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Chemical Papers 65 (4) 519–526 (2011)
DOI: 10.2478/s11696-011-0028-z

ORIGINAL PAPER

An efficient and novel one-pot synthesis of 2,4,5-triaryl-1*H*-imidazoles catalyzed by $UO_2(NO_3)_2 \cdot 6H_2O$ under heterogeneous conditions

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Received 15 November 2010; Revised 2 February 2011; Accepted 10 February 2011

An efficient, convenient, and novel one-pot method of 2,4,5-triaryl-1*H*-imidazoles synthesis using benzil, arene carbaldehydes, and ammonium acetate, catalyzed by uranyl nitrate hexahydrate [$UO_2(NO_3)_2 \cdot 6H_2O$] supported on acidic alumina and resulting in good to excellent yields under heterogeneous conditions, is reported. Formation of a reactants–catalyst complex was confirmed by UV-VIS spectral data. Antibacterial (MIC) and antioxidant activity of the synthesized compounds was also studied.

Keywords: 2,4,5-triaryl-1*H*-imidazoles, uranyl nitrate hexahydrate, heterogeneous system, antimicrobial activity, antioxidant activity

Introduction

Imidazole derivatives have been gaining increasing importance in medicinal chemistry and organic synthesis. Synthesis of the imidazole ring system and its derivatives occupies an important place in the realm of natural and synthetic organic chemistry because of their therapeutic and pharmacological activities (Bellina et al., 2007; Hofmann, 1953; Drabu et al., 2005); e.g. anti-HIV, anti-convulsant (Renukadevi et al., 1997), anti-fungal (Maier et al., 1989), calcium antagonist and as inhibitors of thromboxane A_2 synthase (Cozzi et al., 1993), antihistaminic (Mohan & Kumar, 2002), tranquillizing (Shealy et al., 1962), anti-parkinsonism (Meenakshi et al., 1990), anti-inflammatory (Lombardino & Wiseman, 1974; Nagalakshmi, 2008), and MAO inhibiting (Harfenist et al., 1978) activities. Therefore, preparation of imidazoles has attracted considerable attention of synthetic chemists in recent years. Consequently, several methods for the construction of imidazoles have been developed. Among these methods, one-pot reaction of diketones, aldehydes, and ammonium acetate is a typical procedure widely used for the synthesis of substituted triaryl imidazoles. Several procedures reported for the synthesis of triaryl-1*H*-imidazoles through condensation reactions in the presence of H_2SO_4 (Weinmann et al., 2002), HOAc (Sarshar et al., 1996), DMSO (Clark & Cawkill, 1975), organocatalysts in HOAc (Frantz et al., 2004), a variety of solid catalysts (Usyatinsky & Khmelnitsky, 2000; Xu et al., 2004; Sparks & Combs, 2004), protic or Lewis acids (Liu et al., 2003; Shaabani et al., 2007; Kidwai et al., 2007), ionic liquids (Heravi et al., 2007a, 2007b; Siddiqui et al., 2005; Xia & Lu, 2007), and different metal complexes (Heravi et al., 2007a, 2007b; Sangshetti et al., 2008; Wang et al., 2006; Shen et al., 2008; Khosropour, 2008) were examined under different reaction conditions for the synthesis of 2,4,5-triaryl-1*H*-imidazoles (Zhou et al., 2010). However, some of the synthesis protocols reported above suffer from one or more disadvantages, such as harsh reaction conditions, poor yields, prolonged reaction time, the use of expensive equipment, microwave or ultrasonic, and corrosive reagents. Thus, simple, efficient, and flexible protocols for the synthesis of 2,4,5-triaryl-1*H*-imidazoles have to be introduced.

In the present paper, catalytic efficacy of uranyl

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nitrate hexahydrate in one-pot, three component synthesis of 2,4,5-triaryl-1*H*-imidazoles with high yields is reported. The typical procedure includes the reaction between substituted aromatic aldehydes with benzil and ammonium acetate under heterogeneous conditions using catalytic amount of uranyl nitrate hexahydrate supported on acidic alumina, $UO_2(NO_3)_2 \cdot 6H_2O$ $/Al_2O_3$, and heating under reflux. Using UV-VIS absorption spectroscopy, complex formation between reactants and catalyst in the reaction mixture was confirmed. The in vitro antibacterial activities (MIC) of all synthesized compounds (*Ia–In*) were tested against standard pathological bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*) and subjected to antioxidant activity testing using the DPPH free radical scavenging method.

