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Three component one pot synthesis of 5-Substituted 1-Aryl-2,3-diphenyl imidazoles: A novel class of promising antioxidants

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ABSTRACT

A novel series of structurally diverse 5-Substituted 1-Aryl-2,3-diphenyl imidazoles (**2a-j**) was synthesized by treatment of benzoin (**1**) with 4-hydroxy aniline, substituted benzaldehydes and NH_4OAc in polyethylene glycol (PEG-400) under reflux condition in excellent yields. The newly synthesized compounds were characterized by spectral and elemental analysis and screened for their antioxidant properties by employing three *in vitro* assays like 2,2–diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid (ABTS) assay and iron reducing power assay. Ascorbic acid was used as a standard antioxidant and the comparative study with newly synthesized compounds was also done. Among the analogues compounds **2e, 2g** and **2j** bearing hydroxy and methoxy groups on 2-substituted phenyl moiety respectively showed predominant antioxidant activity.

INTRODUCTION

The free radicals are by products of various endogeneous processes that can be stimulated by external factors such as irradiation and xenobiotics (Halliwell *et al.,* 1989). Reactive oxygen species (ROS), including superoxide anion, hydrogen peroxide and hydroxyl radical, are thought to be generated subsequent to the reduction of molecular oxygen in aerobic organisms (Mccord *et al.,* 1985; Clark *et al.,* 1987). They play a crucial role in cellular metabolism and mediate critical biochemical reactions and physiologic effects (Poli *et al.,* 2004). ROS are specific signaling molecules implicated in both physiological and pathophysiological conditions (Zhou *et al.,* 1991). Antioxidants have been widely used as food additives to provide protection against oxidative degradation of foods. They may play an important contributory role in the treatment of many degenerative or chronic diseases, such as atherosclerosis, brain dysfunction, immune system decline and cancer, since considerable experimental evidence, links the production of reactive oxygen species to the initiation and/or progression of those pathologies (Halliwell *et al.,* 1991; Rice-Evans *et al.,* 1993; Behl *et al.,* 1997). Imidazole is the aromatic heterocyclic compound, this ring system is present in important biological building blocks, such as histidine and the related hormone histamine. Imidazole can serve as a base and as a weak acid. Many drugs contain an imidazole ring, such as antifungal drugs (Katritzky *et al.,* 1984; Pozharskii *et al.,* 1997; Gilchrist *et al.,* 1985). Moreover 2-substituted imidazolines are synthetically important due to their use as a synthetic intermediates (Rondu *et al.,* 1997), catalysts (Bousquet *et al.,* 1999), chiral auxiliaries (Ueno *et al.,* 1995), chiral catalysts (Hayashi *et al.,* 1996) in various synthetic reactions. It is also called an important synthon for the preparation of biologically active compounds (Corey *et al.,* 1999). In recent years, the high therapeutic properties of the imidazole related drugs have been attracting the attention of medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Medicinal properties of imidazole containing compounds include anticancer (Davood *et al.,*2008), antimicrobial (Congio *et al.,* 2008), antibacterial (Aridoss *et al.,* 2006), antifungal (Bhandari *et al.,* 2009), and antioxidant activity (Emami *et al.,* 2008).

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Encouraged by these observations and in continuation of our research work to discover new biologically active heterocyclic compounds (Kumar *et al.,* 2010; Kumar *et al.,* 2011; Naik *et al.,* 2011; Rangaswamy *et al.,* 2012), we synthesized a new series of heterocyclic imidazoles, by facile and routine methods, with the hope to get better antioxidant agents.

MATERIALS AND METHODS

Chemistry

All reagents and solvents were purchased from Merck (Darmstadt, Germany) chemical AR grade and were used as provided. DPPH was purchased from Sigma-Aldrich chemical Co. (St. Louis, MO, USA). TLC analysis was performed on alumina sheets precoated with silica gel 60F-254 and SiO_2, 200-400 mesh (Merck) was used for column chromatography. ^{1}H NMR (300 MHz) was obtained AC Bruker spectrometer in the appropriate (DMSO-d_6) solvent.

Melting points were obtained on a reichert thermopan melting point apparatus, equipped with a microscope and are uncorrected. Mass spectra were obtained by Water-Q-TOF ultima spectrometer. Micro analytical data were obtained by elemental-Vario EL-III.

