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# Synthesis, cytotoxic evaluation of novel 2-((1*H*-indol-3-yl) methyl)-5-alkyl-1,3,4-oxadiazole and 2-alkyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole derivatives

Venepally Vijayendar[a,c], Sunitha Rani Routhu[b,c], C Ganesh Kumar[b,c]·& Ram Chandra Reddy Jala[a,c]*

[a] Centre for Lipid Research, CSIR-Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad 500 007, India

[b] Medicinal Chemistry and Biotechnology Division, CSIR-Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad 500 007, India

[c] Academy of Scientific and Innovative Research, New Delhi, India

E-mail: jrcreddy10@gmail.com; ramchandra@iict.res.in

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Interest in the biological applications of oleochemicals has resulted in the development of new heterocyclic compounds from the fatty acids which are renewable raw materials. In the present study the synthesis of hybrid compounds by involving fatty acids, indole-3-acetic acid (heteryl) and trimethoxy benzoic acid (aryl) to derive 2, 5-substituted 1,3,4-oxadiazole moiety using molecular hybridization approach has been carried out. A series of novel 2-((1*H*-indol-3-yl) methyl)-5-alkyl-1,3,4-oxadiazoles **4a-j** and 2-alkyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole **8a-j** analogues have been synthesized and evaluated for their cytotoxicity against A549, MCF-7 and HeLa cell lines. Almost all the tested compounds reveal cytotoxicity against all the cell lines, especially 2-((1*H*-indol-3-yl) methyl)-5-alkyl-1,3,4-oxadiazoles based compounds (**4c, 4d, 4e**) which display potent inhibitory activity with $IC_{50}$ values ranging between 8.26 to 11.36 μM.

**Keywords**: Renewable materials, fatty acids, oxadiazoles, indolyl, cytotoxicity

Cancer remains one of the most life-threatening diseases worldwide. This is one class of disease characterized by an abnormal cell growth and proliferation with the potential to infect surrounding tissues and metastasize to other tissues in the body. Most of the world's population at risk represents a major public health problem due to its morbidity and mortality[1-5]. Therefore, continuous efforts are needed to develop novel compounds with improved selectivity and activity by chemical modifications.

It is well-known that heterocyclic chemistry is one of the most valuable sources of new compounds with diverse biological activity. In this regard, nitrogen and oxygen containing five membered heterocyclic compounds have received considerable attention due to their wide range of biological and pharmacological activities. Among the family of heterocyclic compounds, the five membered oxadiazoles and their derivatives provide a valuable scaffold in medicinal chemistry. In this connection, 1,3,4-Oxadiazoles are of paramount interest of the synthetic and medicinal chemists because they are the important precursors for various heterocycles and also a privileged structural component in a variety of bioactive molecules. 1,3,4-Oxadiazole motif makes up the core structure of numerous biologically active compounds such as anticancer[6], antimicrobial[7], antineoplastic[8], antifungal[9-10], antibacterial activities [11]. In addition, many fatty acids[12] and fatty amides [13] are known to exhibit antimicrobial and cytotoxic activities. Long alkyl/alkenyl chains exhibited antimicrobial activity and some fatty acid derivatives were also known to possess antitumor and anti-depressant activities[14-16].

Meanwhile, methoxy groups on aryl systems have been broadly investigated for their biological effects[17]. These groups are important in cytotoxic and microtubule-binding agents used for cancer chemotherapy[18 - 19]. Recent studies on combretastatin A-4, which is an antitumour drug from the combretastatin group [20], have shown that the 3,4,5-trimethoxy phenyl groups are important for its antitumour activity[21, 22]. Moreover, recently various trimethoxy chalcones and their analogues have antioxidant activities[23]. The incorporation of trimethoxyphenyl moiety in organic compounds has attracted considerable attention due to its naturally derived characterization and wide prevalence in pesticides and medicinal compounds[24 - 26]. In addition to that indole nucleus is a privileged scaffold in natural and synthetic compounds with a wide range of

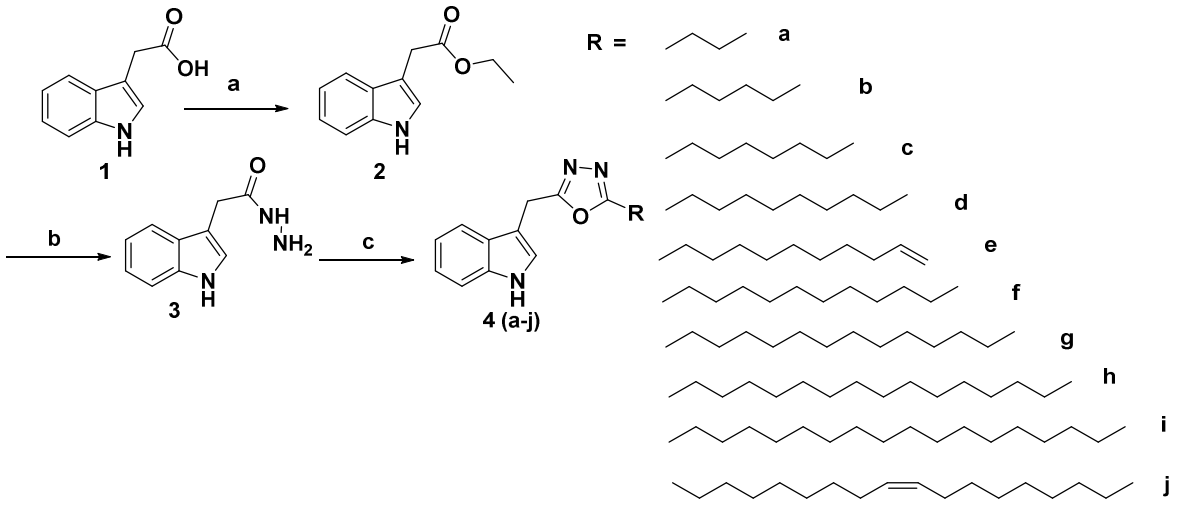
biological activities [27]. Indole is a core structural unit of many natural products and is widely used in agricultural and medicinal chemistry. Compounds containing an indole nucleus display a wide range of biological activities, such as anticancer, antidiabetic, antirheumatoidal, antioxidant and antiviral properties[28]. In that indole-3-acetic acid is a key plant growth hormone[29], tryptophan, an essential amino acid, participates in various biological processes [30] and Indomethacin is a nonsteroidal anti-inflammatory drug [31].

