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Synthesis, Characterization and Antioxidant Activity of Some New 3-(3-(Trifluoromethyl)phenyl)acrylic Acid Derived Hydrazide-Hydrazone Scaffolds

RAMYA KRISHNA PALLAPATI[1], BABY RAMANA MUTCHU[1], UMAMAHESWARA RAO VANGA[2], RAVI VARALA[3] and HARI BABU BOLLIKOLLA[1,*]

[1]Department of Chemistry, Acharya Nagarjuna University, Nagarjuna Nagar-522510, India
[2]Department of Botany & Microbiology, Acharya Nagarjuna University, Nagarjuna Nagar-522510, India
[3]Scrips Pharma, Mallapur, Hyderabad-500076, India

*Corresponding author: E-mail: dr.b.haribabu@gmail.com

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Some new analogues of trifluoromethylphenyl acrylic acid scaffold derived hydrazide-hydrazones (**4a-l**) were produced by using various structurally divergent aromatic aldehydes. All the hydrazones were obtained in moderate to good yields (64-78%) in methanol at a temperature of 45-65 °C. All the compounds were screened for antioxidant activity by DPPH method and the compounds **4c, 4d**, **4e** and **4h** were found to be showed maximum antioxidant activity among the synthesized compounds.

Keywords: Hydrazide-hydrazones, 3-(3-(Trifluoromethyl)phenyl)acrylic acid, Antioxidant activity, Aldehydes.

INTRODUCTION

Hydrazone scaffolds are very important bioactive heterocyclic compounds because of their various biological and clinical applications [1]. The common and traditional method for preparation of the *N*-acyl hydrazones (NAHs) involves the treatment of substituted acid hydrazides and carbonyl compounds in the suitable solvents. All the reported approaches include classical synthetic methodologies and vary in the selectivity and reaction patterns [2]. Further, the acylhydrazones were an adaptable group of nitrogen atom substituted compounds with good chemical reactivity and were also utilized as starting materials and intermediates for many significant heterocyclic compounds [3]. Moreover, because of existence of various significant biological activities the acylhydrazones got wide exposure in present days and can also be used as catalysts [4-6].

The broad range of biological activities of hydrazide-hydrazone derivatives are anticancer, anti-inflammatory, antimicrobial, antitubercular, anticonvulsant, antiprotozoal and antiviral [7-10], hence, it grabbed the attention of several medicinal chemists to produce various hydrazide-hydrazone derivatives and assess them for various biological activities. The general method for synthesizing hydrazide-hydrazone derivatives is heating of suitable hydrazides with aldehydes of different kind in various organic solvents such as methanol, ethanol, *etc*. [11-15].

It was established that the presence of azomethine group (–NH–N=CH–) connected with carbonyl group in these hydrazide-hydrazone organic compounds is responsible for their wide range of biological applications and thus attracted the attention of several medicinal scientists [7]. Moreover, this group is useful for the synthesis of various heterocyclic motifs of medicinal importance such as 1,3,4-oxadiazolines, coumarins, azetidin-2-ones, 1,3-benzothiazin-4-ones, 1,3-thiazolidin-4-ones, *etc*.

In continuation to our research in developing various types of scaffold derived hydrazones for useful medicinal properties such as bezafibrate scaffold [16], 3-(2-hydroxy-5-methylphenyl)-3-phenylpropane hydrazidehydrazone [17], 3-(3-(trifluoromethyl)-phenyl)-3(2-hydroxy-5-methylphenyl)propanehydrazones [18], 3-{[4-(2-methoxyphenyl)piperazin-1-yl]sulfonyl}-benzohydrazide-hydrazone derivatives [19], *etc*. and our interest in developing pharmacologically active novel heterocyclic analogues [20-27], we herein, wish to report the exploitation of acid functional group in forming corresponding trifluoro-

methylphenyl derived hydrazide-hydrazone scaffolds with variation in aldehydes (**Scheme-I**) and to study their use as antioxidants.

