

Original article

Synthesis of (4-benzoyl-phenoxy)-acetic acid derivatives and their efficacy as antioxidant agents

T. Prashanth^a, V. Lakshmi Ranganatha^a, P. Naveen^a, H.D. Gurupadaswamy^a,
A. Bushra Begum^b, Mohammed Al-Ghorbani^a, Shaukath Ara Khanum^{a,*}

^a Department of Chemistry, Yuvaraja College, University of Mysore, Mysore 570 005, Karnataka, India

^b Department of Chemistry, D. Banumai's P U Science College, Mysore 570 024, Karnataka, India

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ABSTRACT

Aim & background: To study the synthesis of a series of (4-benzoyl-phenoxy)-acetic acid derivatives (**6a–k**) and to test their antioxidant activity.

Methods: The newly synthesized compounds were characterized by IR, ¹H NMR and LC–MS analyses. All these compounds were screened for their *in vitro* antioxidant activity by employing 1,1-diphenyl-1-picrylhydrazyl (DPPH), nitric oxide (NO) and hydrogen peroxide (H₂O₂) radical scavenging assays.

Results: Compounds **6h** with chloro substituent in benzoyl ring and **6f** with no substituent in benzoyl ring showed good radical scavenging activity in all the three methods compared to the standard drug ascorbic acid. Whereas compound **6k** with methoxy substituent in benzoyl ring showed good antioxidant activity only in hydrogen peroxide method and remaining compounds showed moderate to mild radical scavenging activity.

Conclusion: Compounds **6f**, **6h** and **6i** showed excellent activity, almost equivalent to that of standard and the remaining compounds showed moderate to mild scavenging activity.

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1. Introduction

The antioxidants that scavenge reactive oxygen species may be of great value in preventing the onset and propagation of oxidative diseases like autoimmune diseases, cardiovascular diseases, neurovascular diseases.¹ *In vivo* molecular oxygen is easily converted to reactive free radicals such as superoxide anions and hydroxyl radicals, which are highly reactive substances that react with lipids, proteins and DNA, provoking irreversible changes of their biomolecular structure.² Reactive oxygen species (ROS) are continuously generated in very low amounts by the transfer of one electron to an oxygen molecule during various physiological processes, such as respiration chain, oxygenase and cellular immunization reactions.^{3,4} It is known that ROS play an important role in tumor initiation.⁵ Elevated ROS levels can initiate DNA damage, and might ultimately lead to carcinogenesis.⁶ Compounds capable of either

scavenging free radicals or suppression of superoxide generation and antioxidant compounds shown cancer chemopreventive effects.⁷ A vast amount of evidence proved that ROS were ascertained to play important multiple roles in tissue damage and loss of function of organs.⁸ These ROS including oxygen free radicals are causative factors in the etiology of degenerative disorders including some hepatopathies and other serious organ damage.⁹ The damage produced by the interaction of free radicals with cellular macromolecules results in cellular senescence and aging.¹⁰ The scavenging activity has been studied in the process of hydrogen atom transfer to the stable free radical DPPH to compare the activity of compounds under investigation with that of widely known antioxidant parameter.¹¹ The investigation of DPPH radical scavenging activity revealed that compounds with electron withdrawing substituents such as Br and Cl displayed very good antioxidant activity.¹² In general, it was observed that halo substituted and unsubstituted compounds exhibited greater activity when compared to nitro substituted compounds.¹³ Nitrogen-containing benzophenone analogs were synthesized and evaluated for inhibition of TNF- α and IL-6 along with good antioxidant activity.¹⁴ Benzophenone derivatives displayed a potent free radical scavenging activity and were able to efficiently protect cells against oxidative stress provoked by tert-butylhydroperoxide.^{15,16} By these

Abbreviations: ROS, reactive oxygen species; DPPH, 1,1-diphenylpicrylhydrazyl; NO, nitric oxide; H₂O₂, hydrogen peroxide; nm, nanometer; mp, melting point; Calcd, calculated.

* Corresponding author. Tel.: +91 99018 88755; fax: +91 821 2419239.