## Results and Discussion

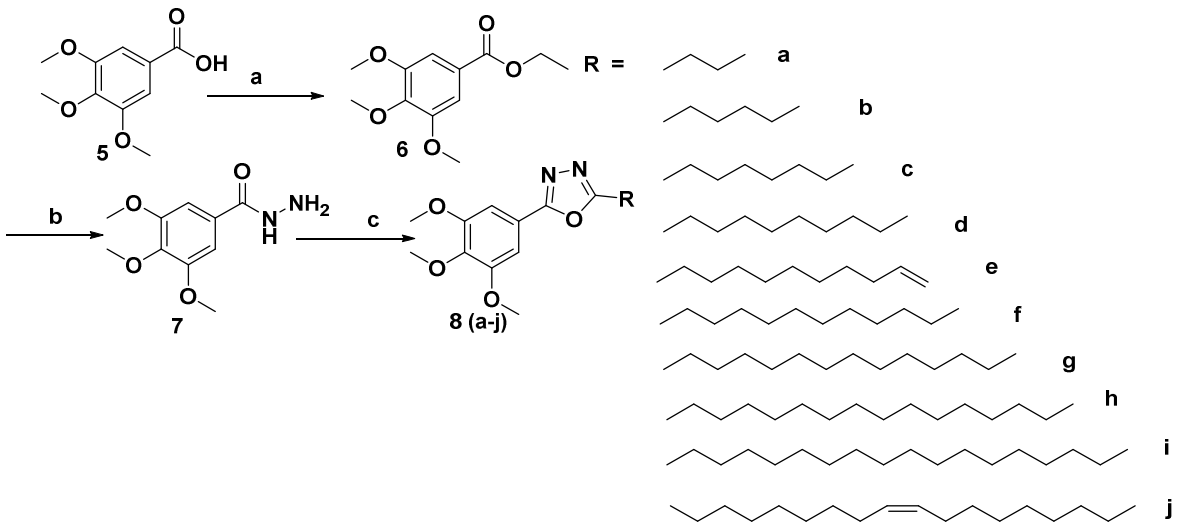
A series of some 2-((*1H-indol-3-yl*) methyl)-5-alkyl-1,3,4-oxadiazoles (**4a-4j**) and 2-alkyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole (**8a–8j**) derivatives were synthesized and as outlined in Scheme I and Scheme II. Aryl and heteroyl acid hydrazides (3, 7) were synthesized by the reaction of 85% hydrazine hydrate and compounds 2, 6 were derived from corresponding acids (1, 5), in ethanol under reflux conditions. Acid hydrazides (3, 7) derived from corresponding acids (1, 5) were cyclized with fatty acids in presence of phosphorus oxychloride to afford 2,5-disubstituted-1,3,4-oxadiazole derivatives (**4a-4j, 8a–8j**). All the compounds were characterized by spectroscopic (IR, $^1$H NMR, $^{13}$C NMR and mass) studies.

The structures of the newly synthesized compounds (**4a-4j**) and (**8a–8j**) were confirmed by spectral data ($^1$H NMR, $^{13}$C NMR, IR, and ESI-MS). All the spectral data of the synthesized compounds were in full agreement with the proposed structures and also discussed for a representative compounds such as (2-((1H-indol-3-yl) methyl)-5-propyl-1,3,4-oxadiazole) (**4a**), 2-propyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole (**8a**). For **4a** derivative, aromatic protons appeared as three distinct regions at 7.62 (d, $J$ = 7.9Hz, 1H, Ar-H), 7.36 (d, $J$ = 7.9Hz, 1H, Ar-H), 7.11-7.22 (m, 3H, Ar-H), where as $CH_2$ protons observed between indole ring and oxadiazole ring resonated as singlet at 4.32 (s, 2H, $CH_2$), $CH_2$ protons containing alkyl chain adjacent to oxadiazole ring resonated as triplet at 2.72-2.76 (t, $J$ = 7.5Hz, 2H, $CH_2$) and remaining aliphatic alkyl chain $CH_2$ protons appeared at 1.73-1.79 (m, 2H, $CH_2$). Further terminal methyl group protons observed as a triplet in the region 0.95 – 0.98 (t, $J$ = 6.7Hz, 3H, $CH_3$) and from the $^{13}$C NMR, peaks at 166.8 and 165.5 were represents oxadiazole moiety. Further, the structure of **4a** was also confirmed by mass spectrum showed a molecular ion peak at m/z 264 $[M+Na]^+$. The observed molecular mass is in agreement with the assigned molecular formula. Finally HRMS spectrum of this compound showed a molecular ion peak *m/z* $[M+H^+]$: calc for $C_{14}H_{16}ON_3$ is 242.12879 found 242.12825 ($C_{14}H_{16}ON_3$) in consistent with its molecular formula.