EXPERIMENTAL

All the experiments were done in oven-dried glassware at 120 °C. The chemicals and solvents obtained from Merck Chemical Co. all reactions were monitored by TLC plates made of silica gel-G (Merck grade) as the adsorbent and the solvent systems were indicated for all reactions. Silica gel of 100-200 mesh grade was used for purification of final products by column chromatography. Proton NMR spectra were obtained on Bruker (400 MHz) spectrometer by use of DMSO-d_6 as solvent.

Synthesis of 4-(3-(trifluoromethyl)phenyl)-3,4-dihydro-6-methylchromen-2-one (2): To a solution of (*E*)-3-(3-(trifluoromethyl)phenyl)acrylic acid (**1**, 20 g, 0.15 mol) in *p*-cresol (15.5 g, 0.15 mol) catalytic amount of conc. H_2SO_4 (4.7 g, 0.05 mol) was added and heated to 120 °C for 15 h. The reaction was monitored by using TLC, after completion of the reaction, the reaction mass was cooled to room temperature and diluted using toluene (2 × 100 mL) and water (100 mL) stirred for 5 min at room temperature. Toluene organic layer was separated first and washed with 10% $NaHCO_3$ solution (2 × 100 mL) at 25 °C. Concentrated the toluene layer to get crude compound. The crude product **2** was filtered and washed with water (100 mL) and dried under vacuum. Finally, the obtained product was recrystallized with isopropyl alcohol to yield 28.55 g pure product (80%) as a white solid having m.p. 50-55 °C.

Synthesis of 3-(3-(trifluoromethyl)phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (3): To a solution of compound **2** (20 g, 0.09 mol) in methanol (100 mL) hydrazine hydrate (15 g, 0.35 mol) was added slowly and heated to 55 °C for about 6 h. The reaction was monitored by using TLC, after completion of the reaction, the reaction mass was cooled to 0-5 °C and the crude product was spontaneously crystallized from the solution. Compound **3** obtained in solid state was filtered and washed with methanol (2 × 10 mL). Finally, the product was dried under vacuum to remove any moisture and recrystallized using ethanol solvent to yield 15 g (80.5 %) of pure product as a white solid. m.p.: 180-185 °C; IR (KBr, ν_{max}, cm^{-1}): 3311, 3301, 3269, 3082, 3049, 2967, 2867, 2811, 1647, 1574, 1509, 1475, 1452, 1440, 1293, 1273, 1262, 1256, 1239, 1221, 1098, 1084; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.23 (s, 1H), 9.01 (s, 1H), 7.53 (t, *J* = 5.0 Hz, 2H), 7.47 (d, *J* = 7.0 Hz, 2H), 6.96 (d, *J* = 2.0 Hz, 1H), 6.80 (q, *J* = 1.5 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.84 (dd, *J* = 7.0, 9.5 Hz, 1H), 4.09 (brs, 2H), 2.86 (dd, *J* = 8.5, 14.5 Hz, 1H), 2.70 (dd, *J* = 8.0, 15.0 Hz, 1H), 2.18 (s, 3H,); ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.7, 152.2, 145.7, 131.7, 129.2, 128.9, 128.8, 128.5, 127.9, 127.7, 127.3, 125.6, 124.2, 124.1, 122.9, 122.5 (2C), 115.1, 37.9, 20.2; ESI-MS: *m/z* 338.9 $(M+H)^+$.

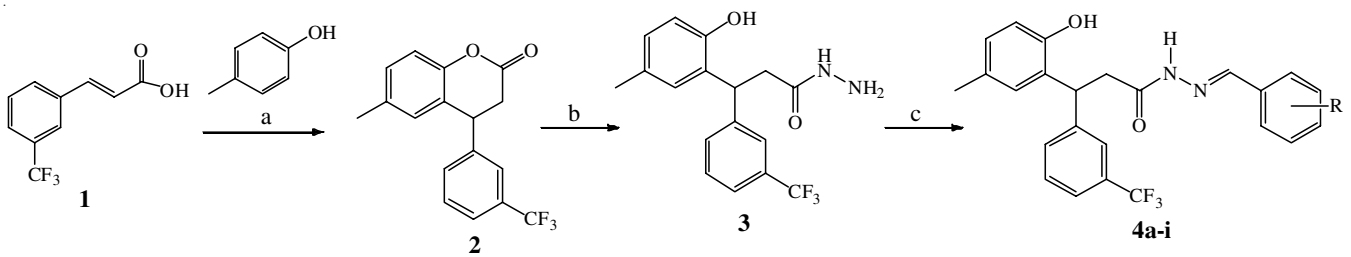
General procedure for the synthesis of titled hydrazone derivatives (4a-i): To a suspension of compound **3** (0.1 g, 0.29 mmol) in solvent methanol (10 mL) at 0-15 °C was added different aromatic aldehydes **(4a-i)** (0.1 g, 0.29 mmol) and heated to 45-65 °C for 5-8 h. The reaction was monitored by using TLC, after the reaction completion the reaction mixture was cooled to 0-5 ºC and maintained for 30 min. The precipitated white solids obtained in each case were filtered at the vaccum pump, dried and purified by using column chromatography.