Procedure for synthesis of benzoin (1)

The mixture of benzaldehyde (2 mmol) and potassium cyanide (0.5 mmol) in methanol (10 ml) was taken in round-bottomed flask fitted with reflux condenser. The mixture was refluxed for 20 min. In the course of about twenty minutes, crystals begin to separate from the hot solution. At the end of the thirty minutes, the solution was cooled, filtered with suction, and washed with water. The obtained crude benzoin was recrystallized from alcohol.

General procedure for the synthesis of 5-Substituted 1-Aryl-2,3-diphenyl imidazoles (2a-j).

A mixture of benzoin (2 mmol), substituted benzaldehydes (2 mmol), 4-hydroxy aniline (2 mmol), NH_4OAc (2 mmol) and PEG (5 mL) was taken in RB flask containing tetrahydrofuran (THF) (10 ml) as solvent, the mixture was refluxed for 6 hrs. The reaction was monitored by thin-layer chromatography (TLC) using hexane:ethylacetate (8:2) as mobile phase, after completion of the reaction, water (10 ml) was added and the mixture was extracted with ethyl acetate (3x10). The extract was dried over anhydrous Na_2SO_4 and concentrated in rotary evaporator, residue was purified by column chromatography to obtain pure 5-substituted 1-aryl-2,3-diphenyl imidazoles **(2a-j)**.

4-(2,4,5-triphenyl-1H-imidazol-1-yl)phenol (2a).

Dark reddish brown solid, IR (KBr)λmax(cm^{-1}): 3154-2915 (Ar-H), 3501 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.95-8.31 (m, 19H, Ar-H), 5.36 (s, 1H, OH); Mass (m/z%): M^+ 388.16; Anal.calcd. for $C_{27}H_{20}N_{2O}$: C, 83.48; H, 5.19; N, 7.21; O, 4.12; Found: C, 83.49; H, 5.21; N, 7.25; O, 4.09%

4-(2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazol-1-yl)phenol (2b).

Reddish brown solid, IR (KBr)λmax(cm^{-1}): 3133.06-2917 (Ar-H), 3495 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 7.42-8.12 (m, 18H, Ar-H), 5.35 (s, 1H, OH); Mass (m/z%): M^+ 422.12; Anal.calcd. for $C_{27}H_{19}ClN_2O$: C, 76.68; H, 4.53; Cl, 8.38; N, 6.62; O, 3.78; Found: C, 76.65; H, 4.55; Cl, 8.40; N, 6.58; O, 3.75%

4-(2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)phenol (2c).

Light yellow solid, IR (KBr)λmax(cm^{-1}): 3123-2919 (Ar-H), 3492 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.95-7.97 (m, 18H, Ar-H), 5.34 (s, 1H, OH), 3.62 (s, 3H, OCH_3); Mass (m/z%): M^+ 418.17; Anal.calcd. for $C_{28}H_{22}N_2O_2$: C, 80.36; H, 5.30; N, 6.69; O, 7.65; Found: C, 80.34; H, 5.28; N, 6.71; O, 7.62%

2-(1-(4-hydroxyphenyl)-4,5-diphenyl-1H-imidazol-2-yl)phenol (2d).

Yellow solid, IR (KBr)λmax(cm^{-1}): 3146-2936 (Ar-H), 3495 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.95-7.79 (m, 18H, Ar-H), 5.34 (s, 2H, OH); Mass (m/z,%): M^+ 404.15; Anal. calcd. for $C_{27}H_{20}N_2O_2$: C, 80.18; H, 4.98; N, 6.93; O, 7.91; Found: C, 80.16; H, 5.10; N, 6.90; O, 7.88%

4,4'-(4,5-diphenyl-1H-imidazole-1,2-diyl)diphenol (2e).

Red solid, IR (KBr)λmax(cm^{-1}): 3122-2925 (Ar-H), 3498 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.95-7.78 (m, 18H, Ar-H), 5.36 (s, 2H, OH); Mass (m/z%): M^+ 404.15; Anal. calcd. for $C_{27}H_{20}N_2O_2$: C, 80.18; H, 4.98; N, 6.93; O, 7.91; Found: C, 80.22; H, 4.88; N, 6.95; O, 7.89%

4-(2-(4-nitrophenyl)-4,5-diphenyl-1H-imidazol-1 -yl)phenol (2f).