Similarly for **8a** derivative, aromatic protons appeared as a singlet at δ 7.26 (s, 2H, Ar-H), where as $OCH_3$ protons of trimethoxy phenyl ring resonated as a singlet at 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), $CH_2$ protons containing alkyl chain adjacent to oxadiazole ring appeared as a triplet at 2.89-2.92 (t, $J$




Scheme I — Reagent and conditions: (a) EtOH, $H_2SO_4$ reflux, 12 h, (b) hydrazine hydrate, EtOH reflux, 10 h, (c) R-COOH, $POCl_3$, reflux, 6 h




Scheme II — Reagent and conditions: (a). EtOH, $H_2SO_4$ reflux, 12 h, (b). hydrazine hydrate, EtOH reflux, 10 h, (c). R-COOH, $POCl_3$, reflux, 6 h

= 7.4Hz, 2H, $CH_2$) and remaining aliphatic alkyl chain $CH_2$ protons observed at 1.86-1.92 (m, 2H, $CH_2$). The terminal methyl group protons appeared as a triplet in the region 1.05-1.09 (t, *J* = 6.8Hz, 3H, $CH_3$) and from the $^{13}C$ NMR, peaks at 166.4 and 164.2 were due to oxadiazole moiety formation. Further, the structure of **8a** was also confirmed by its mass spectrum showed a molecular ion peak at m/z 301 $[M+Na]^+$. The observed molecular mass is in agreement with the assigned molecular formula. Finally HRMS spectrum of this compound showed molecular ion peak *m/z* $[M+H^+]$: calc for $C_{14}H_{19}O_4N_2$ is 279.13393 found 279.13324 ($C_{14}H_{19}O_4N_2$).

## Biology

The cytotoxicity of the newly synthesized compounds (**4a-4j, 8a–8j**) were tested using MTT assay against A549 (human lung cancer cell), MCF-7 (human breast cancer cell), HeLa (human adenocarcinoma cells) and one normal cell line i.e. HEK 293. The selectivity index (SI) was also determined using the following formula: SI = $IC_{50}$ of pure compound in a normal cell line / $IC_{50}$ of the same pure compound in cancer cell line, where $IC_{50}$ is the concentration required to inhibit 50% of the cell population. High SI value (>2) of a compound gives a selective toxicity towards cancer cells, while the compound with SI value <2 is considered to provide general toxicity in which it also can cause cytotoxicity in normal cells[32]. Inhibition of cell proliferation by these active compounds at various concentrations were measured, and their $IC_{50}$ (the concentration that caused 50% cell proliferation inhibition) values were calculated and summarized in Table I. Doxorubicin was used as a positive control. The obtained data revealed that most of the synthesized compounds showed good to promising cytotoxicity on all the tested cell lines (Table I). Among the tested compounds, **4c**, **4d** and **4e** showed promising activity against all the cell lines with $IC_{50}$ values ranging between 8.26 to 11.36 μM, and these results are in good agreement with the previous results obtained for heterocyclic based fatty acid compounds [33, 34]. While the remaining compounds showed moderate activity.

Further, all the tested compounds showed poor cytotoxicity on HEK293 (normal human embryonic kidney cells). Based on the cytotoxicity results against various cell lines, some information on the structure-activity relationship can be derived. Heteryl and fatty acid group substitution on oxadiazole ring favours good activity as compared to aryl and fatty acid group substitution on the oxadiazole ring. Also, the introduction of fatty alkyl chain in both the cases exhibited cytotoxicity. It was observed that the major difference between these molecules considering the variation in the cytotoxicity is due to the variation in carbon chain length and the substitution of heteryl and aryl groups.

## Experimental Section

### Materials and methods

All the chemicals used in this study were obtained from different commercial sources and were used without any further purification. Reactions were