Spectral data

(*E*)-*N*′-(4-Methylbenzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4a): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.38 (s, 1H, O=C-NH), 9.28 (s, 1H, N-N=CH), 8.08 (s, 1H, OH), 7.80 - 7.76 (d, 2H, *J* = 8.0 Hz, H-2,3), 7.68 (d, 1H, *J* = 8.4 Hz, H-5), 7.62 (d, 2H, *J* = 8.8 Hz, H-2′,6′), 7.54 (d, 2H, *J* = 8.0 Hz, H-4′, 5′), 7.26 (d, 2H, *J* = 8.8 Hz, H-2″,6″), 7.09 (d, 2H, *J* = 8.4 Hz, H-3″, 5″), 4.99 - 4.87 (dd, 2H, *J* = 7.6 Hz, C-CH$_2$ (or) H-8), 3.71 (dd, 1H, *J* = 11.2 Hz, H-7), 3.33 (s, 3H, H-4), 2.37 (s, 3H, H-4″); ^{13}C NMR (100 Hz, DMSO-d_6): 133.8, 131.8, 131.7, 131.5, 131.5, 130.0, 129.3, 129.3, 129.0, 128.4, 128.2, 128.1, 128.0, 127.8, 127.8, 127.7, 127.1, 126.9, 126.6, 124.1, 124.1, 124.0, 124.0, 124.0, 111.6, 115.2, 115.1, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 36.2, 28.9, 20.9, 20.9, 20.3, 20.2: ESI-MS: *m/z* 442.1 $(M+H)^+$ for $C_{25}H_{23}N_2O_2F_3$.

(*E*)-*N*′-(4-Trifluoromethylbenzylidene)-3-(3-(trifluoromethyl)phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4b): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.42 (s, 1H, O=C-NH), 9.29 (s, 1H, N-N=CH), 8.21 (s, 1H, OH), 7.93 (d, 2H, *J* = 9.2Hz, H-2,3), 7.80 (d, 1H, *J* = 6.8 Hz, H-5), 7.67 (d, 2H, *J* = 7.6 Hz, H-2′,6′), 7.50 (d, 2H, *J* = 3.6 Hz, H-4′, 5′), 7.09 (d, 2H, *J* = 8.0 Hz, H-2″,6″), 6.68 (d, 2H, *J* = 7.6 Hz, H-3″, 5″), 4.78 (dd, 2H, *J* = 7.6 Hz, C-CH$_2$ (or) H-8), 3.58 (dd, 1H, *J* = 8.4 Hz, H-7), 2.51 (s, 3H, H-4); ^{13}C NMR (100 Hz, DMSO-d_6): 134.2, 130.5, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 28.9, 22.0: ESI-MS: *m/z* 496.1 $(M+H)^+$ for $C_{25}H_{20}N_2O_2F_6$.

