Indian Journal of Chemistry
Vol. 61, July 2022, pp. 703-716

# Synthesis, characterization and antioxidant activities of novel *N*-substituted pyrazoline derivatives bearing 3-benzo[b]thiophene and 5-styryl substituents

Radhakrishnan Krishnan*[a], Karthik Manikandan Pandy[b], Senthil Kumar Paratharaj[b]& Uttam Kumar Ray[b]

[a] Saraswathi Narayanan College of Arts and Science, Madurai Kamaraj University, Madurai 625 022, Tamil Nadu, India

[b] Solara Active Pharma Sciences Limited, R&D Centre, No. 27, Melakottaiyur (PO), Chennai 600 100, Tamil Nadu, India

E-mail: prskradha61@gmail.com

*Received 28 September 2021; accepted (revised) 11 February 2022*

The new series of N-substituted pyrazoline derivatives bearing benzo[b]thiophene and styryl with trifluoromethyl substitution at *para*- and *meta*- positions were synthesized. The structures of newly synthesized compounds were characterized by UV, IR, NMR, Mass and single crystal XRD (SCXRD) and had been screened for antioxidant activity. The *in vitro* antioxidant activities screening revealed that hydroxyl radical scavenging (HRS) activities of compounds **3c, 3f, 4a, 4e, 4f, 5c, 5d 5e** and **5g** are stronger than the other compounds and the compound **5g** shows much better antioxidant activity.

**Keywords**: Pyrazoline, benzo[b]thiophene, N-substituted pyrazolines, antioxidant activity, trifluoromethyl cinnamaldehyde

Pyrazolines are considered to be a top-notch scaffold in medicinal chemistry as their derivatives and their hybrid structures exhibit diverse biological activities like anti-bacterial[1], antifungal[1], anti-viral[2], anti-tubercular[3], anti-inflammatory[4], anti-cancer[3,5], anti-oxidant[6], immunosuppressive[7], analgesic[8], antidiuretic[9], anti-helmentic[9], fungicidal[9], neuropsychiatric and neurodegenerative disorders[9] and also used as brightening agents in synthetic fibres[10], fluorescent probes in chemo-sensors[11], recognition of transitions-metal ions[12], electrophotography and electro-luminescence[13]. Some of the pyrazoline derivatives with various substituents attached to the *N*1 nitrogen atom was found to have displayed significant changes in the photo-physical properties of the compounds[14]. Moreover, the incorporation of electron donors/acceptors into the molecule of interest gives fine tuning of the physico-chemical properties for enhanced applications in various fields[15]. Benzo[b]thiophene is also received a huge attention in medicinal chemistry. Numerous benzo[b]thiophene based compounds are available to treat various types of diseases[17]. The fluorine substitution on organic compounds are now a days widely used strategy in medicinal and applied chemistries as it shows dramatic effects on metabolic stability and physico-chemical properties of the compounds and among the fluorine substitutions, trifluoromethyl substitution will enhance the bioavailability and lipophilicity of the compounds[16]. Having said the importance, enhanced properties and applications of the aforementioned moieties we were attracted to design a new molecular entity bearing all the moieties together and able to synthesize a series of *N*-substituted-2-pyrazoline derivatives bearing styryl[18] with trifluoromethyl substitution and benzo[b]thiophene motifs and studied for their antioxidant activities.

**List of abbreviations**: SCXRD: Single crystal X-ray diffractometer; HRS: Hydroxyl radical scavenging; CCDC: Cambridge Crystallographic Data Centre; RNS: Reactive nitrogen species; ROS: Reactive oxygen species; DPPH: 2,2-diphenyl-1-picrylhydrazyl; ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; TMS: Trimethylsilane; TLC: Thin layer chromatography.

## Results and Discussion

### Chemistry

The designed 5-styryl substituted pyrazolines were synthesized by the reaction of cinnamyl chalcones with hydrazine in ethanol under reflux condition, and the cinnamyl chalcones in turn were obtained from cinnamaldehyde and 1-(benzo[b]thiophene-2-yl)ethan-1-one. In some methods, hydrazones are formed as intermediate which can subsequently cyclized to 2-pyrazolines in the presence of suitable cyclizing agents[19]. Generally, the *N*-substituted pyrazolines were synthesized by direct cyclization of chalcones with substituted hydrazines[20], and acylation

using acetic acid[21], anhydrides[22] and acylchlorides with unsubstituted pyrazolines in presence of a suitable base[23]. The synthesis of pyrazoline derivatives **3-5(a-g)** was carried out according to the steps shown in reaction Scheme I.

In the initial step, compound **1(a-c)** was synthesized *via* the base-catalysed Claisen-Schmidt condensation of 1-(benzo[b]thiophene-2-yl)ethan-1-one with cinnamaldehyde and trifluoromethyl substituted cinnamaldehydes at *para*- and *meta*-positions. The structure of the compounds **1** (a-c) was confirmed from its spectral data. The IR spectrum showed absorption band at 1638-1640 $cm^{-1}$ corresponds to C=O stretching frequency, the band at 1595-1577 $cm^{-1}$ corresponds to conjugated -C=C double bonds stretching. $^{13}C$ NMR spectrum compounds having signal at δ 178.72-183.29 assigned for C=O group conjugated with double bonds.

The compounds **1(a-c)** were further treated with hydrazine hydrate in ethanol under reflux condition, which led to the formation of compounds **2(a-c)**. In the $^{1}H$ NMR of compound **2 (a-c)**, –NH proton appears around at δ 5.8, the $CH_2$ protons of pyrazoline ring appears as a pair of doublets around at δ 3.4-3.3 and 3.0-2.9. The CH ($H_X$) proton appeared as a doublet of doublets around at δ 4.6– 4.5 ($H_X$) due to the vicinal coupling with two magnetically non-equivalent protons of the methylene group at C4 of the pyrazoline ring ($H_A$ and $H_B$) ($^{2}J_{AB}$ = 15.9 Hz, $^{3}J_{AX}$ = 9.9 Hz, $^{3}J_{BX}$ = 8.4 Hz). In the $^{13}C$ NMR of compound **2(a-c)**, the chemical shift values appeared around 59.1 to 63.64 and 34.60 to 39.51 correspond to the pyrazoline ring of CH and $CH_2$ respectively. Aromatic and other carbon atoms were observed at expected chemical shifts range (Figure 1).

In the third step, compounds **2(a-c)** was treated with various *p*-substituted benzoyl chlorides in the presence of triethylamine in dichloromethane solvent,

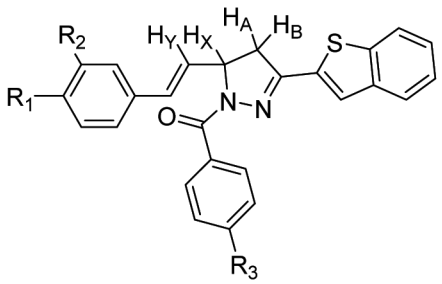
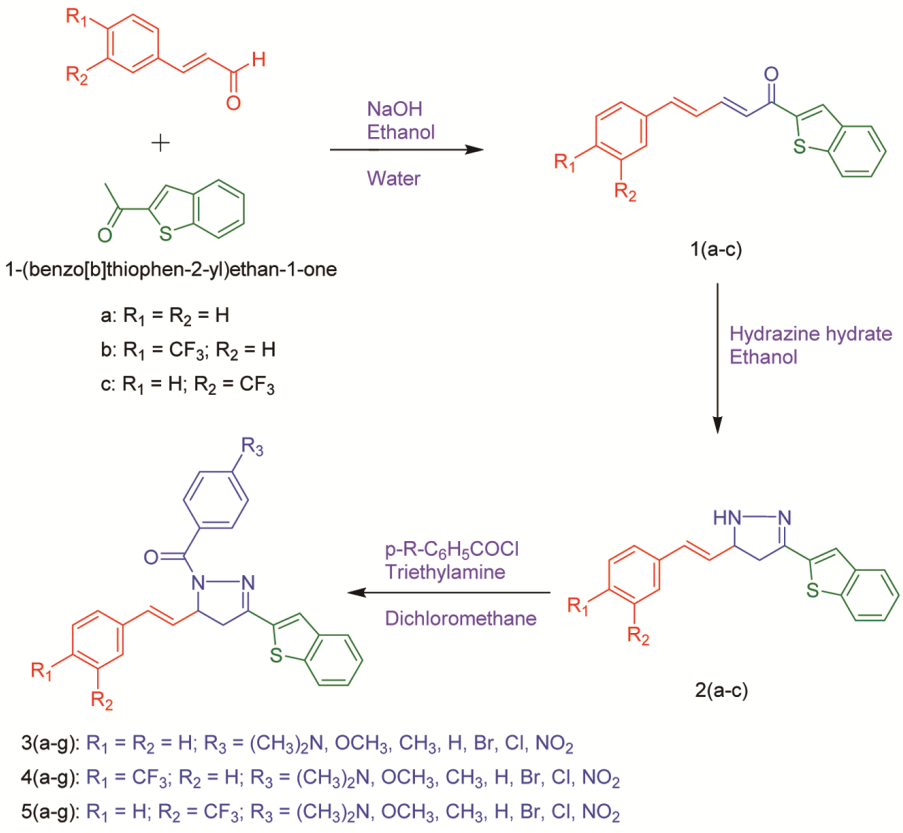



Figure 1 — Pyrazoline ring structure of compounds **3-5(a-g)**




Scheme I — Synthesis of pyrazoline derivatives **3-5(a-g)**

which led to the formation of *N*-substituted pyrazoline derivatives **3-5(a-g)** (Figure 2). The structure of all compounds **3-5(a-g)** was confirmed by its spectral data. The IR spectrum of the compounds **3-5 (a-g)**, showed absorption band around from 1600 to 1688 $cm^{-1}$ due to C=O stretching vibration. The stretching band for aliphatic C-H group observed from 2800 to 2960 $cm^{-1}$. The aromatic -C=C and C=N stretching vibrations were observed between 1480 -1550 $cm^{-1}$ and 1550 - 1600 $cm^{-1}$ respectively.