E-mail address: shaukathara@yahoo.co.in (S.A. Khanum).

literature background we provoked and planned to synthesis these new series of compounds (**6a–k**) and screened for the antioxidant activity.

2. Materials and methods

2.1. Chemistry

Chemicals were purchased from Sigma Aldrich Chemical Co. TLC was performed on aluminum-backed silica plates and visualized by UV-light. Melting points were determined on a Thomas Hoover capillary melting point apparatus with a digital thermometer. IR spectra were recorded on FT-IR Shimadzu 8300 spectrophotometer, ¹H NMR spectra were recorded on a Bruker 400 MHz NMR spectrophotometer in DMSO-d₆ and the chemical shifts were recorded in parts per million down field from tetramethylsilane. Mass spectra were obtained with a VG70-70H spectrophotometer and important fragments are given with the relative intensities in brackets. Results of elemental analysis are within 0.4% of the calculated value.

2.1.1. General procedure for the preparation of phenyl benzoates (**3a–k**)

Substituted benzoates (**3a–k**) were synthesized by benzylation of substituted phenols (**1a–b**) with corresponding benzoyl chlorides (**2a–g**, 1:1) using 10% sodium hydroxide solution. The reaction mass was stirred for 2–3 h at 0 °C. The reaction was monitored by TLC using 4:1 n-hexane: ethyl acetate solvent mixture. After completion of the reaction the oily product was extracted with ether layer. Ether layer was washed with 10% sodium hydroxide solution (3 × 50 ml) followed by water (3 × 30 ml) and then dried over anhydrous sodium sulfate and evaporated the solvent under pressure to afford desired compounds (**3a–k**). Compounds (**3b–k**) were synthesized analogously starting with (**1a–b**) and (**2b–f**) respectively. Compound **3a** is taken as a representative example to explain characterization data.

3a: Yield 90%. IR (Neat): 1715 cm⁻¹ (C=O). ¹H NMR (DMSO-d₆): δ 7.3–7.8 (m, 9H, Ar-H). LC–MS m/z 260.91 (M + 1). Anal. Calcd. for C₁₃H₉BrO₂: C, 59.22; H, 3.70. Found: C, 59.18; H, 3.76%.

2.1.2. General procedure for the preparation of 4-hydroxy benzophenones (**4a–k**)

Substituted 4-hydroxy-diarylmethanone commonly known as hydroxy benzophenones (**4a–k**) were synthesized by Fries rearrangement. Compounds (**3a–k**, 0.001 mol) were treated with anhydrous aluminum chloride (0.002 mol) as a catalyst at 150–170 °C under without solvent condition for about 2–3 h. Then the reaction mixture was cooled to room temperature and quenched with 6N HCl in the presence of ice water. The reaction mixture was stirred for about 2–3 h, filtered the solid and recrystallized it with methanol to obtain desired compounds (**4a–k**). Compounds (**4b–k**) were synthesized analogously starting with (**3b–k**) respectively. Compound **4a** is taken as a representative example to explain characterization data.

4a: Yield 72%. mp 125–128 °C. IR: (KBr, cm⁻¹) 1640 (C=O), 3510–3600 (O–H); ¹H NMR (DMSO-d₆): δ 6.71–7.80 (m, 8H, Ar-H), 4.50 (bs, 1H, –OH). LC–MS m/z 276.9 (M+1). Anal. Calcd. for C₁₃H₉BrO₂: C, 55.92; H, 3.70. Found: C, 56.18; H, 3.69%.

2.1.3. General procedure for the preparation of (4-benzoyl-2-bromo-phenoxy)-acetic acid ethyl ester (**5a–k**)

Compounds (**5a–k**) were obtained by refluxing a mixture of compounds (**4a–k**) (0.013 mol) and ethyl chloroacetate (0.026 mol) in dry acetone (50 ml) and anhydrous potassium carbonate (0.019 mol) for 8–9 h. The reaction mixture was cooled and solvent

was removed by distillation. The residual mass was triturated with cold water to remove potassium carbonate and extracted with ether (3 × 50 ml). The ether layer was washed with 10% sodium hydroxide solution (3 × 50 ml) followed by water (3 × 30 ml) and then dried over anhydrous sodium sulfate and evaporated to dryness to obtain crude solid, which, on recrystallization with ethanol afforded desired compounds (**5a–k**). Compounds (**5b–k**) were synthesized analogously starting with **5b–n**, respectively. Compound **5a** is taken as a representative example to explain characterization data.