(*E*)-*N*′-(3-Methoxy benzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4c): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.45 (s, 1H, O=C-NH), 9.29 (s, 1H, N-N=CH), 8.94 (s, 1H, OH), 7.99-7.68 (d,



Scheme-I: Synthesis of some substituted Hydrazide-Hydrazone derivatives (**4a-i**); **Reaction conditions:** (a) Catalyatic conc. H_2SO_4, 120 °C; (b) hydrazine hydrate, MeOH, 50 °C, (c) aromatic aldehydes, 0-15 °C, MeOH, 45-65 °C

2H, *J* = 6.8Hz, H-2,3), 7.67 (d, 1H, *J* = 7.6 Hz, H-5), 7.53 (d, 2H, *J* = 7.6 Hz, H-2′,6′), 7.18 (d, 2H, *J* = 6.8 Hz, H-4′, 5′), 7.09 (d, 2H, *J* = 8.4 Hz, H-2″,6″), 6.95 (d, 2H, *J* = 8.4 Hz, H-4″, 5″), 4.99-4.62 (dd, 2H, *J* = 7.2 Hz, C-C<u>H</u>$_2$ (or) H-8), 3.57 (dd, 1H, *J* = 10.8 Hz, H-7), 3.30 (s, 3H, H-4), 2.22 (s, 3H, H-4"): ^{13}C NMR (100 Hz, DMSO-d_6): 167.3, 158.7, 156.4, 152.1, 149.3, 142.7, 133.8, 132.9, 131.5, 130.0, 129.7, 129.4, 129.3, 129.2, 129.0, 128.4, 128.3, 128.0, 127.7, 127.4, 126.5, 126.4, 125.0, 124.0, 124.0, 121.6, 120.6, 116.5, 115.1, 112.0,55.8, 40.1, 39.97, 39.7, 39.5, 39.3, 39.1, 39.0, 38.9, 36.0, 21.1, 20.2, 20.2: ESI-MS: *m/z* 457.2 (M+H)$^+$ for $C_{25}H_{23}N_2O_3F_3$.

(*E*)-*N*′-(4-Ethoxybenzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4d): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.37 (s, 1H, O=C-N<u>H</u>), 9.27 (s, 1H, N-N=C<u>H</u>), 8.66(s, 1H, O<u>H</u>), 7.93-7.81 (d, 2H, *J* = 12.0 Hz, H-2,3), 7.67 (d, 1H, *J* = 7.6 Hz, H-5), 7.58 (d, 2H, *J* = 10.8 Hz, H-2′,6′), 7.32 (d, 2H, *J* = 8.4 Hz, H-4′, 5′), 7.09 (d, 2H, *J* = 8.4 Hz, H-2″, 6″), 6.99 (d, 2H, *J* = 8.8 Hz, H-3", 5″), 6.82 (dd, 2H, *J* = 5.2 Hz, C-C<u>H</u>$_2$ (or) H-8), 6.72 (dd, 1H, *J* = 7.6 Hz, H-7), 4.88 (s, 3H, H-4), 3.77 (dd, 2H, *J* = 11.6 HZ, H-4″ O-CH$_2$-CH$_3$′), 2.89 (t, 3H, OCH$_2$-CH$_3$, H-4″); ^{13}C NMR (100 Hz, DMSO-d_6): 167.4, 167.9, 160.3, 152.2, 149.3, 145.8, 142.7, 133.8, 131.7, 131.5, 130.0, 129.9, 129.3, 129.1, 129.0, 128.5, 128.3, 128.2, 128.0, 127.7, 127.3, 126.7, 126.4, 125.0, 124.0, 122.6, 116.5, 115.1, 114.8, 114.7, 63.3, 63.2,40.2,39.7, 39.5, 39.3, 39.1, 38.9, 38.9, 36.0, 20.3, 20.2, 14.5: ESI-MS: *m/z* 470.1 (M+H)$^+$ for $C_{26}H_{25}N_2O_3F_3$.