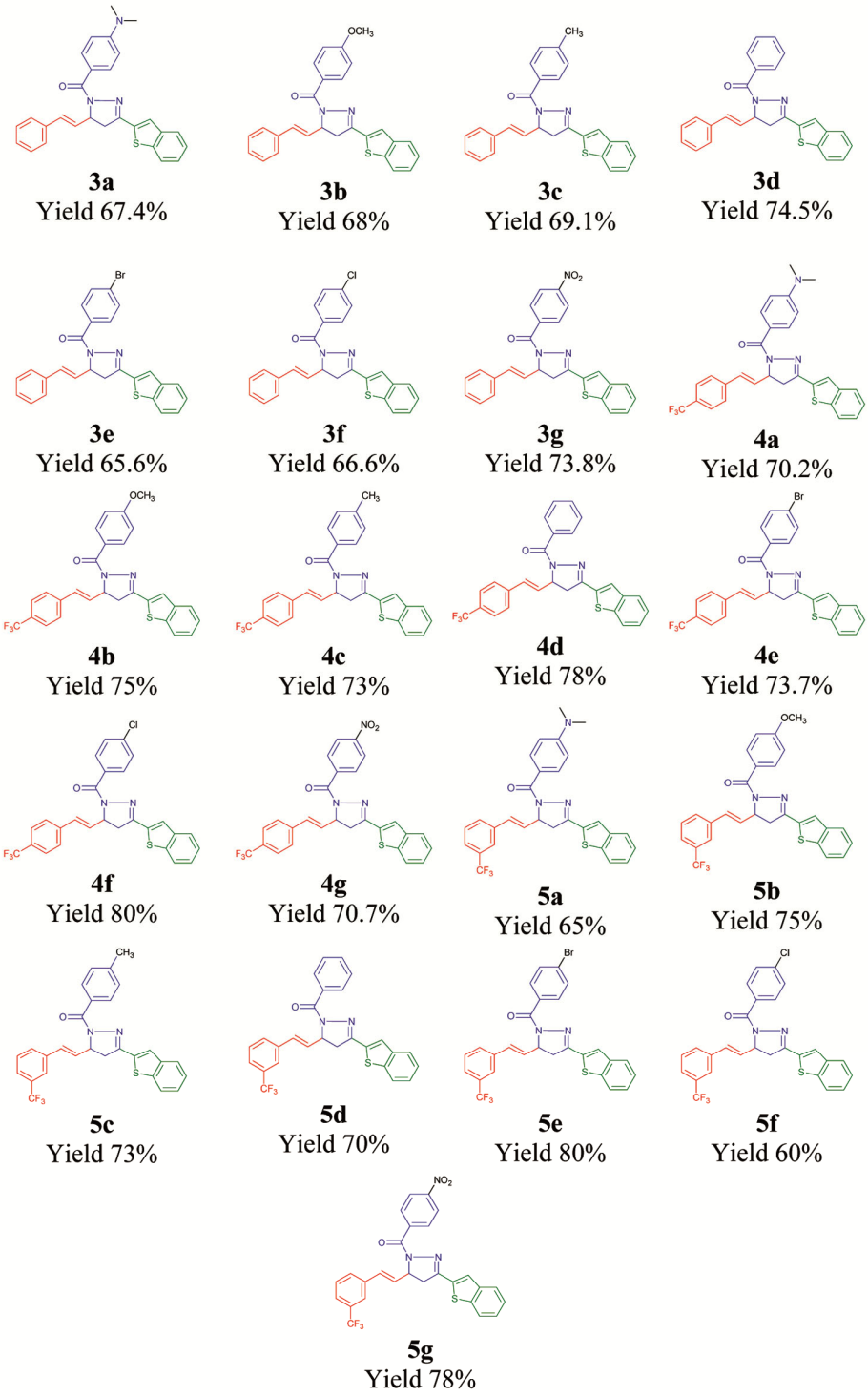



Figure 2 — Structures of compounds **3-5(a-g)** and their yield

The $^{1}$H NMR of compounds **3-5(a-g)**, –NH proton signal around at δ 5.8 was not observed, which reveals that the substitution occurred at *N*1 position. The $CH_2$ protons of *N*-substituted pyrazoline derivatives appeared as a pair of doublets around at δ 3.7-3.5 and 3.3-3.0 ($J_{AB}$ = 17.4-17.4 Hz, $J_{AX}$ = 11.4 – 11.1 Hz, $J_{BX}$ = 5.1-5.4 Hz). The CH proton appeared as a multiplet around at δ 5.62– 5.29 ($H_X$) due to the vicinal coupling with two magnetically non-equivalent protons of the methylene group of the pyrazoline ring ($H_A$ and $H_B$) and styryl group proton ($H_Y$) as mentioned in the Figure 1. In the $^{13}$C NMR of compound **3-5(a-g)**, the chemical shift values corresponding to the carbonyl carbon appeared around at δ 164 - 167, which confirms the amide carbonyl group. Aromatic and other carbon atoms were observed at expected chemical shift ranges. The structures of compound **3-5(a-g)** and the corresponding yield is mentioned in the Figure 2.

The single crystals were obtained for one of the compounds, (3-benzo[b]thiophene-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)phenyl)methanone **3d** from saturated methanol solution. The single crystal X-ray diffraction analysis of compound **3d** shows the three-dimensional structure of the molecules (CCDC number 2089498). Ortep diagram was generated and shown in Figure 3. The crystalline state along with their intermolecular interactions is shown in Figure 4 (Ref. 24). From the single crystal analysis, it was found that the compound **3d** having a monoclinic system with the lattice parameters, a=5.8842Å, b=23.776Å, c=14.982Å and α=90°, β=90.903° and γ=90°. Crystal data and refinement details are mentioned in Table I.

## Pharmacology

### Antioxidant activity

Free radicals such as reactive nitrogen species (RNS) and reactive oxygen species (ROS), including hydrogen peroxide, reactive hydroxyl radicals are produced by normal cellular metabolism and causes various diseases such as cancer, diabetes, cardiovascular disorders, neurodegenerative diseases, inflammation, age related diseases and osteoporosis. The excessive production of such ROS/RNS species in living cells originates the oxidative stress condition, where oxidants overpower the antioxidant productive system which may lead to imbalance between the production of antioxidants and the production of free radicals. This would cause damage to lipids, protein, DNA resulting in an alteration of cell structures and functions and thus may lead to various diseases[25]. The risk of such chronic diseases can be controlled by antioxidants. Antioxidants are compounds that can interact with free radicals in a safer manner, terminate the reaction, and convert them to a harmless molecule by offering an electron. Antioxidants therefore reduce the oxidative stress and

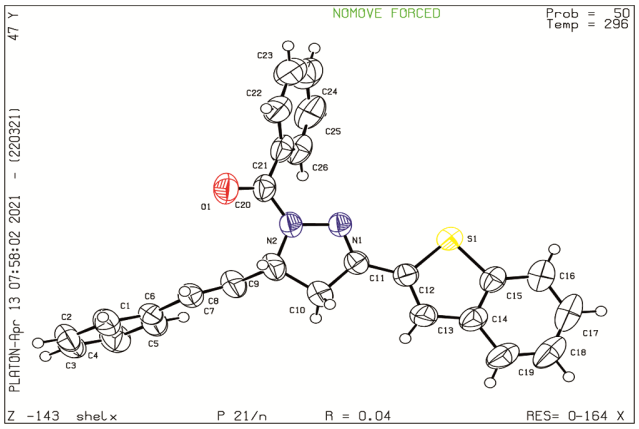



Figure 3 — Ortep diagram of compound **3d**, showing 50% probability ellipsoids and the atom numbering scheme

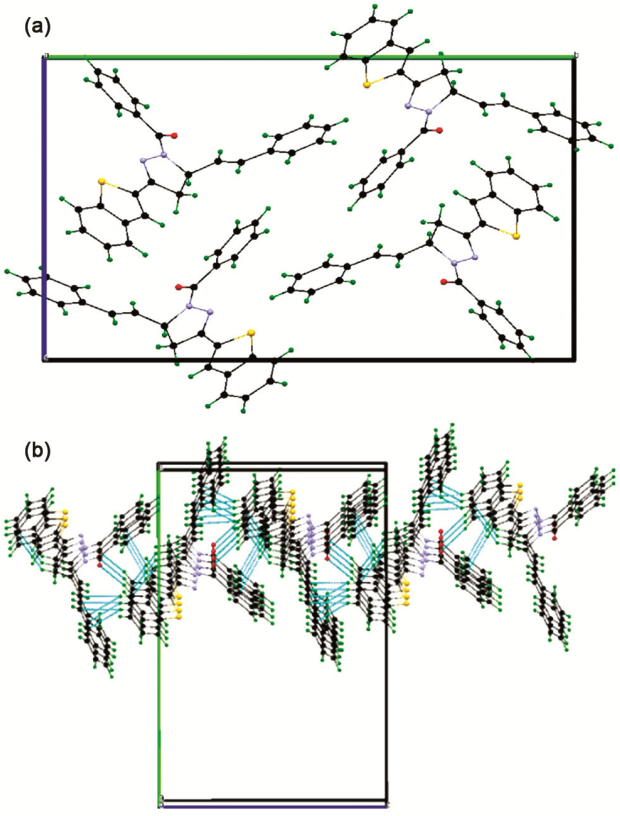



Figure 4 — (a) Packing diagram of molecule **3d** and (b) dash lines indicates intermolecular interactions

thus protecting the cells from oxidative damage[26]. Phytochemicals such as vitamins, polyphenols, carotenoids and flavonoids are known as scavengers of free radicals[27].