5a: Yield 90%. mp 49–52 °C. IR (Nujol, cm⁻¹): 1664 (C=O), 1760 (ester, C=O). ¹H NMR (DMSO-d₆): δ 1.2 (t, 3H, CH₃ of ester), 4.1 (q, 2H, CH₂ of ester), 4.9 (s, 2H, OCH₂), 6.9–7.7 (m, 8H, Ar-H). LC–MS m/z 299 (M + 1). Anal. Calcd. For C₁₇H₁₅BrO₄: C, 56.47; H, 4.04. Found: C, 56.26; H, 4.12%.

2.1.4. General procedure for the preparation of (4-benzoyl-2-bromo-phenoxy)-acetic acid (**6a–k**)

Compounds (**5a–k**) (6.0 mmol) was dissolved in ethanol (15 ml) and treated with a solution of sodium hydroxide (15 mmol) in water (5 ml). The reaction mixture was refluxed for 5–6 h, cooled, and acidified with 1 N hydrochloric acid. The precipitate was filtered, washed with water and finally crystallized from methanol to afford desired compounds (**6a–k**) with good yield. Compounds (**6b–k**) were synthesized analogously starting with (**5b–n**) respectively. The characterization data of the compounds (**6a–k**).

6a: Yield 75%. mp 130–132 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 4.86 (s, 2H, OCH₂), 6.9–7.7 (m, 8H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 334.9 (M + 1). Anal. Calcd for C₁₅H₁₁BrO₄: C, 53.71; H, 3.30. Found: C, 53.68; H, 3.33.26%.

6b: Yield 70%. mp 125–128 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 2.34 (s, 3H, CH₃), 4.86 (s, 2H, OCH₂), 6.8–7.7 (m, 7H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 349 (M + 1). Anal. Calcd for C₁₆H₁₃BrO₄: C, 55.71; H, 3.30. Found: C, 55.68; H, 3.33.26%.

6c: Yield 73%. mp 160–162 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 4.86 (s, 2H, OCH₂), 6.7–7.7 (m, 7H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 370.9 (M + 1). Anal. Calcd for C₁₅H₁₀BrClO₄: C, 48.71; H, 2.30. Found: C, 48.68; H, 2.33.26%.

6d: Yield 78%. mp 178–180 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 4.86 (s, 2H, OCH₂), 6.7–7.8 (m, 7H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 412.9 (M+1). Anal. Calcd for C₁₅H₁₀Br₂O₄: C, 43.71; H, 2.30. Found: C, 43.68; H, 2.33.26%.

6e: Yield 75%. mp 210–212 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 4.88 (s, 2H, OCH₂), 6.9–7.7 (m, 7H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 353 (M + 1). Anal. Calcd for C₁₅H₁₀BrFO₄: C, 51.71; H, 2.30. Found: C, 51.68; H, 2.33.26%.

6f: Yield 80%. mp 121–125 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 2.34 (s, 6H, CH₃), 4.9 (s, 2H, OCH₂), 7.2–7.7 (m, 7H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 285.2 (M + 1). Anal. Calcd for C₁₇H₁₆O₄: C, 71.71; H, 5.30. Found: C, 71.68; H, 5.33.26%.

6g: Yield 85%. mp 178–180 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 2.34 (s, 9H, CH₃), 4.9 (s, 2H, OCH₂), 7.2–7.6 (m, 6H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 299 (M + 1). Anal. Calcd for C₁₈H₁₈O₄: C, 72.71; H, 6.30. Found: C, 72.68; H, 6.33.26%.

6h: Yield 88%. mp 165–169 °C. FT-IR (KBr, cm⁻¹): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ¹H NMR (DMSO): δ 2.34 (s, 6H, CH₃), 4.9 (s, 2H, OCH₂), 7.2–7.6 (m, 6H, Ar-H), 9.5 (s, 1H, COOH).

Table 1
In vitro antioxidant activity of compounds **6a–k** in DPPH method.