(*E*)-*N*′-(3-Fluoro-4-methyl benzylidene)-3-(3-(trifluoromethyl)phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4e): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.49 (s, 1H, O=C-N<u>H</u>), 9.25 (s, 1H, N-N=C<u>H</u>), 8.08(s, 1H, O<u>H</u>), 7.69 (d, 2H, *J* = 7.6 Hz, H-2,3), 7.62 (d, 1H, *J* = 7.6 Hz, H-5), 7.52 (d, 2H, *J* = 8.0 Hz, H-2′,6′), 7.48 (d, 2H, *J* = 5.2 Hz, H-4′, 5′), 7.26 (d, 2H, *J* = 8.4 Hz, H-2″,6″), 7.09 (d, 2H, *J* = 8.8 Hz, H-5″), 4.97-4.88 (dd, 2H, *J* = 5.2 Hz, C-C<u>H</u>$_2$ (or) H-8), 3.78 (dd, 1H, *J* = 12.4 Hz, H-7), 3.23 (s, 3H, H-4), 2.34 (s 3H, H-4″),);^{13}C NMR (100 Hz, DMSO-d_6): 167.4, 161.5, 159.0, 152.2, 149.3, 142.7, 133.8, 131.8, 131.7, 131.5, 130.0, 129.7, 129.5, 129.3, 129.0, 128.4, 128.2, 127.7, 127.4, 125.1, 125.1, 125.0, 124.0, 116.5, 115.4, 115.1, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 36.0,31.2, 28.9, 28.6, 28.4, 22.0, 20.3, 20.2, 14.2, 14.2, 13.8: ESI-MS: *m/z* 458.4 (M+H)$^+$ for $C_{25}H_{22}N_2O_2F_4$.

(*E*)-*N*′-(4-Fluorobenzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4f): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.44 (s, 1H, O=C-N<u>H</u>), 9.27 (s, 1H, N-N=C<u>H</u>), 8.72 (s, 1H, O<u>H</u>), 7.97 (d, 2H, *J* = 6.0 Hz, H-2,3), 7.78 (d, 1H, *J* = 5.6 Hz, H-5), 7.62 (d, 2H, *J* = 9.6 Hz, H-2′,6′), 7.54 (d, 2H, *J* = 8.0 Hz, H-4′, 5′), 7.38 (d, 2H, *J* = 8.4 Hz, H-2″,6″), 7.09 (d, 2H, *J* = 8.4 Hz, H-3″, 5″), 4.98-4.77 (dd, 2H, *J* = 720 Hz, C-C<u>H</u>$_2$ (or) H-8), 3.86 (dd, 1H, *J* = 10.4 Hz, H-7), 2.99 (s, 3H, H-4): ^{13}C NMR, (100 Hz, DMSO-d_6): 152.2, 152.2, 150.4, 145.7, 145.5, 130.6, 130.6, 130.0, 129.3, 129.1, 129.0, 128.4, 127.7, 124.4, 124.2, 124.1, 124.0, 117.4, 116.5, 116.1, 115.9, 115.8, 115.6, 115.1, 100.7, 95.8, 88.8, 87.7, 83.2, 80.8, 69.8, 51.5, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 31.2, 28.9, 22.0, 20.3, 13.8: ESI-MS: *m/z* 445.1 (M+H)$^+$ for $C_{24}H_{20}N_2O_2F_4$.

(*E*)-*N*′-(2-Hydroxybenzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4g): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.44 (s, 1H, O=C-N<u>H</u>), 9.26 (s, 1H, N-N=C<u>H</u>), 8.08 (s, 1H, O<u>H</u>), 7.97 (s, 1H, O<u>H</u>), 7.78-7.68 (d, 2H, *J* = 5.6 Hz, H-2,3), 7.62 (d, 1H, *J* = 9.2 Hz, H-5), 7.29 (d, 2H, *J* = 8.8 Hz, H-2′,6′), 7.09 (d, 2H, *J* = 8.4 Hz, H-4′, 5′),6.88 (d, 2H, *J* = 6.88 Hz, H-3″,6″), 6.69 (d, 2H, *J* = 6.8 Hz, H-4″, 5″), 4.99-4.88 (dd, 2H, *J* = 7.2 Hz, C-C<u>H</u>$_2$ (or) H-8), 3.42 (dd, 1H, *J* = 6.8 Hz, H-7), 3.01 (s, 3H, H-4); ^{13}C NMR, (100 Hz, DMSO-d_6): 172.4, 152.2, 131.9, 131.7, 131.5, 130.6, 130.0, 129.3, 129.3, 129.0, 129.0, 128.8, 128.4, 128.2, 128.1, 127.7, 127.3, 124.2, 124.1, 116.5, 115.9, 115.8, 115.6, 115.2, 115.1, 58.9, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 36.5, 31.2, 28.9, 28.9, 28.8, 28.6, 28.5, 22.0, 20.3, 20.2, 13.8; ESI-MS: *m/z* 443.1 (M+H)$^+$ for $C_{24}H_{21}N_2O_3F_3$.