Table I — Results of cytotoxicity of the synthesized compounds

| | $IC_{50}$ values (μM) | | | | | | |
|---|---|---|---|---|---|---|---|
| | A549 | SI† | MCF 7 | SI† | HeLa | SI† | HEK293 |
| **4a** | 18.36 ± 0.03 | 5.15 | 16.79 ± 0.92 | 5.63 | 20.18 ± 0.06 | 4.68 | 94.56 ± 0.12 |
| **4b** | 19.20 ± 0.96 | 4.90 | 18.87 ± 0.63 | 4.99 | 20.31 ±0.32 | 4.63 | 94.23 ± 0.52 |
| **4c** | 9.05 ± 0.59 | 9.86 | 9.50 ± 0.86 | 9.39 | 10.26 ± 0.98 | 8.69 | 89.24 ± 0.08 |
| **4d** | 8.26 ± 0.49 | 10.84 | 10.18 ± 0.36 | 8.80 | 10.26 ± 0.56 | 8.73 | 89.61 ± 0.46 |
| **4e** | 9.31 ± 0.97 | 9.25 | 9.24 ± 0.84 | 9.33 | 11.36 ± 0.06 | 7.58 | 86.21 ± 0.31 |
| **4f** | 25.13 ± 0.02 | 3.94 | 20.92 ± 0.98 | 4.74 | 18.26 ± 0.26 | 5.43 | 99.23 ± 0.16 |
| **4g** | 23.06 ± 0.09 | 4.20 | 19.21 ± 0.92 | 5.05 | 20.23 ± 0.58 | 4.79 | 97.08 ± 0.89 |
| **4h** | 31.03 ± 0.25 | 2.72 | 29.78 ± 0.32 | 2.83 | 30.20 ± 0.36 | 2.80 | 84.56 ± 0.93 |
| **4i** | 63.06 ± 0.46 | 1.40 | 61.79 ± 0.69 | 1.43 | 62.31 ± 0.89 | 1.41 | 88.46 ± 0.13 |
| **4j** | 17.65 ± 0.96 | 4.73 | 13.85 ± 0.36 | 6.03 | 19.26 ± 0.26 | 4.33 | 83.56 ± 0.59 |
| **8a** | 19.93 ± 0.42 | 4.82 | 17.67 ± 0.06 | 5.44 | 20.01 ± 0.12 | 4.81 | 96.26 ± 0.92 |
| **8b** | 20.63 ± 0.96 | 4.33 | 18.60 ± 0.93 | 4.80 | 21.97 ± 0.86 | 4.06 | 89.36 ± 0.36 |
| **8c** | 22.30 ± 0.45 | 4.36 | 19.22 ± 0.23 | 5.06 | 18.10 ± 0.23 | 5.37 | 97.26 ± 0.46 |
| **8d** | 21.49 ± 0.32 | 3.54 | 19.77 ± 0.96 | 3.85 | 18.03 ± 0.29 | 4.22 | 76.26 ± 0.76 |
| **8e** | 26.16 ± 0.51 | 3.40 | 24.51 ± 0.33 | 3.63 | 27.06 ± 0.31 | 3.29 | 89.16 ± 0.89 |
| **8f** | 35.18 ± 0.51 | 2.73 | 33.57 ± 0.32 | 2.86 | 39.98 ± 0.66 | 2.40 | 96.26 ± 0.21 |
| **8g** | 17.69 ± 0.18 | 4.94 | 18.22 ± 1.93 | 4.80 | 16.96 ± 0.69 | 5.16 | 87.56 ± 0.26 |
| **8h** | 16.34 ± 0.84 | 6.06 | 15.74 ± 0.95 | 6.29 | 18.18 ± 0.98 | 5.44 | 99.03 ± 0.79 |
| **8i** | 19.76 ± 0.72 | 3.87 | 16.50 ± 0.36 | 4.64 | 23.60 ± 0.12 | 3.24 | 76.56 ± 0.25 |
| **8j** | 17.94 ± 0.65 | 4.88 | 16.75 ± 0.09 | 5.23 | 21.09 ± 0.35 | 4.15 | 87.65 ± 0.13 |
| **Doxorubicin** | 2.10 ± 0.09 | 37.26 | 3.12 ± 0.12 | 25.08 | 1.78 ± 0.24 | 43.96 | 78.26 ± 0.89 |

$IC_{50}$ is the concentration required to inhibit 50% of the cell population; A549: human alveolar adenocarcinoma epithelial cells (ATCC No. CCL-185), MCF-7: human breast adenocarcinoma cells (ATCC No. HTB-22), HeLa: human cervical cancer cell line (ATCC No. CCL-2); HEK293: normal human embryonic kidney cells (ATCC No. CRL-1573)

†Selectivity index (SI) = $IC_{50}$ of pure compound in a normal cell line / $IC_{50}$ of the same pure compound in cancer cell line, where $IC_{50}$ is the concentration required to inhibit 50% of the cell population

monitored on micro TLC with UV detection. Final purification was carried out using silica gel 60-120 mesh (Rankem). All $^{1}H$ and $^{13}C$ NMR spectra were recorded on AVANCE (300 and 500 MHz for $^{1}H$ NMR and 75 MHz for $^{13}C$NMR). Chemical shifts are reported in ppm with reference to internal standard TMS. Molecular weights of unknown compounds were identified by ESI-MS and HRMS (Electron spray ionization technique). IR spectra were recorded in chloroform on a Perkin-Elmer FT-IR spectrum BX.

**Synthesis of ethyl 2-(1*H*-indol-3-yl) acetate, 2**

The ester was prepared by refluxing 2-(1H-indol-3-yl) acetic acid (5 g, 1 mmol) in excess of absolute ethanol (50 mL) in the presence of few drops of conc. sulphuric acid for 12 h and the progress of reaction was monitored by TLC. After 12 h reaction time, the solvent was evaporated under reduced pressure, water was added and the product was extracted with ethyl acetate and dried over anhydrous sodium sulphate. The crude product was purified by using column chromatography to afford the title compound in 86% yield. $^{1}H$ NMR (300 MHz, $CDCl_3$): δ 8.11 (Broad-singlet, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.22 (m, 3H, Ar-H), 4.13-4.19 (m, 2H, $CH_2$), 1.23-1.27 (t, *J* = 7.1Hz, 3H, $CH_3$); MS (ESI, *m/z*) $[M+Na]^+$ 226.

**Synthesis of 2-(1*H*-indol-3-yl) acetohydrazide, 3**

A mixture of ethyl 2-(1*H*-indol-3-yl) acetate (2 g, 1 mmol), hydrazine hydrate (6 mL, 15 mmol) and 20 mL of ethanol was refluxed on an oil bath for 10 h and the progress of reaction was monitored by TLC. After 10 h reaction time, the solvent was evaporated under reduced pressure and the concentrated solution was quenched to ice cold water. The solid separated was filtered, washed and dried. The crude product was purified by recrystalization from ethanol which afforded the title compound in 74% yield. $^{1}H$ NMR (300 MHz, $CDCl_3$): δ 8.11 (Broad- singlet, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), δ 7.53 (Broad-singlet, 1H, NH), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.22 (m, 3H, Ar-H), 4.13-4.19 (m, 2H, $CH_2$), 4.12 (Broad-singlet, 2H, $NH_2$),1.23-1.27 (t, 3H, $CH_3$); MS (ESI, *m/z*) $[M+H]^+$ 190.