Experimental

All reagents were purchased from Aldrich (India), Hi Media (India), and Qualigens (India) and used without further purification. $UO_2(NO_3)_2 \cdot 6H_2O$ was purchased from LOBA Chemie (India) and used as received. IR spectra (in KBr pellets, in the range of 400–4000 cm^{-1}) were recorded at room temperature at the resolution of 4 cm^{-1}, using Avatar 330 spectrometer (Thermo Fisher Scientific) with a DTGS detector. ^1H (300 MHz for compounds *Ia*, *Ie–Ij*, *Il*, and 500 MHz for compounds *Ib–Id*, *Ik*, *Im*, *In*) and ^{13}C (125.75 MHz) NMR spectra were recorded on a Bruker AVANCE III instrument using approximately 0.03 M solutions in $CDCl_3$ and DMSO-d_6 with TMS as the internal reference at room temperature. Mass spectra were obtained using a JEOL GC MATE II HRMS (Spinco Biotech) (EI) and an ESI mass spectrometer (Thermo Finnigan). Electronic absorption spectra were measured using a HITACHI U-2800 model, double beam UV-VIS spectrophotometer in the region of 200–800 nm using ethanol as the solvent. Melting points were determined using open capillaries and are uncorrected.

General procedure for the synthesis of 2,4,5-triaryl-1H-imidazoles (Ia–In)

A mixture of uranyl nitrate hexahydrate (10 mole % per 0.05 g of Al_2O_3), ammonium acetate (4 mmol), and benzil (1 mmol) was dissolved in ethanol (20 mL) followed by the addition of an arene carbaldehyde (1.2 mmol). The reaction mixture was then stirred and heated under reflux until completed. Progress of the reaction was monitored by TLC. The mixture was then cooled to room temperature and poured into ice-water. The solid obtained was filtered and washed thoroughly with methanol to separate the product from Al_2O_3. The filtrate was evaporated under diminished pressure and the product was purified using HPLC to give corresponding 2,4,5-triaryl-1*H*-imidazole. The solid separated was filtered and dissolved in methanol to remove Al_2O_3. The separated solid was filtered and washed with methanol. The washed filtrate was dried to get the corresponding 2,4,5-triaryl-1*H*-imidazole.

Antibacterial activity screening

The in vitro antibacterial effect was tested against 24-h cultures of *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 25619, and *Staphylococcus aureus* ATCC 25923 at 2.0 mg mL^{-1}, 1.5 mg mL^{-1}, 1.0 mg mL^{-1}, 0.5 mg mL^{-1}, and 0.25 mg mL^{-1} concentrations, respectively, in the Mueller–Hinton agar medium by the agar well diffusion method. A stock solution (10 mg mL^{-1}) was prepared by dissolving the compounds in DMSO and the solutions were serially diluted in order to determine the MIC values. Bacterial strains employed in the study were obtained from the National Institute of Cholera and Enteric Diseases (NICED), Kolkata, India. The medium and Petri plates were sterilized by autoclaving at 120 °C (103.4 kPa). About 25 mL of the Mueller–Hinton agar medium were transferred aseptically into each sterilized Petri plate. The plates were left at room temperature to allow solidification. The prepared culture plates were inoculated with different selected strains of bacteria using the streak plate method. Wells were made on the agar surface with a 6 mm cork borer. The wells were filled with different concentrations of the test solutions using a micropipette and the plates were incubated for 24 h at (37 ± 1) °C. Antibacterial activity was determined by measuring the diameter of the area in which bacterial growth was inhibited around the well. Compounds showing antibacterial activity were subjected to the minimum inhibitory concentration (MIC) assay using the serial two-fold dilution method (Florey et al., 1989). MIC was interpreted as the lowest concentration of the sample at which there is no visible growth (turbidity) of microorganisms. Tetracycline was used as standard drug for comparison in the antibacterial studies. Furthermore, control experiments using DMSO were done for antibacterial activity studies.