(*E*)-*N*′-(4-Butylbenzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4h): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.42 (s, 1H, O=C-N<u>H</u>), 9.32 (s, 1H, N-N=C<u>H</u>), 8.13 (s, 1H, O<u>H</u>), 7.90 (d, 2H, *J* = 8.0 Hz, H-2,3), 7.71 (d, 1H, *J* = 8.0 Hz, H-5), 7.58 (d, 2H, *J* = 8.4 Hz, H-2′,6′), 7.48 (d, 2H, *J* = 8.0 Hz, H-4′, 5′), 7.37 (d, 2H, *J* = 7.6 Hz, H-2″,6″), 7.13 (d, 2H, *J* = 8.4 Hz, H-3″, 5″), 6.92 (dd, 2H, *J* = 6.4 Hz, C-C<u>H</u>$_2$ (or) H-8), 6.72 (dd, 1H, *J* = 6.0 Hz, H-7), 4.83-4.66 (s, 3H, H-4), 2.41 (s, 2H, H-4″), 2.27 (s, 2H, H-4″), 2.21 (s, 2H, H-4″), 1.66 (s, 3H, H-4″): ^{13}C NMR, (100 Hz, DMSO-d_6): 167.3, 161.0, 149.3, 146.0, 142.7, 133.8, 131.7, 131.5, 131.4, 130.0, 129.7, 129.4, 129.3, 129.3, 129.0, 128.7, 128.6, 128.4, 128.3, 128.3, 125.0, 124.0, 124.0, 116.5, 115.1, 55.1, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 39.0, 38.9, 26.0, 34.7, 32.7, 29.2, 28.9, 28.8, 21.6, 20.2, 20.2, 13.6; ESI-MS: *m/z* 483.2 (M+H)$^+$ for $C_{28}H_{29}N_2O_2F_3$.

(*E*)-*N*′-(4-Trimethyl benzylidene)-3-(3-(trifluoromethyl)-phenyl)-3-(2-hydroxy-5-methylphenyl)propanehydrazide (4i): ^{1}H NMR: (400 MHz, DMSO-d_6): δ 11.38 (s, 1H, O=C-N<u>H</u>), 9.29 (s, 1H, N-N=C<u>H</u>), 8.68 (s, 1H, O<u>H</u>), 7.94 (d, 2H, *J* = 8.4 Hz, H-2,3), 7.82 (d, 1H, *J* = 8.0 Hz, H-5), 7.67 (d, 2H, *J* = 7.6 Hz, H-2′,6′), 7.62 (d, 2H, *J* = 6.8 Hz, H-4′, 5′), 7.58 (d, 2H, *J* = 7.6 Hz, H-2″,6″), 7.47 (d, 2H, *J* = 8.0 Hz, H-3″, 5″), 4.90-4.62 (dd, 2H, *J* = 8.0 Hz, C-C<u>H</u>$_2$ (or) H-8), 3.77 (dd, 1H, *J* = 8.8 Hz, H-7), 3.29 (s, 3H, H-4), 1.36-1.15 (Bs, 9H, H-4″): ^{13}C NMR, (100 Hz, DMSO-d_6): 167.3, 152.2, 149.3, 142.7, 133.8, 131.5, 131.1, 130.0, 129.4, 129.2, 129.1, 129.0, 128.4, 128.2, 128.1, 127.7, 126.7, 126.5, 125.6, 125.5, 125.2, 125.0, 124.2, 124.0, 124.0, 116.0, 115.1, 54.8, 40.1, 39.9, 39.7, 39.5, 39.3, 39.1, 39.0, 38.9, 36.0, 34.6, 34.5, 30.9, 30.8, 30.8, 20.3, 20.2; ESI-MS: *m/z* 483.1 (M+H)$^+$ for $C_{28}H_{29}N_2O_2F_3$.