Compounds	Concentration ($\mu\text{g/ml}$)				
	25	50	75	100	IC ₅₀
6a	51.87 \pm 1.70	57.95 \pm 1.00	60.68 \pm 0.90	66.99 \pm 1.58	22.83 \pm 1.45
6b	68.77 \pm 1.04	70.79 \pm 0.85	75.95 \pm 1.30	80.58 \pm 1.03	17.89 \pm 1.05
6c	63.98 \pm 1.42	67.89 \pm 1.19	72.92 \pm 1.54	76.78 \pm 0.93	18.68 \pm 1.11
6d	58.98 \pm 1.15	63.85 \pm 1.22	67.89 \pm 0.86	71.86 \pm 0.93	19.99 \pm 0.76
6e	67.95 \pm 1.24	71.97 \pm 1.39	73.81 \pm 1.56	78.67 \pm 1.02	17.77 \pm 1.08
6f	75.85 \pm 0.26	78.85 \pm 0.47	82.92 \pm 0.59	84.89 \pm 0.76	15.78 \pm 0.26
6g	63.86 \pm 1.03	68.86 \pm 1.38	72.88 \pm 0.80	76.69 \pm 1.61	18.57 \pm 1.05
6h	72.94 \pm 0.17	76.78 \pm 0.43	78.95 \pm 0.44	82.79 \pm 0.68	15.67 \pm 0.58
6i	69.84 \pm 0.24	73.85 \pm 0.41	76.69 \pm 0.63	80.56 \pm 0.68	16.85 \pm 0.59
6j	62.56 \pm 0.69	66.74 \pm 1.30	70.69 \pm 1.27	75.77 \pm 1.32	18.78 \pm 1.21
6k	71.83 \pm 0.34	74.74 \pm 0.58	77.68 \pm 0.68	82.84 \pm 0.84	16.78 \pm 0.50
Ascorbic acid	81.98 \pm 0.11	82.99 \pm 0.37	84.88 \pm 0.43	86.79 \pm 0.52	14.98 \pm 0.43
Blank	–	–	–	–	–

(–) Showed no scavenging activity. Values were the means of three replicates \pm SD.

LC–MS m/z 319.1 ($M + 1$). Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{ClO}_4$: C, 64.71; H, 4.30. Found: C, 64.68; H, 4.33.26%.

6i: Yield 74%. mp 140–145 °C. FT-IR (KBr, cm^{-1}): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ^1H NMR (DMSO): δ 2.34 (s, 6H, CH_3), 4.86 (s, 2H, OCH_2), 7.2–7.7 (m, 6H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 363 ($M + 1$). Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{BrO}_4$: C, 56.71; H, 4.30. Found: C, 56.68; H, 4.33.26%.

6j: Yield 69%. mp 218–220 °C. FT-IR (KBr, cm^{-1}): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ^1H NMR (DMSO): δ 2.34 (s, 6H, CH_3), 4.86 (s, 2H, OCH_2), 7.2–7.7 (m, 6H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 303.1 ($M + 1$). Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{FO}_4$: C, 67.71; H, 6.30. Found: C, 67.68; H, 6.33.26%.

6k: Yield 75%. mp 201–204 °C. FT-IR (KBr, cm^{-1}): 1675 (C=O), 1730 (acid C=O), 3400–3500 (acid OH). ^1H NMR (DMSO): δ 2.34 (s, 6H, CH_3), 3.72 (s, 3H, OCH_3), 4.86 (s, 2H, OCH_2), 6.7–7.7 (m, 6H, Ar-H), 9.5 (s, 1H, COOH). LC–MS m/z 315.1 ($M + 1$). Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{O}_5$: C, 68.71; H, 5.30. Found: C, 68.61; H, 5.33.26%.

2.2. Pharmacological screening

2.2.1. Antioxidant screening (in vitro)

Compounds (**4a–k**) were tested for *in vitro* antioxidant property by 1,1-diphenylpicrylhydrazyl (DPPH),^{17,18} nitric oxide (NO)^{19,20} and hydrogen peroxide (H_2O_2)²¹ methods which were summarized in Tables 1–3 respectively.