**General procedure for the synthesis of target compounds, 4a-j**

A mixture of 2-(1*H*-indol-3-yl) acetohydrazide (3) (1mmol), fatty acids (1mmoL) and phosphorous

oxychloride (2.5mL) was refluxed for 6 h. The excess solvent was distilled off under reduced pressure and the residue was quenched with ice cold water and the product was extracted with ethyl acetate and dried over anhydrous sodium sulphate. The crude product was purified by using column chromatography to afford the title compounds.

**2-((1*H*-Indol-3-yl) methyl)-5-propyl-1,3,4-oxadiazole, 4a**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 43% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 8.25 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.22 (m, 3H, Ar-H), 4.32 (s, 2H, $CH_2$), 2.72-2.76 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.73-1.79 (m, 2H, $CH_2$), 0.95 – 0.98 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.8, 165.5, 135.8, 126.4, 122.8, 122.0, 119.4, 118.2, 111.0, 107.9, 26.8, 21.8, 19.5, 13.25; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3441, 3015, 2936, 2872, 1574, 1498, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+Na]^+$ 264; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{14}H_{16}ON_3$ is 242.12879 found 242.12825 ($C_{14}H_{16}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-pentyl-1,3,4-oxadiazole, 4b**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 48% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 8.30 (s, 1H, NH), 7.63 (d, *J* = 7.9Hz, 1H, Ar-H), 7.37 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.22 (m, 3H, Ar-H), 4.31 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.69-1.75 (m, 2H, $CH_2$), 1.28-1.33 (m, 4H, $(-CH_2-)_2$), 0.84 – 0.87 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.6, 166.0, 136.4, 127.0, 123.2, 122.7, 120.1, 118.9, 111.5, 108.7, 31.3, 26.3, 25.5, 22.4, 14.0; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3442, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+Na]^+$ 292; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{16}H_{20}ON_3$ is 270.16009 found 270.15958 ($C_{16}H_{20}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-heptyl-1,3,4-oxadiazole, 4c**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 50% yield as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.23 (m, 3H, Ar-H), 4.32 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.75 (m, 2H, $CH_2$), 1.21-1.33 (m, 8H, $(-CH_2-)_4$), 0.84 – 0.88 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.6, 166.0, 136.4, 127.0, 123.4, 122.5, 120.0, 118.8, 111.6, 108.4, 31.8, 29.1, 26.6, 25.5, 22.8, 22.3, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3441, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+H]^+$ 298; HR-MS (ESI) *m/z* $[M+Na^+]$: calc for $C_{18}H_{23}ON_3Na$ is 320.17333 found 320.17257 ($C_{18}H_{23}ON_3Na$).

**2-((1*H*-Indol-3-yl) methyl)-5-nonyl-1,3,4-oxadiazole, 4d**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 56% yield as a semi solid**.** $^1$H NMR (300 MHz, $CDCl_3$): δ 8.17 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.37 (d, *J* = 7.9Hz, 1H, Ar-H), 7.12-7.24 (m, 3H, Ar-H), 4.32 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.75 (m, 2H, $CH_2$), 1.24-1.31 (m, 12H, $(-CH_2-)_6$), 0.85 – 0.89 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.6, 166.0, 136.4, 127.0, 123.4, 122.6, 120.0, 118.8, 111.6, 108.5, 32.0, 29.2, 26.6, 25.5, 22.9, 22.3, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3442, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+H]^+$ 326; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{20}H_{28}ON_3$ is 326.22269 found 326.22208($C_{20}H_{28}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-(dec-9-en-1-yl)-1,3,4-oxadiazole, 4e**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 58% yield as a semi solid**.** $^1$H NMR (300 MHz, $CDCl_3$): δ 8.15 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.23 (m, 3H, Ar-H), 5.76-5.84 (m, 1H, $CH_2$-*CH*=$CH_2$), 4.91-5.00 (m, 2H, $CH_2$-*C*H=*CH*$_2$), 4.32 (s, 2H, $CH_2$), 2.73-2.76 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.98-2.04 (m, 2H, $CH_2$), 1.68-1.74 (m, 2H, $CH_2$), 1.25-1.35 (m, 10H, $(-CH_2-)_5$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.2, 165.7, 136.1, 131.4, 126.7, 124.6, 123.0, 122.3, 119.8, 118.6, 114.1, 111.2, 108.4, 32.4, 29.4, 28.8, 26.3, 25.2, 22.0, 17.8, 13.9; IR (KBr $\nu_{max}$ $cm^{-1}$): 3297, 2925, 2850, 1732, 1597, 1567, 1461, 1165, 1102, 966, 741; MS (ESI, *m/z*) $[M+H]^+$ 338; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{21}H_{28}ON_3$ is 338.22269 found 338.22207 ($C_{21}H_{28}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-undecyl-1,3,4-oxadiazole, 4f**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 48% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 8.23 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.12-7.22 (m, 3H, Ar-H), 4.31 (s, 2H, $CH_2$), 2.73-2.76 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.74 (t, *J* =7.4Hz, 2H, $CH_2$), 1.23-1.32 (m, 16H,