The antioxidant activity of organic compounds can be assessed using various methods such as DPPH assay, hydroxyl radical scavenging (HRS) activity, super oxide anion radical and ABTS assay. In this study, the newly synthesized compounds were assessed with hydroxyl radical scavenging (HRS) activity. Hydroxyl radical is one of the potent reactive oxygen species in the biological system. It reacts with polyunsaturated fatty acid moieties of cell membrane phospholipids and cause damage to cell[28].

The antioxidant activity of the newly synthesized compounds was determined with various concentrations according to the method reported by Klein *et al*.[29] The results were tabulated in Table II, Table III and Table IV.

The percentage of inhibition was determined and tabulated for all the compounds **3-5(a-g)**.

$$\% \text{ of inhibition} = \frac{(\text{Absorbance of control} - \text{Absorbance of test sample})}{\text{Absorbance of control}} \times 100$$

## Structure activity relationship (SAR)

All the compounds were measured for percentage inhibition activity for HRS at different concentration

Table I — Crystal data and structure refinement details for compound **3d**

| Identification code | Shelx | |
|---|---|---|
| Empirical formula | $C_{26}H_{20}N_2OS$ | |
| Formula weight | 408.5 | |
| Temperature | 296(2) K | |
| Wavelength | 1.54178 Å | |
| Crystal system | Monoclinic | |
| Space group | P 21/n | |
| Unit cell dimensions | a = 5.8842(8) Å | α = 90°. |
| | b = 23.776(3) Å | β = 90.903(6)°. |
| | c = 14.982(2) Å | γ = 90°. |
| Volume | 2095.8(5) Å3 | |
| Z | 4 | |
| Density (calculated) | 1.295 $Mg/m^3$ | |
| Absorption coefficient | 1.521 $mm^{-1}$ | |
| F(000) | 856 | |
| Crystal size | 0.300 × 0.250 × 0.200 mm3 | |
| Theta range for data collection | 3.487 to 72.282°. | |
| Index ranges | −7<=h<=7, −29<=k<=29, −18<=l<=18 | |
| Reflections collected | 43245 | |
| Independent reflections | 4133 [R(int) = 0.0687] | |
| Completeness to theta = 67.679° | 100.00% | |
| Absorption correction | Multi | |
| Max. and min. transmission | 0.7536 and 0.5740 | |
| Refinement method | Full-matrix least-squares on F2 | |
| Data / restraints / parameters | 4133 / 81 / 271 | |
| Goodness-of-fit on F2 | 1.03 | |
| Final R indices [I>2sigma(I)] | R1 = 0.0386, wR2 = 0.1009 | |
| R indices (all data) | R1 = 0.0692, wR2 = 0.1067 | |
| Largest diff. peak and hole | 0.125 and −0.297 e.Å−3 | |

Table II — Antioxidant activity of compounds **3(a-g)** by hydroxyl radical scavenging assay

| Sample Concentration | Percentage of inhibition **3(a-g)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | $(CH_3)_2N$ | $OCH_3$ | $CH_3$ | H | Br | Cl | $NO_2$ |
| | **3a** | **3b** | **3c** | **3d** | **3e** | **3f** | **3g** |
| 20 µg | 12.18 | 5.77 | 31.41 | 11.54 | 1.92 | 16.67 | 3.21 |
| 40 µg | 32.69 | 17.95 | 43.59 | 21.79 | 10.9 | 25 | 10.9 |
| 60 µg | 51.92 | 35.26 | 50.64 | 28.21 | 41.67 | 42.95 | 26.92 |
| 80 µg | 62.18 | 64.74 | 71.15 | 33.97 | 49.36 | 71.79 | 38.46 |
| 100 µg | 73.08 | 78.85 | 81.41 | 42.31 | 62.82 | 85.26 | 58.97 |

Table III — Antioxidant activity of compounds **4(a-g)** by hydroxyl radical scavenging assay

| Sample Concentration | Percentage of inhibition **4(a-g)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | $(CH_3)_2N$ | $OCH_3$ | $CH_3$ | H | Br | Cl | $NO_2$ |
| | **4a** | **4b** | **4c** | **4d** | **4e** | **4f** | **4g** |
| 20 µg | 8.33 | 1.92 | 11.54 | 3.21 | 1.92 | 4.49 | 0.64 |
| 40 µg | 45.51 | 10.26 | 24.36 | 8.97 | 17.95 | 19.23 | 12.82 |
| 60 µg | 53.21 | 17.95 | 35.26 | 23.08 | 37.18 | 36.54 | 19.23 |
| 80 µg | 66.03 | 34.62 | 69.23 | 39.1 | 66.03 | 62.18 | 24.36 |
| 100 µg | 84.62 | 37.18 | 76.28 | 57.69 | 84.62 | 86.54 | 55.13 |

Table IV — Antioxidant activity of compounds **5(a-g)** by hydroxyl radical scavenging assay

| Sample Concentration | Percentage of inhibition **5(a-g)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | $(CH_3)_2N$ | $OCH_3$ | $CH_3$ | H | Br | Cl | $NO_2$ |
| | **5a** | **5b** | **5c** | **5d** | **5e** | **5f** | **5g** |
| 20 µg | 2.56 | 26.92 | 56.41 | 36.54 | 25.64 | 23.08 | 18.59 |
| 40 µg | 37.18 | 50 | 58.97 | 48.08 | 37.18 | 46.79 | 35.26 |
| 60 µg | 51.92 | 62.18 | 68.59 | 69.23 | 51.28 | 64.1 | 62.18 |
| 80 µg | 55.13 | 65.38 | 73.08 | 71.15 | 64.1 | 67.95 | 75.64 |
| 100 µg | 62.18 | 76.92 | 81.41 | 85.9 | 83.33 | 79.49 | 92.31 |

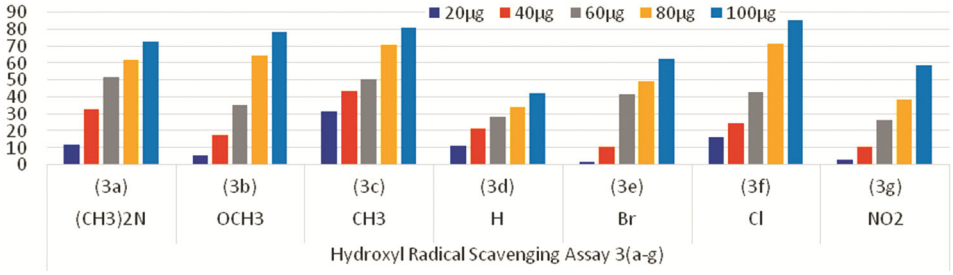



Figure 5 — Comparison of HRS activity of compounds **3(a-g)** at different concentrations

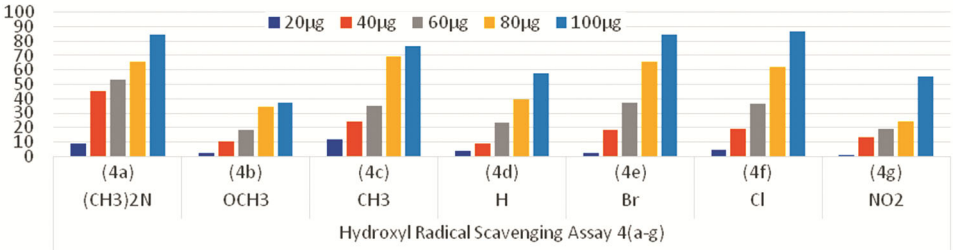



Figure 6 — Comparison of HRS activity of compounds **4(a-g)** at different concentrations

levels from 20 µg to 100 µg. The results of antioxidant activity of all compounds based on the electron donating and electron withdrawing group in the *para* position of the benzoyl group and the presence $CF_3$ in *para* and *meta* position of the styryl group have been studied and all the compounds have exhibited significant effect on the HRS activity.