2.2.2. DPPH radical scavenging activity

The hydrogen atom or electron donating ability of the compounds was measured from the bleaching of the purple colored

methanol solution of DPPH. The spectrophotometric assay uses the stable radical DPPH as a reagent. 1 ml of various concentrations of the test compounds (25, 50, 75, 100 and 100 $\mu\text{g/ml}$) in methanol was added to 4 ml of 0.004% (w/v) methanol solution of DPPH. After a 30 min incubation period at room temperature, the absorbance was read against blank at 517 nm. The percent of inhibition (I%) of free radical production from DPPH was calculated by the following equation

$$\% \text{ of scavenging} = \left[\frac{(A_{\text{control}} - A_{\text{sample}})}{A_{\text{blank}}} \right] \times 100 \quad (1)$$

where A_{control} is the absorbance of the control reaction (containing all reagents except the test compound) and A_{sample} is the absorbance of the test compound. Tests were carried at in triplicate.

2.2.3. Nitric oxide (NO) scavenging activity

Nitric oxide scavenging activity was measured by slightly modified methods of Green et al and Marocci et al Nitric oxide radicals (NO) were generated from sodium nitroprusside. 1 ml of sodium nitroprusside (10 mM) and 1.5 ml of phosphate buffer saline (0.2 M, pH 7.4) were added to different concentrations (25, 50, 75 and 100 $\mu\text{g/ml}$) of the test compounds and incubated for 150 min at 25 °C and 1 ml of the reaction mixture was treated with 1 ml of Griess reagent (1% sulfanilamide, 2% H_3PO_4 and 0.1% naphthylethylenediamine dihydrochloride). The absorbance of the chromophore was measured at 546 nm. Nitric oxide scavenging activity was calculated using Eq. (1).

Table 2
The *in vitro* antioxidant activity of compounds **6a–k** in nitric oxide (NO) method.