Reddish brown solid, IR(KBr)λmax(cm^{-1}): 3108-2913 (Ar-H), 3496 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.70-7.27 (m, 18H, Ar-H), 5.32 (s, 1H, OH); Mass (m/z%): M^+ 433.14; Anal.calcd. for $C_{27}H_{19}N_3O_3$: C, 74.81; H, 4.42; N, 9.69; O, 11.07; Found: C, 74.79; H, 4.45; N, 9.71; O, 11.13%

4- (2- (3, 4 -dimethoxyphenyl) -4,5-diphenyl -1H-imidazol-1-yl)phenol (2g).

Reddish brown solid, IR (KBr)λmax(cm^{-1}): 3119-2936 (Ar-H), 3499 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.98-7.97 (m, 17H, Ar-H), 5.35 (s, 1H,OH), 3.83 (s, 6H, OCH_3); Mass (m/z%): M^+ 448.18; Anal.calcd. for $C_{29}H_{24}N_2O_3$: C, 77.66; H, 5.39; N, 6.25; O, 10.70; Found: C, C, 77.68; H, 5.35; N, 6.26; O, 10.68%

4-(4,5-diphenyl-2-(3,4,5-trimethoxyphenyl)-1H-imidazol-1-yl)phenol (2h).

Yellow semi solid, IR (KBr)λmax(cm^{-1}): 3128-2916 (Ar-H), 3500 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.87-8.59 (m, 16H, Ar-H), 5.35 (s, 1H, OH), 3.83 (s, 9H, OCH_3); Mass

(m/z%): M^+ 478.19; Anal.calcd. for $C_{30}H_{26}N_2O_4$: C, 75.28; H, 5.50; N, 5.86; O, 13.39; Found: C, 75.31; H, 5.45; N, 5.86; O, 13.38%.

4-(4,5-diphenyl-2-p-tolyl-1H-imidazol-1-yl)phenol (2i).

Reddish brown solid, IR(KBr)λmax(cm^{-1}): 3124-2917 (Ar-H), 3497 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.70-8.27 (m, 18H, Ar-H), 5.35 (s, 1H, OH), 2.32 (s, 3H, CH_3); Mass (m/z%): M^+ 402.17; Anal.calcd. for $C_{28}H_{22}N_2O$: C, 83.56; H, 5.51; N, 6.96; O, 3.98; Found: C, 83.53; H, 5.49; N, 6.92; O, 3.91%

4- (1- (4- hydroxyphenyl) -4, 5-diphenyl-1H-imidazol-2-yl)-2-methoxyphenol (2j).

Light brown solid, IR (KBr)λmax(cm^{-1}): 3112.06-2917 (Ar-H), 3498 (OH); ^{1}H NMR (300 MHz) ($CDCl_3$) δ (ppm): 6.98-7.97 (m, 17H, Ar-H), 3.83 (s, 3H, OCH_3), 5.35 (s, 2H, OH); Mass (m/z%): M^+ 434.16; Anal.calcd. for $C_{28}H_{22}N_2O_3$: C, 77.40; H, 5.10; N, 6.45; O, 11.05; Found: C, 77.39; H, 5.12; N, 6.42; O, 11.01%

Antioxidant activity

DPPH free radical scavenging assay

The evaluation of antioxidant activity of newly synthesized compounds **(2a-j)** was done by DPPH radical scavenging assay (Blois *et al.*, 1958). Internal standard Ascorbic acid and the synthesized compounds of different concentrations were prepared in distilled ethanol, 1 mL of each compound solutions having different concentrations (10 µM, 25 µM, 50 µm, 100 µM, 200 µM and 500 µM) were taken in different test tubes. 4 mL of 0.1 mM ethanol solution of DPPH was added and shaken vigorously.

The tubes were then incubated in the dark room at RT for 20 min. A DPPH blank was prepared without compound, and ethanol was used for the baseline correction. Changes (decrease) in the absorbance at 517 nm were measured using a UV-visible spectrophotometer and the remaining DPPH was calculated. The percent decrease in the absorbance was recorded for each concentration, and percent quenching of DPPH was calculated on the basis of the observed decreased in absorbance of the radical. The radical scavenging activity was expressed as the inhibition percentage and was calculated using the formula:

Radical scavenging activity (%) = $[(A_o-A_1)/A_o \times 100]$

Where A_o is the absorbance of the control (blank, without compound) and A_1 is the absorbance of the compound.