All the compounds at high concentration level (100 µg) showed excellent inhibition effects except unsubstituted compounds showing that the substitution plays an important role in the inhibition activity. Compounds bearing electron releasing groups (**3a, 3b, 3c)** and Cl **(3f)** were exhibited good HRS activity and –Br (**3e)** and $–NO_2$ (**3d)** exhibited moderate HRS activity than the compound **3d** (Figure 5). It reveals that the presence of substituents in the *para* position of the benzoyl group shows significant changes in the HRS activity irrespective of electron donating and electron withdrawing nature.

Similarly, in the *p*-trifluoromethyl styryl series, the compounds **4a, 4e, 4f** exhibited excellent HRS activity (Figure 6), at highest concentration level (100 µg) than the compound **3a**, **3e** and **3f**. It is observed that the introduction of $CF_3$ at *para* position of styryl group did not affect much on HRS activity.

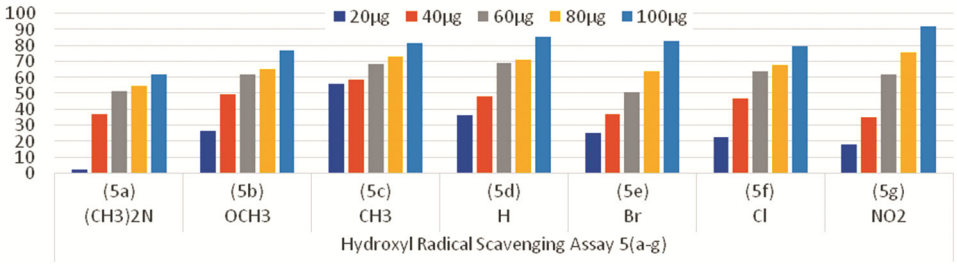



Figure 7 — Comparison of HRS activity of compounds **5(a-g)** at different concentrations

In the *m*-trifluoromethyl styryl series, almost all the compounds exhibited excellent inhibition effect at maximum concentration level except the compound with $N(Me)_2$ substituent **(5a)**. The introduction of $CF_3$ group at *m*-position of the styryl group enhances the inhibitory activity when compared to *p*-$CF_3$ substituted and unsubstituted series. The HRS activity of compound **5g** shows superior activity than the **3g** and **4g**, proves that the presence of $CF_3$ groups enhances the activity than the other compounds (Figure 7).

As whole, compounds **3c, 3f, 4a, 4e, 4f, 5c, 5d, 5e** and **5g** shows good antioxidant property than the other compounds. Compound **5g** is more potent inhibition of hydroxyl radical than the other compounds. The above study indicates that the presence of substitution in the benzoyl ring and $CF_3$ substitution in the styryl group shows significant changes in the HRS activity.

## Experimental Section

The reagents were purchased from Aldrich and used without further purification and solvents were purchased from commercial suppliers and used without further purification. $^1$H NMR and $^{13}$C NMR spectra were obtained on a Bruker Avance instrument in $CDCl_3$ using TMS as an internal standard, operating at 300 MHz and 75 MHz respectively. Chemical shifts (δ) are expressed in ppm and coupling constants *J* are given in Hz. For $CDCl_3$ solutions the chemical shifts are reported as parts per million (ppm) to residual proton or carbon of the solvents; $CDCl_3$ ($\delta_H$ 7.26) and $CDCl_3$ ($\delta_C$ 77.03). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q =quartet, dd = doublet of doublets, m = multiplet. UV-Vis spectra were recorded between 200 to 800 nm on Shimadzu (1650) UV–Vis spectrophotometer using $CH_2Cl_2$ as solvent. IR spectra were collected neat in the solid state on a Bruker Spectrum-1. Melting points were obtained on a Melting point instrument. LC-MS spectra were obtained on Thermoscientific LTQ Xcallibur 2.2 LCMS spectrometer equipped with an ESI/APCI source.

### General procedure for the preparation of compounds 1a-c

**Synthesis of 1-(benzo[b]thiophen-2-yl)-5-phenylpenta-2,4-dien-1-one, 1a**

A mixture of cinnamaldehyde (20.0 g, 0.151 mol), 1-benzo[b]thiophen-2-yl-ethanone (22.7 g, 0.129 mol) in absolute alcohol (150.0 mL) and demineralized water (75 mL) was stirred under drop wise addition of 20% NaOH solution (25.0 mL, 0.125 mol) at 10-15°C for 30 minutes. The reaction mixture was stirred for 60 minutes at 25-30°C and completion of the reaction was confirmed by TLC. Upon reaction completion the precipitated solid was filtered, washed with 1:1 mixture of ethanol and water (50.0 mL). The crude product was purified using ethanol (40.0 mL) to obtain **1a**. Yellow solid. Yield 65%. m.p. 130-132°C. UV-Vis ($CH_2Cl_2$): λmax (ε) = 356 nm; IR (KBr): 3053-3026, 1640, 1582, 1515-1430, 1353, 1187-1144, 1000 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.92-7.87 (m, 2H), 7.72-7.64 (m, 1H), 7.53-7.33 (m, 8H), 7.14-7.04 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 178.72, 140.59, 139.63, 137.89, 137.83, 134.58, 131.32, 124.64, 124.16, 123.86, 122.66, 122.60, 121.92, 121.22, 120.26, 119.74 and 118.26; LC-MS: *m/z* 291.10 [M+H]. Anal. Calcd for: $C_{19}H_{14}OS$: C, 78.59; H, 4.86. Found: C, 78.58; H, 4.84%.

**1-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl) phenyl)penta-2,4-dien-1-one, 1b**: Yellow solid. Yield 65% (24.4 g). m.p.166-168°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 348 nm; IR (KBr): 3064, 1638-1612, 1581, 1577, 1514-1416, 1323, 1148, 1065 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.93-7.88 (m, 2H), 7.70 (m, 5H), 7.51-7.39 (m, 2H), 7.19-7.02 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 183.26, 145.10, 143.31, 142.70, 140.26, 139.40, 139.38, 139.27, 131.33, 130.90, 130.47, 130.04, 129.40,

128.91, 128.88, 127.51, 127.39, 126.02, 125.87, 125.82, 125.77, 125.72, 125.09, 123.00, 122.19 and 118.59; LC-MS: *m/z* 359.13 [M+H]. Anal. Calcd for: $C_{20}H_{13}F_3OS$: C, 67.03; H, 3.66. Found: C, 67.01; H, 3.64%.

**1-(Benzo[b]thiophen-2-yl)-5-(3-(trifluoromethyl) phenyl)penta-2,4-dien-1-one, 1c**: Yellow solid. Yield 65% (11.6 g). m.p.154-156°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 346 nm; IR (KBr): 3053-3018, 1640, 1581, 1515-1429, 1325, 1121, 1006 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.93-7.88 (m, 2H), 7.76 (s, 1H), 7.70-7.76 (m, 3H), 7.54-7.39 (m, 3H), 7.19-7.02 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 183.29, 145.12, 143.35, 142.69, 140.27, 139.27, 136.80, 132.00, 131.5, 131.1, 130.7, 130.42, 129.3, 129.07, 128.8, 128.3, 127.4, 126.02, 125.7, 125.66, 125.58, 125.5, 125.06, 123.79, 123.64, 122.99, 122.14 and 118.52; LC-MS: *m/z* 359.15 [M+H]. Anal. Calcd for: $C_{20}H_{13}F_3OS$: C, 67.03; H, 3.66. Found: C, 67.02; H, 3.65%.

**General procedure for the preparation of compounds 2a-c**

**Synthesis of 3-(benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazole, 2a**: A mixture of compound **1a** (21.0 g, 0.072 mol) in absolute alcohol (100.0 mL) and hydrazine monohydrate (7.24 g, 0.145 mol) were heated to 75-80°C and maintained for 7 hours. The progress of the reaction was monitored by TLC. Upon reaction completion the reaction mixture was cooled to 0-5°C. The precipitated solid was filtered, washed with ethanol (40.0 mL). The crude product was purified using methanol (50.0 mL) to obtain compound **2a**. Pale yellow solid. Yield 77%. m.p.136-138°C. UV-Vis (CH2Cl2): λmax (ε) = 325 nm; IR (KBr): 3331, 3053-3022, 2895-2858, 1642, 1522-1494, 1437, 1354, 1180-1158, 1032, 974 $cm^{-1}$; 1H NMR (300 MHz, $CDCl_3$): δ 7.80-7.70 (m, 2H), 7.40-7.22 (m, 8H), 6.62-6.57 (d, 1H, *J* = 15.6), 6.35-6.27 (dd, 1H, $J_1$ = 15.6 Hz, $J_2$ = 8.4 Hz), 5.82 (bs, 1H), 4.62-4.53 (dd, 1H, $J_1$ = 17.7 Hz, $J_2$ = 8.4 Hz), 3.39-3.30 (dd, 1H, , $J_1$ = 15.9 Hz, $J_2$ = 9.9 Hz), 3.05-2.97 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 8.4 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 143.36, 135.27, 134.95, 132.21, 131.51, 127.45, 123.94, 123.83, 123.27, 121.78, 120.50, 119.77, 119.02, 118.33, 117.65, 59.20 and 34.61; LC-MS: *m/z* 305.18 [M+H]. Anal. Calcd for: $C_{19}H_{16}N_2S$: C, 74.97; H, 5.30; N, 9.20. Found: C, 74.95; H, 5.28; N, 9.19%.

