprofen</td>
<td>0.030 ± 0.0044</td>
<td>86.35 ± 2.033*</td>
</tr>
<tr>
<td>3a</td>
<td>0.093 ± 0.0042</td>
<td>57.57 ± 1.916*</td>
</tr>
<tr>
<td>3b</td>
<td>0.090 ± 0.0044</td>
<td>59.08 ± 2.033*</td>
</tr>
<tr>
<td>3c</td>
<td>0.083 ± 0.0061</td>
<td>62.11 ± 2.794*</td>
</tr>
<tr>
<td>3d</td>
<td>0.060 ± 0.0073</td>
<td>72.72 ± 3.319*</td>
</tr>
<tr>
<td>3e</td>
<td>0.073 ± 0.0042</td>
<td>66.66 ± 1.916*</td>
</tr>
<tr>
<td>3f</td>
<td>0.106 ± 0.0066</td>
<td>51.51 ± 3.030*</td>
</tr>
<tr>
<td>3g</td>
<td>0.073 ± 0.0042</td>
<td>66.66 ± 1.916*</td>
</tr>
<tr>
<td>3h</td>
<td>0.110 ± 0.0044</td>
<td>49.99 ± 2.033*</td>
</tr>
<tr>
<td>3i</td>
<td>0.073 ± 0.0066</td>
<td>66.66 ± 3.030*</td>
</tr>
<tr>
<td>3j</td>
<td>0.060 ± 0.0073</td>
<td>72.72 ± 3.319*</td>
</tr>
<tr>
<td>3k</td>
<td>0.070 ± 0.0044</td>
<td>68.17 ± 3.033*</td>
</tr>
<tr>
<td>3l</td>
<td>0.067 ± 0.0042</td>
<td>69.69 ± 1.916*</td>
</tr>
<tr>
<td>3m</td>
<td>0.087 ± 0.0042</td>
<td>60.60 ± 1.916*</td>
</tr>
<tr>
<td>3n</td>
<td>0.080 ± 0.0073</td>
<td>63.63 ± 3.319*</td>
</tr>
<tr>
<td>3q</td>
<td>0.067 ± 0.0042</td>
<td>69.69 ± 1.916*</td>
</tr>
</tbody>
</table>

CONCLUSION
In this paper, I disclose the synthesis of 5-(2,4,6Trichlorophenoxy methyl)-2-substituted phenyl 1,3,4-oxadiazole (3a-q) and evaluated for anti-inflammatory activity by carageenin-induced rat paw edema method of Winter et al. Compounds (3a-n) & (3q) showed anti-inflammatory activity ranging from 49.99% to 72.72% at 70mg/Kg oral dose after 4 hours, whereas the standard drug Ibuprofen showed 86.35% inhibition of rat paw edema at the same oral dose.
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