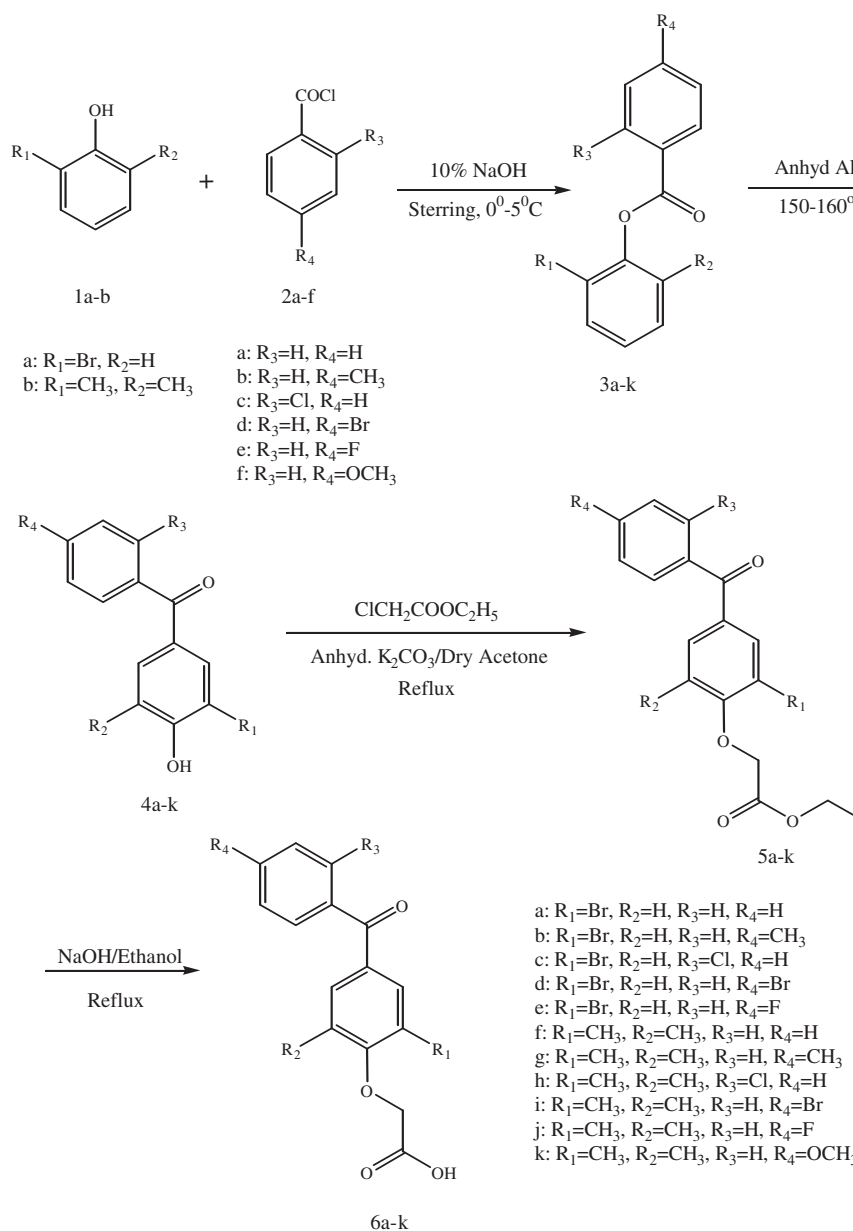
Compounds	Concentration ($\mu\text{g/ml}$)				
	25	50	75	100	IC ₅₀
6a	59.67 \pm 1.50	62.78 \pm 1.19	66.83 \pm 1.29	71.56 \pm 0.69	19.97 \pm 0.92
6b	70.98 \pm 0.86	73.69 \pm 1.05	76.79 \pm 1.39	81.64 \pm 1.25	16.86 \pm 0.93
6c	67.96 \pm 0.88	69.89 \pm 1.37	73.95 \pm 0.93	78.96 \pm 1.19	17.89 \pm 1.03
6d	61.79 \pm 1.39	65.74 \pm 1.54	69.46 \pm 0.76	72.25 \pm 1.05	19.68 \pm 0.95
6e	71.48 \pm 0.83	73.78 \pm 0.92	77.82 \pm 1.04	81.96 \pm 1.39	16.88 \pm 0.54
6f	77.58 \pm 0.26	82.84 \pm 0.45	83.73 \pm 0.59	85.79 \pm 0.78	14.62 \pm 0.75
6g	62.83 \pm 1.30	70.84 \pm 1.22	75.79 \pm 1.02	77.41 \pm 0.77	18.72 \pm 1.10
6h	74.75 \pm 0.24	78.92 \pm 0.35	81.71 \pm 0.55	84.82 \pm 0.70	15.86 \pm 0.54
6i	70.63 \pm 0.15	75.82 \pm 0.33	78.93 \pm 0.52	82.85 \pm 0.67	16.84 \pm 0.90
6j	63.85 \pm 1.16	68.95 \pm 1.55	73.82 \pm 1.39	78.92 \pm 0.69	18.77 \pm 1.21
6k	72.86 \pm 0.24	77.83 \pm 0.43	81.79 \pm 0.60	83.68 \pm 0.77	16.67 \pm 0.89
Ascorbic acid	83.63 \pm 0.17	84.65 \pm 0.35	87.54 \pm 0.51	89.97 \pm 0.68	13.97 \pm 0.54
Blank	–	–	–	–	–

(–) Showed no scavenging activity. Values were the means of three replicates \pm SD.

Table 3
The *in vitro* antioxidant activity of compounds **6a–k** in hydrogen peroxide (H₂O₂) method.