**3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl) styryl)-4,5-dihydro-1*H*-pyrazole, 2b**: Pale yellow solid. Yield 80% (14.2 g). m.p.174-176°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 318 nm; IR (KBr): 3332, 3262, 3052, 2866, 1613, 1414, 1329, 1160, 1115, 1067, 1037 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.82-7.70 (m, 2H), 7.59-7.46 (m, 5H), 7.37-7.26 (m, 4H), 6.66-6.60 (d, 1H, *J* = 15.9 Hz), 6.44-6.36 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 8.4 Hz), 5.87 (bs, 1H), 4.65-4.56 (dd, 1H, $J_1$ = 18.0 Hz, $J_2$ = 8.4 Hz), 3.42-3.33 (dd, 1H, , $J_1$ = 15.9 Hz, $J_2$ = 9.9 Hz), 3.06-2.98 (dd, 1H, , $J_1$ = 15.9 Hz, $J_2$ = 8.4 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 148.13, 140.02, 139.73, 139.64, 136.71, 131.25, 130.80, 130.42, 129.99, 129.56, 129.13, 126.69, 125.92, 125.71, 125.66, 125.61, 125.56, 125.35, 125.24, 124.57, 123.80, 123.23, 123.03, 122.40, 122.31, 63.65 and 39.34; LC-MS: *m/z* 373.17 [M+H]. Anal. Calcd for: $C_{20}H_{15}F_3N_2S$: C, 64.50; H, 4.06; N, 7.52. Found: C, 64.51; H, 4.05; N, 7.51%.

**3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluoromethyl) styryl)-4,5-dihydro-1*H*-pyrazole, 2c**: Pale yellow solid. Yield 80% (8.3 g). m.p.147-149°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 319 nm; IR (KBr): 3324, 3063-3039, 2919-2864, 1661, 1523-1493, 1338, 1115, 1029 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.83-7.77 (m, 1H), 7.77-7.70 (m, 1H), 7.62 (s, 1H), 7.56-7.40 (m, 3H), 7.36-7.31 (m, 2H), 7.27 (s, 1H), 6.65-6.60 (d, 1H, *J* = 15.9 Hz), 6.42-6.34 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 8.1 Hz), 5.84 (bs, 1H), 4.64-4.55 (dd, 1H, $J_1$ = 18.3 Hz, $J_2$ = 8.4 Hz), 3.41-3.32 (dd, 1H, , $J_1$ = 15.9 Hz, $J_2$ = 9.9 Hz), 3.06-2.97 (dd, 1H, , $J_1$ = 15.9 Hz, $J_2$ = 8.4 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 148.11, 140.01, 139.66, 137.07, 136.74, 131.74, 131.32, 130.89, 130.74, 130.59, 130.46, 129.64, 129.14, 125.86, 125.32, 124.56, 124.52, 124.47, 124.42, 124.31, 123.80, 123.29, 123.22, 123.14, 122.39, 122.25, 118.2, 63.63 and 39.31; LC-MS: *m/z* 373.18 [M+H]. Anal. Calcd for: $C_{20}H_{15}F_3N_2S$: C, 64.50; H, 4.06; N, 7.52. Found: C, 64.48; H, 4.05; N, 7.51%.

**General procedure for the preparation of compounds 3-5a-g**

**Synthesis of (3-(benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(4-(dimethylamino) phenyl)methanone, 3a**

A mixture of compound **2a** (1.0 g, 0.003 mol) in dichloromethane (15 mL) with triethylamine (0.698 g, 0.007 mol) was cooled to 0-5°C. 4-dimethyl amino benzoyl chloride (1.206 g, 0.006 mol) was slowly

added to the reaction mixture for 10 minutes. The progress of the reaction was monitored by TLC. Upon reaction completion, reaction mixture was quenched using chilled water (15 mL) and layer was separated. Organic layer was washed with 5% sodium bicarbonate solution (15 mL) followed by water (15 mL) and organic layer was dried over sodium sulphate and evaporated to dryness. The product was crystallized from the residue using methanol (10 mL). The crystallized product was filtered and dried to obtain compound **3a**. yellow solid. Yield 67.4%. m.p. 173-175°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 336 nm; IR (KBr): 3053-3026, 2918-2818, 1750, 1688, 1639-1602, 1527-1491, 1392-1361, 1314, 1247, 1158, 1012 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.15-8.10 (m, 2H), 7.83-7.74 (m, 2H), 7.43-7.20 (m, 8H), 6.73-6.64 (m, 3H), 6.38-6.30 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.60-5.52 (m, 1H), 3.65-3.55 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.21-3.14 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.1 Hz), 3.05 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 163.43, 154.08, 149.66, 140.58, 139.52, 136.40, 135.83, 132.58, 132.49, 131.74, 128.50, 127.79, 127.41, 126.71, 125.92, 125.31, 124.75, 124.19, 122.40, 120.59, 115.66, 110.85, 110.46, 60.20, 40.11 and 38.52; LC-MS: *m/z* 452.33 [M+H]. Anal. Calcd for: $C_{28}H_{25}N_3OS$: C, 74.47; H, 5.58; N, 9.31. Found: C, 74.46; H, 5.57; N, 9.30%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(4-methoxyphenyl)methanone, 3b**: light pink solid. Yield 68% (0.98 g). m.p. 182-184°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 334nm; IR (KBr): 3053-3007, 2961-2930, 2834, 1615, 1524-1506, 1444, 1403, 1332-1302, 1253, 1175, 1027 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.14-8.09 (m, 2H), 7.82-7.76 (m, 2H), 7.45 (s, 1H), 7.40-7.19 (m, 8H), 6.99-6.94 (m, 2H), 6.75-6.70 (d, 1H, $J$ = 15.9 Hz), 6.37-6.30 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.51 (m, 1H), 3.89 (s, 3H), 3.68-3.59 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.25-3.18 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.78, 161.10, 150.39, 140.63, 139.43, 136.23, 135.45, 132.53, 132.14, 128.54, 127.93, 126.91, 126.71, 126.23, 126.09, 125.68, 124.82, 124.25, 122.45, 113.01, 60.10, 55.38 and 38.75; LC-MS: *m/z* 439.27 [M+H]. Anal. Calcd for: $C_{27}H_{22}N_2O_2S$: C, 73.95; H, 5.06; N, 6.39. Found: C, 73.91; H, 5.01; N, 6.43%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(p-tolyl)methanone, 3c**: Off-White solid. Yield 69.1% (0.96 g). m.p. 184-186°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 331nm; IR (KBr): 3029, 2971-2923, 1633, 1568, 1520-1492, 1443-1413, 1322, 1185-1155, 1124, 1071-1020 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.99-7.25 (m, 14H), 6.77-6.72 (d, 1H, $J$ = 15.6 Hz), 6.46-6.38 (dd, 1H, $J_1$ = 15.6 Hz, $J_2$ = 6.9 Hz), 5.60-5.52 (m, 1H), 3.71-3.61 (dd, 1H, $J_1$ = 17.4Hz, $J_2$ = 11.4Hz), 3.26-3.18 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz), 2.42 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.44, 150.55, 141.58, 140.67, 139.42, 136.23, 135.42, 132.19, 131.20, 130.45, 128.57, 128.44, 127.96, 126.82, 126.73, 126.11, 125.75, 124.83, 124.27, 122.46, 60.01, 38.85, and 21.61; LC-MS: *m/z* 423.27 [M+H]. Anal. Calcd for: $C_{27}H_{22}N_2OS$: C, 76.75; H, 5.25; N, 6.63. Found: C, 76.73; H, 5.24; N, 6.61%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(phenyl)methanone, 3d**: White solid. Yield 74.5% (1.0 g). m.p. 156-158°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 332 nm; IR (KBr): 3059, 3026, 2981-2926, 1633, 1520-1492, 1448-1410, 1322, 1187-1154, 1126, 1071, 1021 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.05-8.03 (m, 2H), 7.81-7.76 (m, 2H), 7.53-7.43 (m, 4H), 7.41-7.35 (m, 4H), 7.34-7.20 (m, 3H), 6.76-6.71 (d, 1H, $J$ = 15.9 Hz), 6.37-6.30 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.52 (m, 1H), 3.70-3.61 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.1 Hz), 3.27-3.20 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.50, 150.81, 140.69, 139.39, 136.20, 135.30, 134.13, 132.32, 131.18, 130.31, 128.59, 128.01, 127.73, 126.75, 126.68, 126.16, 125.88, 124.85, 124.30, 122.48, 59.98 and 38.94; LC-MS: *m/z* 409.28 [M+H]. Anal. Calcd for: $C_{26}H_{20}N_2OS$: C, 76.44; H, 4.93; N, 6.86. Found: C, 76.43; H, 4.91; N, 6.85%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(4-bromophenyl)methanone, 3e**: Off White solid. Yield 65.6% (1.05 g). m.p. 206-208°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 330 nm; IR (KBr): 3040, 1785, 1623, 1526-1486, 1404-1418, 1324, 1177-1155, 1125, 1069, 1004 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.95-7.92 (m, 2H), 7.83-7.77 (m, 2H), 7.62-7.58 (m, 2H), 7.48 (s, 1H), 7.41-7.23 (m, 7H), 6.74-6.77 (d, 1H, $J$ = 15.9 Hz), 6.36-6.28 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.58-5.50 (m, 1H), 3.72-3.62 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.285-3.211 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.40, 151.16, 140.69, 139.33, 136.05, 135.03, 132.90, 132.58, 131.97, 130.96, 128.59, 128.08, 126.73, 126.36, 126.28, 126.09,