$ABTS^{\cdot+}$ radical scavenging assay

The ability of the test sample to scavenge $ABTS^{\cdot+}$ radical cation was determined according to the literature method (Re *et al.*, 1999). The $ABTS^{\cdot+}$ radical cation was pregenerated by mixing 7 mM $ABTS^{\cdot+}$ stock solution with 2.45 mM potassium persulfate (final concentration) and incubating for 12–16 hrs in the dark at room temperature until the reaction was complete and the absorbance was stable. The absorbance of the $ABTS^{\cdot+}$ solution was equilibrated to 0.70 (± 0.02) by diluting with water at room temperature, then 1 mL was mixed with different concentration of the test sample (10–500 µM) and the absorbance was measured at 734 nm after 6 min. The scavenging capability of $ABTS^{\cdot+}$ radical was calculated using the following equation:.

$ABTS^{\cdot+}$ scavenging effect (%) = $[(A_c-A_s)/A_c] \times 100$

Where, A_c is the initial concentration of the $ABTS^{\cdot+}$ and A_s is the absorbance of the remaining concentration of $ABTS^{\cdot+}$ in the presence of compounds.

Reducing power assay (Iron reducing activity)

The reducing power of synthesized compounds **(2a-j)** was determined according to the method of Oyaizu (Oyaizu *et al.*, 1986). The compounds having different concentration were mixed with 2.5 mL of phosphate buffer (0.2 M, pH 6.6) and 2.5 mL of 1% potassium ferri cyanide, and then incubated at 50 ^oC for 20 min. To this mixture 2.5 mL of 10% trichloroacetic acid was added and the mixture was centrifuged at 3000 rpm for 20 min. The upper layer (2.5 mL) was mixed with 2.5 mL of distilled water and 0.5 mL of 0.1% ferric chloride and the absorbance was taken at 700 nm. Increased absorbance of the reaction mixture indicates an increased reducing power.

Statistical analysis

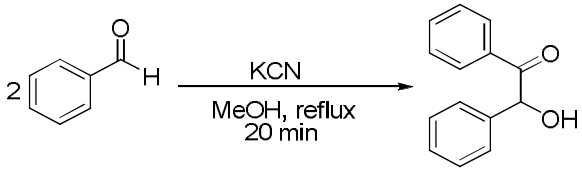
Assays were carried out in triplicate for 3-5 separate experiments. The amount of compound needed to inhibit DPPH free radicals and ABTS free radical concentration by 50% (IC_{50}) was graphically estimated using a linear regression algorithm.