Compounds	Concentration (μg/ml)				
	25	50	75	100	IC ₅₀
6a	50.84 ± 1.14	53.78 ± 0.84	57.83 ± 0.95	62.91 ± 0.61	23.79 ± 1.02
6b	60.63 ± 0.84	62.61 ± 1.56	67.83 ± 1.05	70.84 ± 1.35	19.67 ± 1.21
6c	57.59 ± 1.10	61.69 ± 1.15	64.47 ± 1.45	68.63 ± 1.53	20.86 ± 1.05
6d	52.88 ± 0.87	55.76 ± 1.37	58.74 ± 0.76	63.69 ± 1.03	22.79 ± 0.40
6e	59.76 ± 1.04	62.69 ± 1.25	66.73 ± 1.55	69.48 ± 0.81	19.97 ± 0.50
6f	67.84 ± 0.26	70.58 ± 0.43	73.76 ± 0.59	78.74 ± 0.80	17.69 ± 0.93
6g	53.66 ± 1.17	57.73 ± 0.86	61.81 ± 1.47	65.73 ± 0.80	21.65 ± 0.67
6h	62.63 ± 0.28	64.84 ± 0.44	67.52 ± 0.63	71.74 ± 0.76	18.93 ± 1.24
6i	63.83 ± 0.25	66.76 ± 0.62	68.68 ± 0.67	71.75 ± 0.78	18.94 ± 0.24
6j	60.76 ± 1.30	63.83 ± 1.16	67.84 ± 1.05	70.66 ± 1.55	19.76 ± 0.76
6k	65.84 ± 1.10	68.68 ± 1.29	70.88 ± 0.58	73.85 ± 0.69	17.64 ± 0.58
Ascorbic acid	75.96 ± 0.17	77.75 ± 0.32	81.48 ± 0.60	85.62 ± 0.70	15.73 ± 0.25
Blank	–	–	–	–	–

(–) Showed no scavenging activity. Values were the means of three replicates ± SD.



Scheme 1. Synthesis of (4-benzoyl-phenoxy)-acetic acid derivatives (**6a–k**).

2.2.4. Hydrogen peroxide (H₂O₂) scavenging activity

The H₂O₂ scavenging activity of the test compound was determined according to the method of Ruch et al. A solution of H₂O₂ (40 μM) was prepared in phosphate buffer (pH 7.4). 25, 50, 75 and 100 μg/ml concentrations of the test compounds in 3.4 ml phosphate buffer were added to H₂O₂ solution (0.6 ml, 40 μM). The absorbance value of the reaction mixture was recorded at 230 nm. The percentage of scavenging activity of H₂O₂ was calculated using Eq. (1).

3. Result and discussion

Series of (4-benzoyl-2-methyl-phenyl)-acetic acid derivatives (**6a–k**) were prepared by reported procedure²² with different substituents in good yields. Compounds (**4a–k**) were tested for *in vitro* antioxidant property by DPPH^{16,17}, NO^{18,19} and H₂O₂²⁰ methods which were summarized in Tables 1–3 respectively. Compounds **6h** with chloro substituent at benzoyl ring and **6f** with no substituent at benzoyl ring showed good radical scavenging activity in all three methods compared to the standard drug ascorbic acid. Whereas compound **6k** with methoxy substituent in benzoyl ring showed good antioxidant activity only in H₂O₂ method. Whereas the one more compound **6i** with bromo substituent displayed moderate activity in all the three methods. The IC₅₀ value of the standard ascorbic acid was found to be 14.98 ± 0.43, 13.97 ± 0.54 and 15.73 ± 0.25 in DPPH, NO and H₂O₂ methods respectively, whereas the IC₅₀ values of the compounds **6f** and **6h** were found to be 15.78 ± 0.26 and 15.67 ± 0.58 in DPPH, 14.62 ± 0.75 and 15.86 ± 0.54 in NO and 17.69 ± 0.93 and 18.93 ± 1.24 in H₂O₂. IC₅₀ value for compound **6k** is 17.64 ± 0.58. Further Tables 1–3 indicate that remaining compounds showed moderate to mild radical scavenging activity in DPPH, NO and H₂O₂ methods.

4. Conclusion

In conclusion, a new series of (4-benzoyl-phenyl)-acetic acid derivatives (**6a–k**) were prepared by reported procedure²¹ with different substituents in good yields and studied for their antioxidant activity. It was observed that halo substituted and unsubstituted compounds **6f**, **6h** and **6k** exhibited greater activity in which same conclusion was expressed by (Kotaiah et al, 2012) for pyrimidine and oxadiazole derivatives. Compound **6i** displayed

moderately good activity for the same reason. The investigation of antioxidant screening data reveals that among all the compounds screened, compounds **6f**, **6h** and **6i** showed excellent, almost equivalent to that of standard and the remaining compounds showed moderate to mild scavenging activity. Scheme 1

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