125.91, 124.90, 124.33, 122.49, 60.06 and 38.97; LC-MS: *m/z* 487.19 [M+H]. Anal. Calcd for: $C_{26}H_{19}BrN_2OS$: C, 64.07; H, 3.93; N, 5.75. Found: C, 64.05; H, 3.95; N, 5.74%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(4-chlorophenyl)methanone, 3f**: Off White solid. Yield 66.6% (0.97 g). m.p. 178-180°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 327 nm; IR (KBr): 3037, 2924,-2852, 1677, 1622, 1526-1485, 1445-1420, 1336-1302, 1177-1153, 1125-1109, 1089, 1015, 834 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.10-8.00 (m, 2H), 7.79-7.76 (m, 2H), 7.48-7.21 (m, 10H), 6.77-6.71 (d, 1H, $J$ = 15.9 Hz), 6.36-6.28 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.51 (m, 1H), 3.72-3.63 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.29-3.21 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.35, 151.11, 140.69, 139.32, 137.33, 136.04, 135.03, 132.58, 132.38, 131.78, 131.56, 128.88, 128.56, 128.06, 12797, 126.71, 126.35, 126.25, 126.04, 124.88, 124.30, 122.48, 60.05 and 39.0; LC-MS: *m/z* 443.29 [M+H]. Anal. Calcd for: $C_{26}H_{19}ClN_2OS$: C, 70.50; H, 4.32; N, 6.32. Found: C, 70.50; H, 4.30; N, 6.31%.

**(3-(Benzo[b]thiophen-2-yl)-5-styryl-4,5-dihydro-1*H*-pyrazol-1-yl)(4-nitrophenyl)methanone, 3g**: Yellow solid. Yield 73.8% (1.1 g). m.p. 202-203°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 257, 318 nm; IR (KBr): 3056, 3024-2844, 1632, 1596, 1519, 1445-1421, 1334, 1180-1158, 1123-1106, 1014 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.33-8.30 (m, 2H), 8.18-8.15 (m, 2H), 7.83-7.78 (m, 2H), 7.51-7.25 (m, 8H), 6.80-6.75 (d, 1H, $J$ = 15.6 Hz), 6.36-6.29 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.5 Hz), 5.60-5.52 (m, 1H), 3.77-3.67 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.1 Hz), 3.34-3.26 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 164.37, 152.03, 149.06, 140.74, 139.99, 139.36, 135.89, 134.58, 133.08, 131.17, 128.65, 128.24, 126.76, 126.60, 126.49, 125.86, 12501, 124.44, 122.86, 122.52, 60.11 and 39.18; LC-MS: *m/z* 454.23 [M+H]. Anal. Calcd for: $C_{26}H_{19}N_3O_3S$: C, 68.86; H, 4.22; N, 9.27. Found: C, 68.85; H, 4.21; N, 9.26%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl) styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-(dimethy lamino)phenyl)methanone, 4a**: Pale yellow solid. Yield 70.2% (0.98 g). m.p. 191-194°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 310 nm; IR (KBr): 3057, 2990-2819, 1916, 1731, 1625-1602, 1527, 1394, 1321, 1160, 1112, 1065, 1013 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.11-8.01 (d, 2H), 7.83-7.76 (m, 2H), 7.63-7.34 (m, 7H), 6.76-6.56 (m, 3H), 6.46-6.38 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 6.9 Hz), 5.62-5.54 (m, 1H), 3.69-3.59 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.23-3.16 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.4 Hz), 3.06 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.07, 152.43, 149.63, 140.59, 139.91, 139.46, 135.63, 132.57, 132.50, 130.39, 130.11, 129.72, 129.29, 126.84, 125.99, 125.50, 125.45, 125.40, 124.79, 124.19, 122.41, 120.30, 60.04, 40.08, 40.02 and 38.44; LC-MS: *m/z* 520.30 [M+H]. Anal. Calcd for: $C_{29}H_{24}F_3N_3OS$: C, 67.04; H, 4.66; N, 8.09. Found: C, 67.03; H, 4.64; N, 8.09%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoro methyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-methoxyphenyl)methanone, 4b**: Pale brown solid. Yield 75% (1.02 g). m.p. 118-120°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 332 nm; IR (KBr): 3057, 2999-2836, 1905, 1629-1, 1509, 1487, 1444, 1404, 1312, 1252, 1155, 1125, 1060, 1033 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.10-8.00 (m, 2H), 7.78-7.76 (m, 2H), 7.63-7.60 (m, 2H), 7.48-7.30 (m, 5H), 7.12-7.07 (m, 1H), 7.0-6.95 (m, 2H), 6.41-6.33 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 6.9 Hz), 5.62-5.54 (m, 1H), 3.89 (s, 3H), 3.73-3.63 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.28-3.20 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.4 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.96, 162.02, 150.24, 140.67, 139.40, 135.47, 135.30, 132.47, 131.83, 131.67, 127.94, 127.69, 127.56, 126.09, 125.78, 125.69, 124.81, 124.25, 122.44, 113.01, 59.88, 55.37 and 38.68.; LC-MS: *m/z* 507.31 [M+H]. Anal. Calcd for: $C_{28}H_{21}F_3N_2O_2S$: C, 66.39; H, 4.18; N, 5.53. Found: C, 66.37; H, 4.16; N, 5.52%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluorometh yl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(p-tolyl)methanone, 4c**: Off-White solid. Yield 73% (0.96 g). m.p. 177-179°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 256, 331 nm; IR (KBr): 3054, 2979-2920, 1920, 1649, 1520, 1408, 1324, 1157, 1123, 1067, 1014 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.98-7.95 (d, 2H, $J$ = 8.4 Hz), 7.81-7.74 (m, 2H), 7.45-7.19 (m, 9H), 6.75-6.70 (d, 1H, $J$ = 15.6 Hz), 6.37-6.29 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.29 (m, 1H), 3.69-3.59 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.25-3.18 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.1 Hz), 2.42 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.48, 150.54, 141.76, 140.67, 139.71, 139.36, 135.20, 130.96, 130.84, 130.44, 130.31, 130.09, 129.88, 129.58,

129.50, 129.11, 129.02, 128.74, 128.47, 126.87, 126.19, 125.97, 125.85, 125.56, 125.51, 125.46, 125.41, 124.87, 124.28, 122.46, 122.37, 59.84, 38.77 and 21.58; LC-MS: *m/z* 491.3 [M+H]. Anal. Calcd for: $C_{28}H_{21}F_3N_2OS$: C, 68.56; H, 4.32; N, 5.71. Found: C, 68.54; H, 4.30; N, 5.70%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl) styryl)-4,5-dihydro-1*H*-pyrazol-1-yl) (phenyl) methanone, 4d**: White solid. Yield 78% (1.0 g). m.p. 134-136°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 256, 336 nm; IR (KBr): 3060, 2927, 1918, 1633, 1522, 1448, 1412, 1324, 1158, 1122, 1066, 1015 $cm^{-1}$; $^1H$ NMR (300 MHz $CDCl_3$): δ 8.06-8.03 (m, 2H), 7.83-7.75 (m, 2H), 7.56-7.26 (m, 8H), 6.79-6.74 (d, 1H, $J$ = 15.9 Hz), 6.47-6.39 (dd, 1H, $J_1$ = 15.6 Hz, $J_2$ = 6.9 Hz), 5.61-5.54 (m, 1H), 3.74-3.65 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.29-3.21 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.56, 150.77, 140.70, 139.66, 139.33, 135.08, 133.87, 131.31, 130.98, 130.29, 129.32, 127.76, 126.88, 126.23, 125.97, 125.54, 125.49, 124.88, 124.30, 122.48, 59.79, 38.88; LC-MS: *m/z* 477.27 [M+H]. Anal. Calcd for: $C_{27}H_{19}F_3N_2OS$: C, 68.06; H, 4.02; N, 5.88. Found: C, 68.04; H, 4.01; N, 5.89%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-bromophenyl)methanone, 4e**: Off White solid. Yield 73.7% (1.1 g). m.p. 180-182°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 257, 329 nm; IR (KBr): 3062-2927, 1914, 1646, 1587, 1522, 1482, 1414, 1327, 1239, 1158, 1120, 1067, 1007 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.10-7.90 (m, 2H), 7.82-7.77 (m, 2H), 7.70-7.47 (m, 7H), 7.43-7.36 (m, 2H), 6.79-6.74 (d, 1H, $J$ = 15.9 Hz), 6.45-6.37 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.51 (m, 1H), 3.75-3.65 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.29-3.22 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.45, 151.13, 140.71, 139.55, 139.29, 134.82, 132.68, 132.39, 131.96, 131.92, 131.82, 131.22, 131.01, 130.21, 130.03, 129.60, 129.06, 127.53, 126.88, 126.36, 126.20, 126.07, 125.92, 125.56, 125.51, 125.46, 124.95, 124.35, 122.50, 122.32, 59.90 and 38.89; LC-MS: *m/z* 557.2 [M+H]. Anal. Calcd for: $C_{27}H_{18}BrF_3N_2OS$: C, 58.39; H, 3.27; N, 5.04. Found: C, 58.38; H, 3.25; N, 5.05%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-chlorophenyl)methanone, 4f**: White solid. Yield 80% (1.1 g). m.p. 168-170°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 255, 327 nm; IR (KBr): 3057, 2926, 1924, 1786, 1721, 1648, 1591, 1523, 1485, 1415, 1327, 1241, 1159, 1122-1070, 1009, 837 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.10-8.00 (m, 2H), 7.83-7.76 (m, 9H), 6.79-6.74 (d, 1H, $J$ = 15.6 Hz), 6.45-6.38 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.60-5.54 (m, 1H), 3.75-3.65 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.29-3.22 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 165.35, 151.11, 141.42, 140.70, 139.56, 139.30, 137.49, 134.84, 132.20, 131.88, 131.80, 131.20, 130.02, 129.59, 129.38, 129.10, 128.71, 128.02, 127.09, 126.88, 126.35, 126.19, 125.92, 125.55, 125.50, 125.45, 124.94, 124.35, 122.49, 122.32, 59.90, 38.88; LC-MS: *m/z* 511.20 [M+H]. Anal. Calcd for: $C_{27}H_{18}ClF_3N_2OS$: C, 63.47; H, 3.55; N, 5.48. Found: C, 63.46; H, 3.54; N, 5.47%.