($-CH_2-)_8$), 0.86 – 0.89 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.0, 167.6, 136.4, 127.0, 123.3, 122.6, 120.1, 118.9, 111.5, 108.6, 32.2, 29.9, 26.6, 25.6, 22.9, 22.4, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3441, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+H]^+$ 354; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{22}H_{32}ON_3$ is 354.25399 found 354.25335 ($C_{22}H_{32}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-tridecyl-1,3,4-oxadiazole, 4g**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 51% yield as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.21 (s, 1H, NH), 7.64 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.12-7.21 (m, 3H, Ar-H), 4.32 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.75 (t, *J* =7.4Hz, 2H, $CH_2$), 1.23-1.31 (m, 20H, ($-CH_2-)_{10}$), 0.84 – 0.88 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.0, 165.4, 135.8, 126.3, 122.7, 121.9, 119.4, 118.2, 110.9, 107.7, 31.5, 29.2, 26.0, 24.9, 22.3, 21.7, 13.7; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3442, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+H]^+$ 382; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{24}H_{36}ON_3$ is 382.28529 found 382.28515 ($C_{24}H_{36}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-pentadecyl-1,3,4-oxadiazole, 4h**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 48% yield as a semi solid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.14 (s, 1H, NH), 7.63 (d, *J* = 7.9Hz, 1H, Ar-H), 7.37 (d, *J* = 7.9Hz, 1H, Ar-H), 7.12-7.24 (m, 3H, Ar-H), 4.32 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.75 (t, *J* =7.4Hz, 2H, $CH_2$), 1.23-1.25 (m, 24H, ($-CH_2-)_{12}$), 0.86 – 0.89 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.0, 165.4, 135.8, 126.5, 122.7, 122.1, 119.5, 118.3, 111.0, 108.1, 31.6, 28.8, 26.1, 25.0, 22.4, 21.8, 13.8; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3442, 3015, 2960, 2937, 1574, 1499, 1464, 1419, 1217, 1130, 1002, 755, 666; MS (ESI, *m/z*) $[M+H]^+$ 410; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{26}H_{40}ON_3$ is 410.31659 found 410.31581 ($C_{26}H_{40}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-heptadecyl-1,3,4-oxadiazole, 4i**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 58% yield as a semi solid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.18 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.38 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.23 (m, 3H, Ar-H), 4.31 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.68-1.75 (t, *J* =7.4Hz, 2H, $CH_2$), 1.23-1.33 (m, 28H, ($-CH_2-)_{14}$), 0.86 – 0.89 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.3, 165.6, 136.1, 126.7, 122.9, 122.4, 119.8, 118.6, 111.2, 108.4, 31.8, 29.6, 28.9, 26.3, 25.3, 22.6, 22.0, 14.1; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3449, 3015, 2936, 1574, 14989, 1463, 1419, 1217, 1130, 755, 666; MS (ESI, *m/z*) $[M+Na]^+$ 460; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{28}H_{44}ON_3$ is 438.34789 found 438.34713 ($C_{28}H_{44}ON_3$).

**2-((1*H*-Indol-3-yl) methyl)-5-(heptadec-8-en-1-yl)-1,3,4-oxadiazole, 4j**

The title compound was obtained in hexane: ethyl acetate (60: 40, v/v) solvent with 52% yield as a semi solid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.22 (s, 1H, NH), 7.62 (d, *J* = 7.9Hz, 1H, Ar-H), 7.36 (d, *J* = 7.9Hz, 1H, Ar-H), 7.11-7.23 (m, 3H, Ar-H), 5.33-5.38 (m, 2H, -*CH*= *CH*-),4.31 (s, 2H, $CH_2$), 2.73-2.77 (t, *J* = 7.5Hz, 2H, $CH_2$), 1.93-2.04 (m, 4H, -$CH_2$-CH= CH-$CH_2$-), 1.68-1.75 (t, *J* =7.4Hz, 2H, $CH_2$), 1.25-1.31 (m, 20H, ($-CH_2-)_{10}$), 0.85 – 0.89 (t, *J* = 6.7Hz, 3H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 167.0, 165.4, 135.9, 130.0, 126.4, 122.7, 122.0, 119.4, 118.2, 111.0, 107.9, 32.2, 31.5, 29.3, 28.6, 26.9, 25.0, 22.3, 14.1; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3272, 2922, 2851, 1722, 1599, 1567, 1463, 1164, 1105, 965, 741; MS (ESI, *m/z*) $[M+Na]^+$ 458; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{28}H_{42}ON_3$ is 436.33224 found 436.33150 ($C_{28}H_{42}ON_3$).

**Synthesis of ethyl 3,4,5-trimethoxybenzoate, 6**

The ester was prepared by refluxing 3,4,5-trimethoxybenzoic acid (5 g, 1 mmol) in excess of absolute ethanol (50 mL) in the presence of a few drops of conc. sulphuric acid for 12 h and the progress of reaction was monitored by TLC. After 12 h reaction time, the solvent was evaporated under reduced pressure, water was added and the product was extracted with ethyl acetate and dried over anhydrous sodium sulphate. The crude product was purified by using column chromatography to afford the title compound in 86% yield. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.30 (s, 2H, Ar-H), 4.39-4.37 (m, 2H, $CH_2$), 3.91 (s, 6H, $OCH_3$), 3.90 (s, 3H, $OCH_3$), 1.38-1.41 (t, *J* = 7.1Hz, 3H, $CH_3$); MS (ESI, *m/z*) $[M+Na]^+$ 263.