RESULT AND DISCUSSION

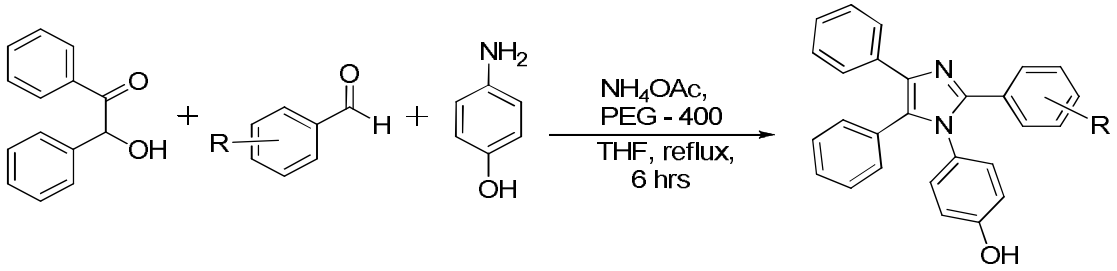
Chemistry

In this communication, the starting molecule benzoin (**1**) was synthesized by known method **(Scheme 1)** with slight modification (Wohler *et al.*, 1832; Arnold *et al.*, 1936). Further, reaction of 4-hydroxy aniline and substituted benzaldehydes with model compound benzoin **(1)** in the presence of ammonium acetate to accomplished 5-Substituted 1-Aryl-2,3-diphenyl imidazoles **(2a-j) Scheme 2** (Biswanath *et al.*, 2010). The mechanism involves initially, benzoin heated alone under reflux in PEG, benzoin was converted to benzyl within a few minutes. Aerial oxygen acts as the oxidant as the present conversion could not proceed in the absence of air (**Scheme 3 Step 1**). Further, condensation reaction between substituted benzaldehydes and 4-hydroxy aniline in the presence of ammonium acetate (NH_4OAc) afforded 4-(amino(phenyl)methylamino)phenol. Further scaffold 4-(amino(phenyl)methylamino)phenol cyclization with benzoin furnished 5-Substituted 1-Aryl-2,3-diphenyl Imidazoles **(Scheme 3 Step 2)**. The synthesized compounds was characterized by various physico-chemical and spectroscopic techniques. IR spectrum reveals that the absence of benzoin OH stretching at 3200-3389 cm^{-1} and also the presence of C-N amine stretching at 1340-1020 cm^{-1} and also all the target analogues revealed the

presence of aromatic peaks (Ar-H) at the respective region 3154-2913 cm^{-1} stretch confirm the formation of a 2-hydroxy-1,2-di(phenyl)ethanone into imidazole derivatives. ^1H NMR spectra of all conjugated analogues **(2a-j)** showed the signal due to phenolic OH appeared as singlet at about 5.32-5.36 ppm and methoxy protons present in the compound resonated as singlet at 3.62-3.83 ppm, other aromatic protons were observed at expected regions 6.70-8.59 ppm.