**(3-(Benzo[b]thiophen-2-yl)-5-(4-(trifluoromethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-nitrophenyl)methanone, 4g**: Yellow solid. Yield 70.7% (0.99 g). m.p. 197-199°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) = 260, 321 nm; IR (KBr): 3207, 3117-2849, 1940, 1624, 1595, 1519, 1444, 1419, 1324, 1158, 1123, 1066, 1015 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.34-8.29 (m, 2H), 8.19-8.15 (m, 2H), 7.83-7.78 (m, 2H), 7.58-7.26 (m, 7H), 6.84-6.78 (d, 1H, $J$ = 15.9 Hz), 6.46-6.38 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.5 Hz), 5.61-5.53 (m, 1H), 3.80-3.70 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.1 Hz), 3.35-3.27 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 164.43, 152.05, 149.12, 140.76, 139.75, 139.39, 139.22, 134.36, 131.71, 131.18, 130.17, 129.74, 128.56, 126.92, 126.73, 126.58, 125.61, 125.56, 125.51, 125.05, 124.47, 122.88, 122.53, 59.95 and 39.11; LC-MS: *m/z* 522.2 [M+H]. Anal. Calcd for: $C_{27}H_{18}F_3N_3O_3S$: C, 62.18; H, 3.48; N, 8.06. Found: C, 62.17; H, 3.47; N, 8.04%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluoromethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-(dimethylamino)phenyl)methanone, 5a**: Pale yellow solid. Yield 65% (0.9 g). m.p. 163-165°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 231, 285 nm; IR (KBr): 3059, 2917-2819, 1688, 1568, 1524-1485, 1445-1414, 1327, 1118, 1071$cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): δ 8.05-8.05 (d, 2H), 7.76-7.69 (m, 2H), 7.47-7.37 (m, 5H), 7.34-7.27 (m, 2H), 6.69-6.58 (m, 3H), 6.41-6.33 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 6.9 Hz), 5.55-5.47 (m, 1H), 3.62-3.52 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.15-3.08 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.4 Hz), 2.99 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 166.06, 152.43, 149.68, 140.59, 139.48, 137.19, 135.63, 132.56,

132.51, 131.51, 131.08, 130.66, 130.39, 130.23, 129.90, 129.41, 128.97, 125.99, 125.93, 125.44, 124.78, 124.3, 124.25, 124.22, 123.34, 123.24, 122.40, 122.32, 120.32, 118.71, 110.84, 110.45, 60.4, 40.07 and 38.45; LC-MS: *m/z* 520.34 [M+H]. Anal. Calcd for: $C_{29}H_{24}F_3N_3OS$: C, 67.04; H, 4.66; N, 8.09. Found: C, 67.03; H, 4.64; N, 8.07%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluorom ethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-methoxyphenyl)methanone, 5b**: Pale brown solid. Yield 75% (1.0 g). m.p. 132-135°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 245, 334 nm; IR (KBr): 3060-3000, 2961-2933, 2839, 1622, 1571, 1524-1511, 1422-1406, 1330, 1115, 1254, 1071cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.13-8.10 (m, 2H), 7.82-7.76 (m, 2H), 7.63 (s, 1H), 7.56-7.34 (m, 6H), 6.99-6.94 (m, 2H), 6.78-6.72 (d, 1H, $J$ = 15.9 Hz), 6.44-6.37 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.60-5.52 (m, 1H), 3.89 (s, 3H), 3.70-3.60 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.1 Hz), 3.25-3.18 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.4 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 165.82, 162.10, 150.44, 140.64, 139.39, 137.03, 135.25, 132.57,131.57, 131.14, 130.72, 130.29, 129.93, 129.52, 129.02, 128.92, 126.17, 126.02, 125.91, 125.83, 124.87, 124.45, 124.40, 124.29, 123.33, 123.23, 122.45, 122.30, 118.69, 113.06, 59.95, 55.36 and 38.67; LC-MS: *m/z* 507.31[M+H]. Anal. Calcd for: $C_{28}H_{21}F_3N_2O_2S$: C, 66.39; H, 4.18; N, 5.53. Found: C, 66.38; H, 4.17; N, 5.52%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluorometh yl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(p-tolyl)methanone, 5c**: Off-White solid. Yield 73% (0.96 g). m.p. 159-160°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 242, 333 nm; IR (KBr): 3064, 2963-2928, 1629, 1568, 1524-1485, 1445-1419, 1327, 1118, 1071cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 7.99-7.97 (d, 2H, $J$ = 8.1 Hz), 7.82-7.76 (m, 2H), 7.64 (s, 1H), 7.56-7.54 (d, 1H, $J$ = 7.8 Hz), 7.49-7.34 (m, 5H), 7.28-7.26 (d, 2H), 6.78-6.73 (d, 1H, $J$ = 15.9 Hz), 6.45-6.37 (dd, 1H, $J_1$ = 15.6 Hz, $J_2$ = 6.9 Hz), 5.60-5.53 (m, 1H), 3.72-3.63 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.1 Hz), 3.27-3.19 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz), 2.43 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.49, 150.48, 141.73, 140.68,139.36, 136.99, 135.23, 131.19, 130.95, 130.88, 130.76, 130.44, 129.93, 129.02, 128.77, 128.45, 126.16, 125.88, 125.80, 124.85, 124.48, 124.43, 124.26, 123.34, 123.29, 122.45, 122.27, 59.81, 38.81 and 21.58; LC-MS: *m/z* 491.27 [M+H]. Anal. Calcd for: $C_{28}H_{21}F_3N_2OS$: C, 68.56; H, 4.32; N, 5.71. Found: C, 68.55; H, 4.31; N, 5.70%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluorometh yl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(phenyl)methanone, 5d**: White solid. Yield 70%. m.p. 160-162°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 330 nm; IR (KBr): 3066, 2931, 1637, 1526-1490, 1416-1449, 1326, 1123, 1073 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.06-8.04 (m, 2H), 7.82-7.77 (m, 2H), 7.64 (s, 1H), 7.57-7.35 (m, 9H), 6.80-6.75 (d, 1H, $J$ = 15.9 Hz), 6.45-6.38 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.62-5.54 (m, 1H), 3.74-3.65 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 11.4 Hz), 3.29-3.22 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 166.55, 150.78, 140.71, 139.35, 136.97, 135.11, 133.90, 131.62, 131.29, 131.19, 130.99, 130.76, 130.32, 129.95, 129.51, 129.05, 128.65, 127.75, 126.22, 125.97, 125.90, 124.88, 124.52, 124.47, 124.31, 123.39, 123.34, 123.29, 123.24, 122.47, 122.29, 118.68, 59.80 and 38.88; LC-MS: *m/z* 477.20 [M+H]. Anal. Calcd for: $C_{27}H_{19}F_3N_2OS$: C, 68.06; H, 4.02; N, 5.88. Found: C, 68.04; H, 4.01; N, 5.87%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluorom ethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-bromophenyl)methanone, 5e**: Off White solid. Yield 80% (1.2 g). m.p. 162-164°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 242, 318 nm; IR (KBr): 3056, 2928, 1646, 1591, 1523-1485, 1446-1417, 1331, 1119, 1071cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.0-7.90 (d, 2H), 7.81-7.77 (m, 2H), 7.69-7.54 (m, 4H), 7.50-7.35 (m, 5H), 6.80-6.74 (d, 1H, $J$ = 15.9 Hz), 6.43-6.35 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.2 Hz), 5.59-5.51 (m, 1H), 3.74-3.65 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.29-3.22 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 165.41, 151.18, 140.70, 139.31, 136.85, 134.84, 132.72, 132.00,131.62, 131.22, 131.01, 130.77, 130.34, 129.97, 129.50, 129.08, 128.39, 126.36, 126.24, 126.05, 125.89, 124.96, 124.65, 124.60, 124.55, 124.50, 124.38, 123.39, 123.34, 123.29, 123.24, 122.50, 122.28, 118.67, 59.92 and 38.88; LC-MS: *m/z* 557.17 [M+H]. Anal. Calcd for: $C_{27}H_{18}BrF_3N_2OS$: C, 58.39; H, 3.27; N, 5.04. Found: C, 58.38; H, 3.26; N, 5.02%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluoromethy l) styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-chlorophenyl)methanone, 5f**: Off White solid. Yield 60% (0.82 g). m.p. 148-150°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε)= 242, 333 nm; IR (KBr): 3057, 2926-2851, 1645, 1593, 1523-1489,1446-1418, 1330, 1119, 1091, 835cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.04-8.0 (d,