RESULTS AND DISCUSSION

In this report, the synthesis of some new 3-(3-(trifluoro methyl)phenyl)acrylic acid scaffold derived from hydrazide-hydrazones are presentd as shown in **Scheme-I**. Initially, in the first step, the starting material 3-(3-(trifluoromethyl)-phenyl)acrylic acid was treated with *p*-cresol in the presence of conc. H_2SO_4 in catalytic quantity at 120 °C to give the corresponding chromenone (**2**). Compound **2** was further treated with hydrazine hydrate in solvent methanol to afford respective acid hydrazide compound **3**. Finally, it was reacted with structurally

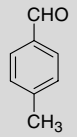
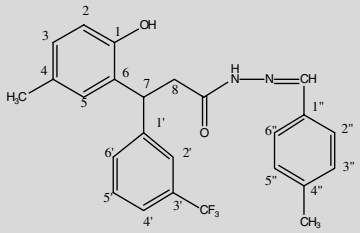
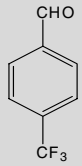
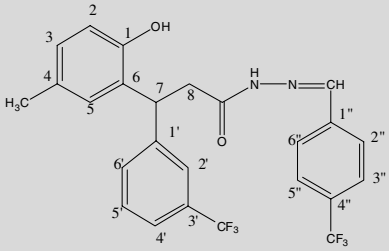
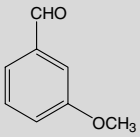
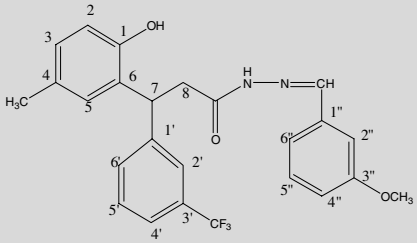
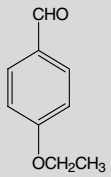
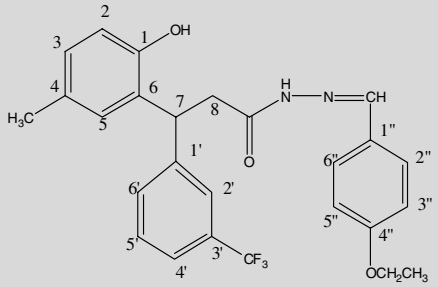
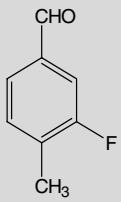
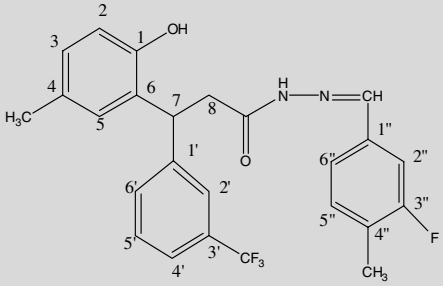
divergent aromatic aldehydes to furnish the resultant hydrazide-hydrazones (**4a-i**) in moderate to good isolated yields.

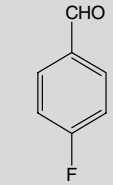
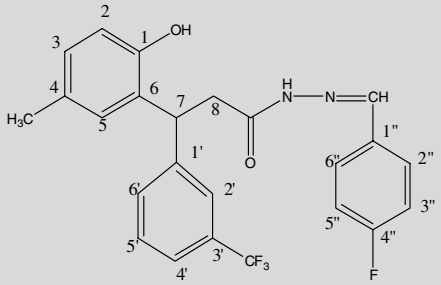
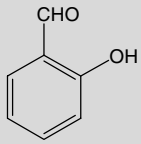
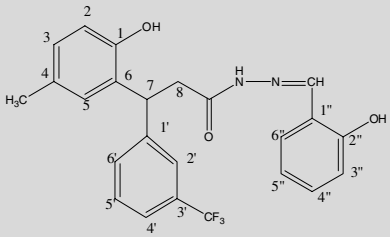
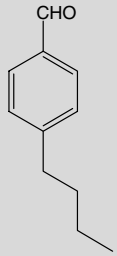
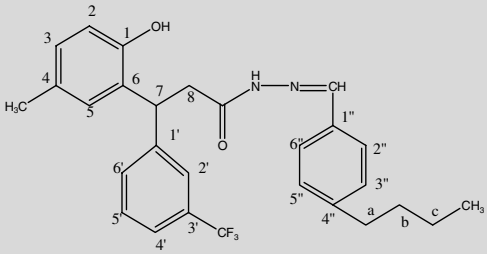
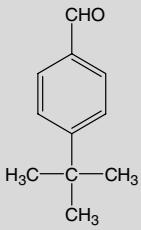
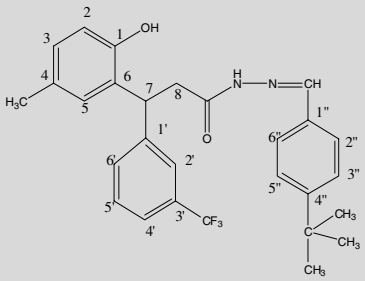
A series of 9 new 3-(3-(trifluoro methyl) phenyl) propionic derived hydrazide-hydrazones were prepared with yields ranging from 64-78%. All the compounds were well characterized by IR, NMR and mass spectral analyses and physical constants. Further, the details of the yields, TLC mobile phase and R_f values of each individual compound were provided in Table-1.