**Synthesis of 3,4,5-trimethoxybenzohydrazide, 7**

A mixture of ethyl 3,4,5-trimethoxybenzoate (2 g, 1 mmol), hydrazine hydrate (6 mL, 15 mmol) and 20 mL of ethanol was refluxed on an oil bath for 10 h and the progress of reaction was monitored by TLC. After 10 h reaction time, the solvent was evaporated under reduced pressure and the concentrated solution

was quenched to ice cold water. The solid separated was filtered, washed and dried. The crude product was purified by recrystalization from ethanol, which afforded the title compound in 74% yield. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.53 (Broad-singlet, 1H, NH), 6.98 (s, 2H, Ar-H), 4.12 (Broad-singlet, 2H, $NH_2$), 3.89 (s, 6H, $OCH_3$), 3.88 (s, 3H, $OCH_3$); MS (ESI, *m/z*) $[M+Na]^+$ 249.

**General procedure for the synthesis of target compounds, 8a-j**

A mixture of 3,4,5-trimethoxybenzohydrazide (7) (1mmol), fatty acids (1mmol) and phosphorous oxychloride (2.5mL) was refluxed for 6 h. The excess solvent was distilled off under reduced pressure and the residue was quenched with ice cold water and the product was extracted with ethyl acetate and dried over anhydrous sodium sulphate. The crude product was purified by using column chromatography by eluting with ethyl acetate: hexane (30:70 v/v), which afforded the title compound in 81-87% yield.

**2-Propyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8a**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 48% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.89-2.92 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.86-1.92 (m, 2H, $CH_2$), 1.05-1.09 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.4, 164.2, 153.2, 140.5, 118.8, 103.6, 60.6, 56.0, 26.9, 19.8, 13.2; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3253, 2927, 2864, 1594, 1458, 1107, 753, 666; MS (ESI, *m/z*) $[M+Na]^+$ 301; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{14}H_{19}O_4N_2$ is 279.13393 found 279.13324 ($C_{14}H_{19}O_4N_2$).

**2-Pentyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8b**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 54% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.94 (t, *J = 7.4Hz,* 2H, $CH_2$), 1.82-1.88 (m, 2H, $CH_2$), 1.38-1.44 (m, 4H, $(-CH_2-)_2$), 0.91-0.94 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.9, 164.5, 153.5, 140.7, 119.1, 103.9, 60.9, 56.3, 31.2, 26.2, 25.3, 22.1, 13.8; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3253, 2927, 2864, 1594, 1458, 1107, 753, 666; MS (ESI, *m/z*) $[M+Na]^+$ 329; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{16}H_{23}O_4N_2$ is 307.16523 found 307.16443 ($C_{16}H_{23}O_4N_2$).

**2-Heptyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8c**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 60% yield as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.94 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.81-1.89 (m, 2H, $CH_2$), 1.25-1.35 (m, 8H, $(-CH_2-)_4$), 0.87-0.90 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.2, 164.8, 153.9, 141.1, 119.5, 104.2, 61.2, 56.6, 31.9, 29.0, 26.9, 25.7, 22.8, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3251, 2925, 2865, 1646, 1596, 1568, 1425, 1394, 1166, 1125, 1107, 740; MS (ESI, *m/z*) $[M+H]^+$ 335; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{18}H_{27}O_4N_2$ is 335.19653 found 335.19579 ($C_{18}H_{27}O_4N_2$).

**2-Nonyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8d**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 63% yield as a semi solid**.** $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.81-1.88 (m, 2H, $CH_2$), 1.25-1.35 (m, 12H, $(-CH_2-)_6$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.2, 164.8, 153.9, 141.1, 119.5, 104.2, 61.2, 56.6, 32.1, 29.3, 26.9, 25.7, 22.9, 14.4; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3250, 2924, 2865, 1640, 1596, 1425, 1107, 739, 714; MS (ESI, *m/z*) $[M+H]^+$ 363; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{20}H_{31}O_4N_2$ is 363.22783 found 363.22720 ($C_{20}H_{31}O_4N_2$).

**2-(Dec-9-en-1-yl)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8e**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 68% yield as a semi solid**.** $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 5.37-5.42 (m, 1H, $CH_2$-*CH*=$CH_2$), 4.08-4.14 (m, 2H, $CH_2$-*CH*=*CH*$_2$), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$),2.90-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.94-2.01 (m, 2H, $CH_2$),1.81-1.87 (m, 2H, $CH_2$), 1.28-1.39 (m, 10H, $(-CH_2-)_5$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.6, 164.2, 153.3, 140.5, 131.8, 124.3, 103.6, 60.6, 56.0, 31.9, 28.6, 26.2, 25.1, 22.3, 17.5, 13.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 2930, 2853, 1727, 1573, 1497, 1419, 1237, 1129, 1005, 770; MS (ESI, *m/z*) $[M+H]^+$ 375; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{21}H_{31}O_4N_2$ is 375.22783 found 375.22735 ($C_{21}H_{31}O_4N_2$).

**2-(3,4,5-Trimethoxyphenyl)-5-undecyl-1,3,4-oxadiazole, 8f**

The title compound was obtained in hexane: ethyl acetate (55: 45, v/v) solvent with 65% yield as a semi

solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.81-1.88 (m, 2H, $CH_2$), 1.25-1.35 (m, 16H, $(-CH_2-)_8$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 165.3, 162.7, 152.0, 139.1, 117.5, 102.3, 59.1, 54.7, 30.2, 27.8, 24.9, 23.7, 20.9, 12.5; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 2920, 2850, 1727, 1574, 1499, 1417, 1236, 1128, 991, 729; MS (ESI, *m/z*) $[M+H]^+$ 391; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{22}H_{35}O_4N_2$ is 391.25913 found 391.25870 ($C_{22}H_{35}O_4N_2$).