2H), 7.83-7.77 (m, 2H), 7.64 (s, 1H), 7.57-7.35 (m, 8H), 6.80-6.75 (d, 1H, $J$ = 15.9 Hz), 6.43-6.36 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.5 Hz), 5.60-5.52 (m, 1H), 3.75-3.65 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.4 Hz), 3.30-3.22 (dd, 1H, $J_1$ = 17.1 Hz, $J_2$ = 5.1 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 165.35, 151.19, 140.70, 139.31, 137.48, 136.86, 134.84, 132.22, 131.84, 131.62, 131.22, 130.77, 130.34, 131.22, 129.96, 129.50, 129.07, 128.39, 128.03, 126.36, 126.24, 125.89, 124.95, 124.59, 124.50, 124.38, 123.39, 123.34, 123.29, 123.24, 122.50, 122.28, 118.67, 59.93 and 38.88; LC-MS: *m/z* 511.20 [M+H]. Anal. Calcd for: $C_{27}H_{18}ClF_3N_2OS$: C, 63.47; H, 3.55; N, 5.48. Found: C, 63.45; H, 3.54; N, 5.46%.

**(3-(Benzo[b]thiophen-2-yl)-5-(3-(trifluoromethyl)styryl)-4,5-dihydro-1*H*-pyrazol-1-yl)(4-nitrophenyl)methanone, 5g**: Yellow solid. Yield 78% (1.1 g). m.p. 202-204°C. UV-Vis ($CH_2Cl_2$): $\lambda_{max}$ (ε) =257, 322 nm; IR (KBr): 3104-3078, 2929-2847, 1649, 1600, 1519, 1492, 1449-1425, 1336, 1112, 1320, 1073cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): δ 8.33-8.30 (d, 2H), 8.19-8.15 (d, 2H), 7.83-7.78 (m, 2H), 7.66 (s, 1H), 7.59-7.36 (m, 6H), 6.84-6.79 (d, 1H, $J$ = 15.9 Hz), 6.44-6.36 (dd, 1H, $J_1$ = 15.9 Hz, $J_2$ = 7.5 Hz), 5.61-5.53 (m, 1H), 3.80-3.70 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 11.1 Hz), 3.35-3.28 (dd, 1H, $J_1$ = 17.4 Hz, $J_2$ = 5.1 Hz); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 164.45, 152.02, 149.13, 140.77, 139.76, 139.22, 136.67, 134.38, 131.76, 131.30, 131.20, 130.87, 130.01, 129.13, 127.83, 126.69, 126.56, 125.82, 125.03, 124.77, 124.45, 123.34, 123.29, 122.89, 122.53, 59.93 and 39.16; LC-MS: *m/z* 522.25 [M+H]. Anal. Calcd for: $C_{27}H_{18}F_3N_3O_3S$: C, 62.18; H, 3.48; N, 8.06. Found: C, 62.17; H, 3.47; N, 8.05%.

## Conclusion

Novel N-substituted pyrazoline derivatives were synthesized from1-(benzo[b]thiophene-2-yl)ethan-1-one and trifluoromethyl substituted cinnamaldehyde at *para*- and *meta*- positions by known methods and characterized by spectral techniques (NMR, Mass and IR). All the compounds show significant antioxidant property. Among them compounds **3c, 3f, 4a, 4e, 4f, 5c, 5d 5e** and **5g** shows good antioxidant property than the other compounds.

## Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/ handle/123456789/ 58776.

## Acknowledgements

The authors are very thankful to the Director, Solara Active Pharma Sciences Limited, Research Centre, Chennai for encouragement and support.

## References

1 Karthikeyan M S, Holla B S & Kumari N S, *European J Med Chem*, 42 (2007) 30.
2 Havrylyuk D, Zimenkovsky B, Vasylenko `O & Lesyk R, *J Heterocycl Chem*, 50 (2013) E55.
3 Joshi H S, Popat K H & Nimavt K S, *Indian J Heterocycl Chem*, 12 (2003) 225.
4 Drabu S, Rana A & Kumar H, *Indian J Heterocycl Chem*, 16 (2007) 399.
5 Shaharyar M, Abdullah M M, Bakht M A & Majeed J, *Eur J Med Chem*, 45 (2010) 114.
6 Tanwer N, Kaur R, Rana D & Singh R, *J Integr Sci Technol*, 3 (2015) 39.
7 Lombardino J G & Otterness I G, *J Med Chem,* 24 (1981) 830.
8 Joshi R S, Mandhane P G, Diwakar S D, Dabhade S K & Gill C H, *Bioorg Med Chem Lett*, 20 (2010) 3721.
9 (a) Ahluwalia V K, Dutt U & Sharma H R, *J Indian Chem Soc*, LXIV (1987) 221; (b) Rangarajan T M & Mathew B, *Curr Top Med Chem*, 21 (2021) 2695.
10 Wagner A, Schellhammer C W & Peterson S, *Angew Chem Int Ed*, 5 (1966) 699.
11 Hu S, Zhang S, Hu Y, Tao Q & Wu A, *Dyes Pigm*, 96 (2013) 509.
12 Kumar C K, Trivedi R, Giribabu L, Niveditha S, Bhanuprakash K & Sridhar B, *J Organomet Chem*, 780 (2015) 20.
13 Jin M, Liang Y J, Lu R, Chuai X H, Yi Z H, Zhao Y & Zhang H J, *Synth Met*, 140 (2004) 37.
14 Pant G J, Singh P, Rawat B S, Rawat M S M & Joshi G C, *Spectrochim Acta A*, 78 (2011) 1075.
15 Singh P, Negi J S, Singh K, Pant G J, Rawat M S M & Joshi G C, *Synth Met*, 162 (2012) 1977.
16 Bohm H J, Banner D, Bendels S, Kansy M, Kuhn B, Muller K, Sander U O & Stahl M, *ChemBioChem,* 5 (2004) 637.
17 Keri R S, Chand K, Budagumpi S, Somappa S B, Patil S A & Nagaraja B M, *Eur J Med Chem*, 138 (2017) 1002.
18 (a) Hampannavar G A, Karpoormath R, Palkar M B, Shaikh M S & Chandrasekaran B, *ACS Med Chem Lett*, 7 (2016) 686; (b) Pathak V N, Joshi R, Sharma J, Gupta N, & Rao V M, *Phosphorus Sulfur Silicon Relat Elem*, 184 (2009) 1854.
19 (a) Knorr L, *Ber Dt Chem Ges*, 26 (1893) 100; (b) Vounauwers K & Muller, *Ber Dt Chem Ges,* 41 (1908) 4230.
20 (a) Han Z, Yan J, Tang H Q, He Y, Zhu Y, & Ge Y Q, *Tetrahedron Lett*, 58 (2017) 1254; (b) Bhat K I & Jainey P J, *Asian J Pharm Clin Res*, 7(4) (2014) 237.
21 Ziani N, Lamara K, Sid A, Willem Q, Dassonneville B & Demonceau A, *Eur J Chem.,* 4 (2013) 176.
22 Lam K W, Tham C L, Liew C Y, Syahida A, Rahman M B A, Israf D A &Lajis N H, *Med Chem Res,* 21 (2012) 333.

23 Bauer U, Egner B J, Nilsson I &Berghult M, *Tetrahedron Lett*, 41 (2000) 2713.
24 Fig. 4 Refer supplementary data.
25 (a) Halliwell B & Gutteridge J M, *Methods Enzymol*, 186 (1990) 1; (b) Halliwell B & Gutteridge J M C, *Free Radicals in Biology & Medicine*, 3rd ed, (Oxford University Press, Oxford) 1999; (c) Chen S K, Hsu C H, Tsai M L, Chen R H &Drummen G P C, *Int J Mol Sci*, 14 (2013) 19399.
26 Beal M F, *Ann Neurol*, 38 (1995) 357.
27 Khalafalla M M, Abdellatef E, Dafalla H M, Nassrallah A A, Aboul-Enein K M, Lightfoot D A, El-Deeb F E & El-Shemy H A, *African J Biotech*, 9 (2010) 8467.
28 Braughler J M, Duncan L A & Chase R L, *J biol chem*, 261 (1986) P10282.
29 Klein S M, Cohen G & Cederbaum A I, *Biochemistry*, 20(21) (1981) 6006.