The compounds **4a** with *para*-CH_3 substitution on phenyl ring, **4b** with *para*-CF_3 substitution on phenyl ring, **4c** with *meta*-OMe substitution on phenyl ring and **4d** with *para*-OC_2H_5 substitution on phenyl ring were found to be obtained with good yields compared to other derivatives, *i.e*. with more than 75% yield. Later the compounds **4e**, **4f** and **4i** were followed with almost 70% yield. The remaining compounds were yielded around 65%. However, there is no distinction was observed between electron withdrawing and releasing groups and both were found to be well undergone to reaction process.

Antioxidant activity: All the synthesized compounds (**4a-i**) were studied for their antioxidant activity at four different concentrations using DPPH method as the compounds obtained from hydrazones were reported to possess antioxidant activity.

TABLE-1
PHYSICAL DATA OF 3-(3-(TRIFLUOROMETHYL)PHENYL)ACRYLIC ACID DERIVED HYDRAZIDE-HYDRAZONES

Compd.	R-CHO	Product	m.p. (°C)	Yield (%)	R_f value	TLC mobile phase
4a			164-166	78.2	0.74	60:40
4b			135-138	75.4	0.69	60:40
4c			140-143	76.4	0.8	50:50
4d			176-178	75.3	0.89	70:30
4e			183-185	69.5	0.68	60:40

4f			197-199	68.4	0.66	80:20
4g			173-175	64.8	0.89	60:40
4h			184-186	64.2	0.76	50:50
4i			170-172	68.9	0.91	60:40

All the synthesized hydrazones were screened for antioxidant activity by following reported literature protocol [28] and results were reported in Table-2.

The compounds showed concentration dependent increased antioxidant activity. At 200 µg concentration, compounds **4c, 4d, 4e** and **4h** showed maximum antioxidant activity. At this concentration (200 µg) except the compounds **4b, 4f** and **4g**, remaining compounds showed more than 40% level of antioxidant activity. However, all the compounds displayed less antioxidant activity when compared to that of positive control, ascorbic acid at any given concentration.

TABLE-2
ANTIOXIDANT ACTIVITY (% INHIBITION) OF THE SYNTHESIZED COMPOUNDS (**4a-i**) BY DPPH METHOD

Compounds	Concentration (µg/mL)			
	25	50	100	200
4a	23.74	33.97	38.79	44.79
4b	10.63	13.82	20.37	27.32
4c	32.77	48.26	54.92	68.61
4d	25.97	41.89	51.92	63.64
4e	37.45	44.54	53.99	66.97
4f	15.16	19.89	24.96	29.39
4g	16.94	18.78	24.52	28.66
4h	13.32	28.37	49.60	64.08
4i	22.25	26.20	34.12	41.60
Ascorbic acid (Std.)	78.74	86.06	92.80	93.25

Conclusion

In conclusion, a total of nine 3-(3-(trifluoromethyl)phenyl)-acrylic derived hydrazide-hydrazones scaffolds were synthesized by using various structurally divergent aromatic aldehydes in moderate to good yields. Compounds **4c, 4d, 4e** and **4h** showed maximum antioxidant activity among all the synthesized compounds.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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