**2-Tridecyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8g**

The title compound was obtained in hexane: ethyl acetate (45: 55, v/v) solvent with 67% yield as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$),2.90-2.94 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.82-1.88 (m, 2H, $CH_2$), 1.25-1.35 (m, 20H, $(-CH_2-)_{10}$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.2, 164.8, 153.8, 141.1, 119.4, 104.2, 61.2, 56.6, 32.1, 29.8, 26.9, 25.7, 22.9, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3250, 2924, 2865, 1568, 1425, 1108, 739, 714; MS (ESI, *m/z*) $[M+H]^+$ 419; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{24}H_{39}O_4N_2$ is 419.29043 found 419.28947 ($C_{24}H_{39}O_4N_2$).

**2-Pentadecyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8h**

The title compound was obtained in hexane: ethyl acetate (45: 55, v/v) solvent with 62% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.81-1.88 (m, 2H, $CH_2$), 1.25-1.35 (m, 24H, $(-CH_2-)_{12}$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.9, 164.5, 153.5, 140.8, 119.1, 103.9, 60.9, 56.3, 31.8, 29.6, 26.6, 25.4, 22.6, 14.0; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3250, 2946, 2924, 2865, 1596, 1569, 1425, 1108, 739, 714; MS (ESI, *m/z*) $[M+H]^+$ 447; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{26}H_{43}O_4N_2$ is 447.32173 found 447.32075 ($C_{26}H_{43}O_4N_2$).

**2-Heptadecyl-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8i**

The title compound was obtained in hexane: ethyl acetate (45: 55, v/v) solvent with 69% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.90-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.81-1.88 (m, 2H, $CH_2$), 1.25-1.31 (m, 28H, $(-CH_2-)_{14}$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.1, 164.7, 153.8, 141.1, 119.4, 104.2, 61.2, 56.5, 32.1, 29.9, 26.8, 25.7, 22.9, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3416, 3250, 2924, 2865, 1709, 1597, 1569, 1425, 1125, 1108, 739; MS (ESI, *m/z*) $[M+H]^+$ 475; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{28}H_{47}O_4N_2$ is 475.35303 found 475.35211 ($C_{28}H_{47}O_4N_2$).

**2-(Heptadec-8-en-1-yl)-5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole, 8j**

The title compound was obtained in hexane: ethyl acetate (45: 55, v/v) solvent with 63% yield as a semi solid. $^1$H NMR (300 MHz, $CDCl_3$): δ 7.26 (s, 2H, Ar-H), 5.34-5.41 (m, 2H, *-CH= CH-*), 3.91 (s, 6H, $OCH_3$), 3.94 (s, 3H, $OCH_3$), 2.89-2.93 (t, *J* = 7.4Hz, 2H, $CH_2$), 1.94-2.00 (m, 4H, $-CH_2$-CH= CH-$CH_2$-), 1.81-1.88 (m, 2H, $CH_2$), 1.25-1.36 (m, 4H, $(-CH_2-)_2$), 0.86-0.89 (t, *J* = 6.8Hz, 3H, $CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 167.2, 164.8, 153.9, 141.1, 130.3, 119.4, 104.2, 61.2, 56.6, 32.8, 32.1, 29.9, 29.3, 26.9, 25.7, 22.9, 14.3; IR ($CHCl_3$ $\nu_{max}$ $cm^{-1}$): 3250, 2946, 2924, 2865, 1710, 1569, 1425, 1166, 1108, 739, 713; MS (ESI, *m/z*) $[M+H]^+$ 473; HR-MS (ESI) *m/z* $[M+H^+]$: calc for $C_{28}H_{45}O_4N_2$ is 473.33738 found 473.33678 ($C_{28}H_{45}O_4N_2$).

**Biological evaluation**

All the synthesized compounds were screened for *in vitro* cytotoxicity on a panel of three different cancer cell lines such as A549 derived from human alveolar adenocarcinoma epithelial cells (ATCC No. CCL-185), HeLa derived from human adenocarcinoma cells (ATCC No. CCL-185) and MCF7 derived from human breast adenocarcinoma cells (ATCC No HTB-22), which were all obtained from the American Type Culture Collection, Manassas, VA, USA. The cytotoxicity was determined using MTT [35].The effects of the different synthesized compounds on the viability of the tumour cell lines were measured at 540 nm using a multimode reader (Infinite® M200, Tecan, Switzerland). The $IC_{50}$ values (50% inhibitory concentration) were calculated from the plotted absorbance data of the dose–response curves. The assay was performed using doxorubicin as positive controls and 1% DMSO as a vehicle control. In order to account for the toxicity of DMSO, the values obtained for the DMSO control were subtracted from those of the test compounds. The $IC_{50}$ values (in mM) are expressed as the average of two independent experiments.

## Conclusions

In conclusion, we have efficiently synthesized two series of 1,3,4-oxadiazole derivatives through simple steps. All the synthesized compounds were evaluated for their cytotoxicity. Antitumor evaluation showed that almost all the tested compounds revealed activity. It is interesting to note that the substitution of heteryl and fatty chain groups on 1,3,4-oxadiazoles-based compounds (**4c, 4d, 4e**) displayed the most potent inhibitory activity when compared to aryl and fatty chain groups on 1,3,4-oxadiazoles.

## Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

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