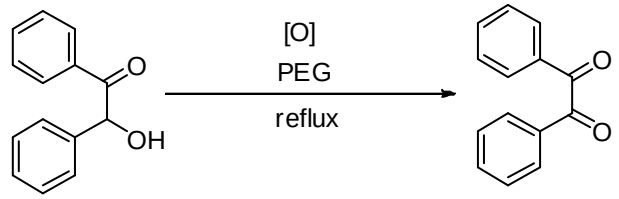


Scheme 1. Synthesis of benzoin **(1)**

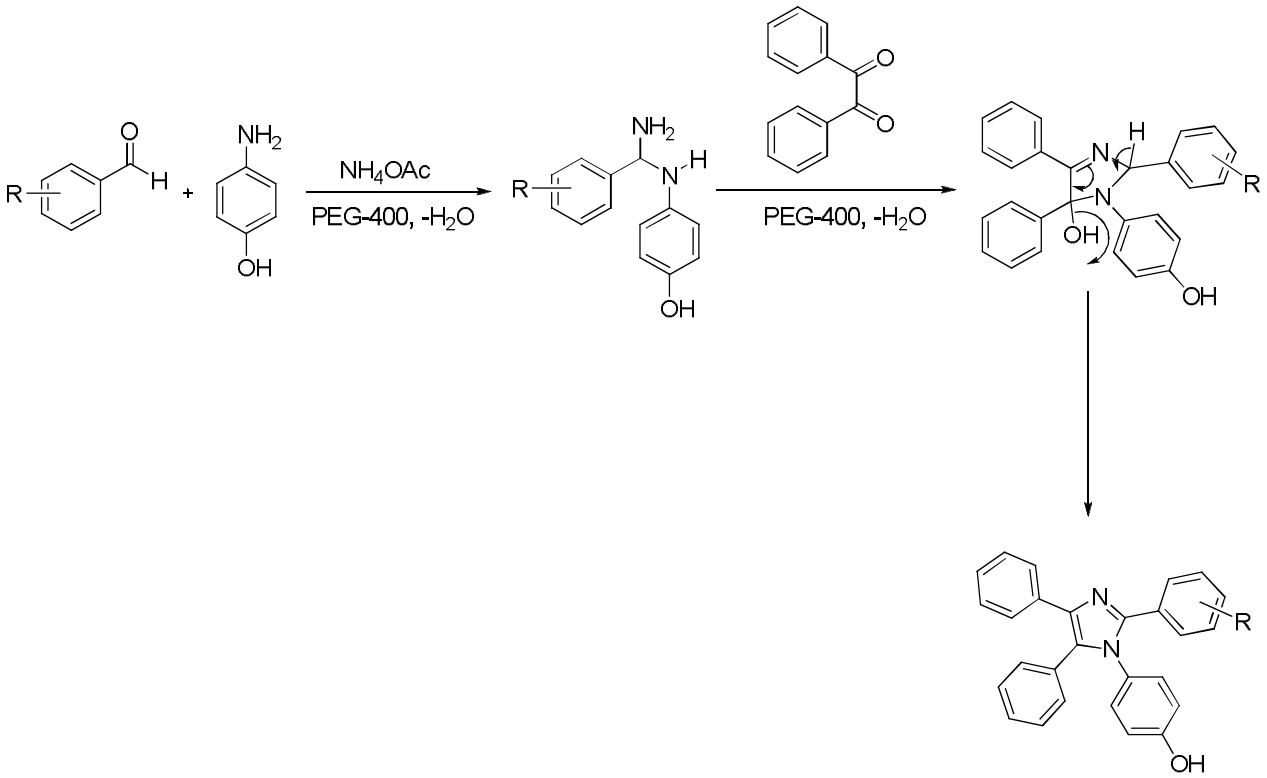


(1) **(2a-j)**

Scheme 2. Reaction protocol for the synthesis of 5-substituted 1-aryl 2,3-diphenyl imidazoles **(2a-j)**



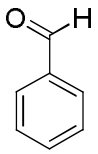
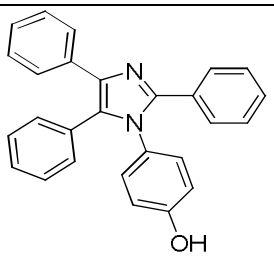
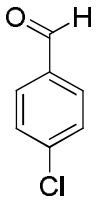
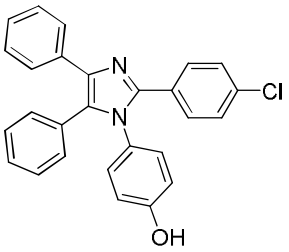
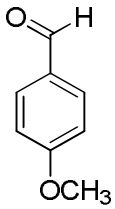
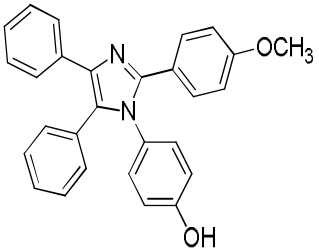
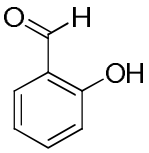
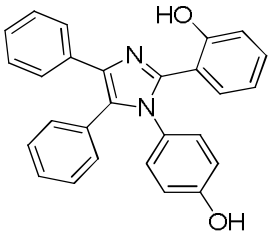
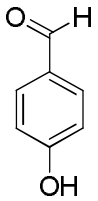
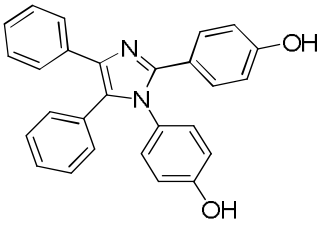
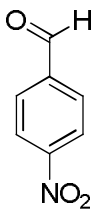
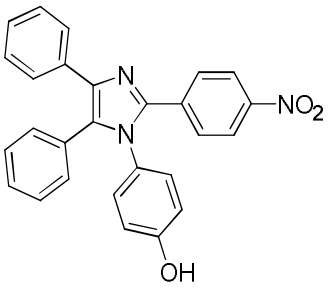
Step 1

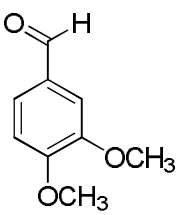
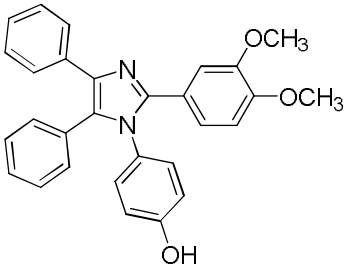
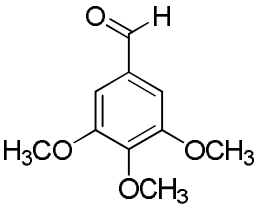
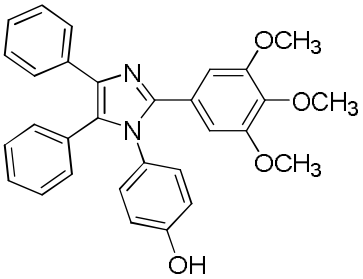
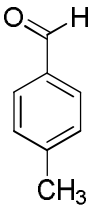
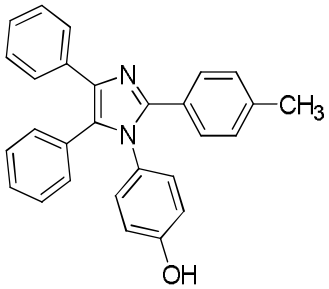
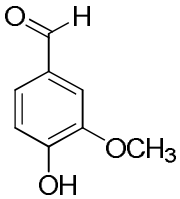
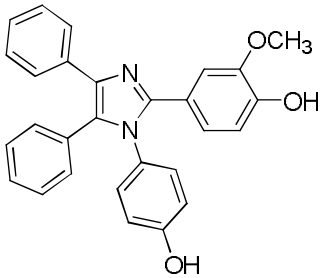


Step 2

Scheme 3. Mechanism involves in obtaining title compounds.

Table 1. Synthesis of 5-Substituted 1-Aryl-2,3-diphenyl Imidazoles **(2a-j)**

Compounds No.	Substituted aldehydes (R^1)	Products	Yield (%)	Melting Point (^oC)
2a			68.45	186-188
2b			72.30	127-129
2c			78.10	190-192
2d			85.20	165-167
2e			81.55	142-145
2f			79.32	175-177

2g			59.00	85-87
2h			72.45	Semisolid
2i			77.60	192-194
2j			81.40	188-190

In order to establish some structure-activity relationship based on position and presence of different substituents and to understand how it affects the antioxidant activity, present research was taken.

Antioxidant activity

DPPH radical scavenging assay

DPPH radical scavenging activity evaluation is a standard assay for the determination of antioxidant activity and offers a rapid technique for screening radical scavenging activity of specific compounds. It is very easy to operate, low cost effective, reproducible, less time consumable and can handle 20 samples at a time. A freshly prepared DPPH solution exhibits a deep purple color with an absorption maximum at 517 nm. When an antioxidant is present in the medium this molecule can quench DPPH free radical (i.e., by providing hydrogen atom or by electron donation, conceivable) and covert them to a colorless or bleached product 2,2'–diphenyl-1-picrylhydrazine or a substituted analogue of hydrazine, resulting in a decrease in absorbance hence more rapidly the absorbance decreases the more potent the antioxidant activity of compound. Percentage (%) activity of ethanolic solution of 5-Substituted 1-Aryl-2, 3-diphenyl Imidazoles **(2a-j)** were examined and compared with the internal standard Ascorbic acid (AA). IC_{50} for all the compounds were calculated and depicted in the **Table 2**. Initially, our model compound **(1)** showed less activity, further construction of imidazole cascade having different functionalities gives the significant change in the activity. All synthesized analogues showed moderate to excellent radical scavenging activity. Among

them compounds **2e**, **2g** and **2j** showed dominant DPPH activity compare to internal standard ascorbic acid (AA) due to the presence of more number of electron donating methoxy and hydroxy groups on 2-substituted phenyl ring at different positions. Compounds **2c** and **2d** having single methoxy and single hydroxy group on the 2,4 position of phenyl ring exhibited slightly less activity compared to standard. Whereas, compounds **2b**, **2f** bearing electron withdrawing chloro and nitro substituent and compound **2i** possessing methyl group does not favors for the enhanced activity. Compound **2h** gathering tri-methoxy group on 2-substituted phenyl ring at *para* and *meta* position displayed the considerable activity, this may be the steric hindrance between the methoxy group. Analogue **2a** doesn't have any substituents on 2-substituted phenyl ring showed less activity. The increasing order of DPPH activity of newly synthesized analogues as fallows,

2j> 2e>2g> BHA>2d>2c>2i>2f>2b>2h>2a>1.

ABTS$^{\cdot+}$ radical scavenging assay

ABTS (2,2'-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) to generate a radical cation, $ABTS^{\cdot+}$, that is green in color and can be measured by absorbance at 734 nm. Antioxidants suppress this reaction by electron donation and inhibit the formation of the colored ABTS radical. The concentration of antioxidant in the test sample is inversely proportional to the ABTS radical formation. In this assay, all the synthesized compounds displayed certain degree of $ABTS^{\cdot+}$ radical scavenging capacity. Compounds **2e, 2g** and **2j** bearing hydroxy and methoxy groups on 2-substituted phenyl skeleton exhibited dominant activity greater than the all synthesized compounds and as well as the standard **(Table 2)**.

On the other hand substitution of electron withdrawing group like Cl, NO_2 in compounds **2b** and **2f** does not affect appreciable changes in the activity. However, **2b** and **2f** possessing electron donating $-OCH_3$ and single hydroxy groups on 2-substituted phenyl core exhibited moderate ABTS radical inhibition capacity. Whereas remaining tetra-substituted imidazole analogues showed considerable activity.

Reducing power assay (Iron reducing activity)

The reducing capacity of compounds can be measured by the direct reduction of Fe^{3+} $(CN^-)_6$ to Fe^{2+} $(CN^-)_6$. The addition of free Fe^{3+} to the reduced product leads to the formation of the intense Perl's Prussian Blue complex, $Fe_4[Fe(CN^-)_6]_3$, which has a strong absorbance at 700 nm. An increase in absorbance of the reaction mixture would indicate an increase in the reducing capacity due to an increase in the formation of the complex. AA was used as standard and the absorbance values of all synthesized compounds are depicted in the **Table 3**.

Compounds **2b** and **2f** having electron withdrawing groups (Cl, NO_2) on the phenyl ring displayed less absorbance values indicated less activity, while for compounds **2e**, **2g** and **2j** possessing -OH and $-OCH_3$ group at *ortho*, *meta* and *para* position of 2-substituted phenyl ring enhance the absorbance value reflecting higher than the standard. The more number of methoxy groups containing compound **2h** and methyl group containing compound **2i** resulted lower ferric ion reducing power than standard. The results of the antioxidant assays revealed that majority of the synthesized compounds exerted a wide range of modest to good antioxidant activity. Interestingly, from all the three antioxidant assays we noted that presence of hydroxy and electron donating groups (EDG) substituents at different C-terminals of imidazole 2-substituted phenyl ring may favors for significant increase in the activity.

Table. 2: 50% Inhibition of DPPH radical and ABTS radical by compounds **(2a-j)**. Each value represents mean ± SD (n=3).

Compounds	IC_{50}(µM)/mL DPPH [a]	ABTS [b]
1	135±0.15	155±0.21
2a	90±0.23	112±0.45
2b	71±0.11	95±0.22
2c	20±0.65	25±0.23
2d	16±0.12	19±0.85
2e	10±0.36	12±0.12
2f	62±0.11	84±0.44
2g	11±0.21	15±0.10
2h	75±0.32	102±0.27
2i	30±0.25	38±0.55
2j	8±0.45	11±0.89
AA	12±0.12	16±0.01

[a] *IC_{50}= the concentration (µM/mL) exhibiting 50% inhibition of DPPH radical*
[b] *IC_{50}= the concentration (µM/mL) exhibiting 50% inhibition of ABTS radical.*

Table 3. Comparison of ferric ions (Fe^{3+}) reducing ability by Fe^{3+}-Fe^{2+} transformation methods of the compounds **(2a-j)** and the standard antioxidant such as AA at the concentration of 10 µM.

Tested compounds	Fe^{3+}-Fe^{2+} reducing ability
1	0.1120
2a	0.1835
2b	0.1968
2c	0.3095
2d	0.3210
2e	0.3490
2f	0.2154
2g	0.3524
2h	0.2766
2i	0.2983
2j	0.3678
AA	0.3415

CONCLUSION

In conclusion, we have synthesized a novel series of 5-Substituted 1-Aryl-2,3-diphenyl Imidazoles **(2a-j)** in good yields and evaluated their antioxidant activity. Interestingly, from all the antioxidant assays we noted that compounds possessed EDG (Electron donating group) hydroxy and methoxy substituents at different C-terminals to 2-substituted phenyl ring resulted a significant increase in the activity. Among the synthesized analogues, compounds **2e, 2g** and **2j** exhibits significant antioxidant potential. Whereas, compounds **2c** and **2d** displayed moderate antioxidant activity. This study extends the knowledge of different substituents at phenyl ring which might be of interest for the identification of novel class of antioxidants. Our investigation may be use full in the treatment of pathologies in which free radical oxidation plays a fundamental role.

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