Antioxidant activity screening

Free radical scavenging activity was determined using the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) according to a protocol given by Brand-Williams et al. (1995). In brief, a solution of each compound (500 μL) containing 0.1 mg of soluble solids per mL was added to a methanol solution of DPPH (0.1 mmol, 3 mL). After a 30 min incubation period at ambient temperature in dark, the absorbance was read at 517 nm. The controls contained all reaction reagents except the synthetic compound or positive control substance. The experiment was carried out in triplicate. The DPPH

Table 1. Synthesis of 2,4,5-triphenyl-1*H*-imidazole (*Ia*) using different catalyst load (CL), solvent, reaction time (t), and reaction conditions[a]

Entry	Catalyst	CL/mole %	Solvent	t/min	Yield[b]/%
1	No catalyst	–	Ethanol	600	5
2	$UO_2(NO_3)_2 \cdot 6H_2O$	5	Ethanol	120	68
3	$UO_2(NO_3)_2 \cdot 6H_2O$	10	Ethanol	90	79
4	$UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$[c]	10	Ethanol	30	93
5	$UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$[c]	10	Methanol	60	89
6	$UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$[c]	10	Dichloromethane	180	54
7	$UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$[c]	10	Acetonitrile	120	91
8	$Sr(NO_3)_2$	20	Ethanol	300	76
9	$Pb(NO_3)_2$	20	Ethanol	300	52
10	Al_2O_3	Excess	Dichloromethane	20[d]	78
11	CAN	5	Methanol	600[e]	75
12	$InCl_3 \cdot 3H_2O$	10	Methanol	498[e]	82

a) Reactants and conditions: benzil (1 mmol), benzaldehyde (1.2 mmol), NH_4OAc (4 mmol); heating under reflux for entries 1–9, MW for entry 10, room temperature for entries 11 and 12; *b*) isolated yield; *c*) 10 mole % of $UO_2(NO_3)_2 \cdot 6H_2O$ per 0.05 g of Al_2O_3; *d*) reported by Usyatinsky and Khmelnitsky (2000); *e*) reported by Sharma et al. (2008).

scavenging activity, expressed as the inhibition of free radical DPPH (I/%), was calculated according to Eq. (1) using optical density (OD) values (measured on the UV spectrophotometer) as described by Tepe et al. (2006).

$$\text{Inhibition (\%)} = [(\text{control OD} - \text{sample OD})/\text{control OD}] \times 100 \quad (1)$$

Results and discussion

To optimize the catalytic system, the synthesis of 2,4,5-triphenyl-1*H*-imidazoles (*Ia*) in the presence of $UO_2(NO_3)_2 \cdot 6H_2O$ was used as a model reaction. Unlike previously reported methods, the present method does not require any expensive reagents, equipments or extensive work-up procedures. The results shown in Table 1 clearly indicate the scope and generality of the reaction with respect to various catalytic systems. In comparison with other catalysts such as Al_2O_3, CAN, and $InCl_3 \cdot 3H_2O$ which have been recently reported in the synthesis of imidazoles, $UO_2(NO_3)_2 \cdot 6H_2O$ shows higher catalytic activity than the others in terms of the amount of catalyst, yield, and reaction time (Table 1). The efficacy of other catalysts such as $Sr(NO_3)_2$ and $Pb(NO_3)_2$ was also studied for this reaction. Yield of the one-pot synthesis of *Ia* using 20 mole % $Sr(NO_3)_2$ as the catalyst and ethanol at reflux temperature for 5 h was 76 %; in the presence of $Pb(NO_3)_2$ under the same conditions it was 52 %. It is notable that $Sr(NO_3)_2$ showed better catalytic efficacy in terms of *Ia* yield than $Pb(NO_3)_2$. Among these catalysts, $UO_2(NO_3)_2 \cdot 6H_2O$ was found to be the best one (Table 1) as 10 mole % of the catalyst were found to be sufficient to achieve the desired product in a good yield.

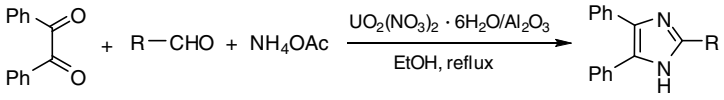
The effect of solvent was studied using ethanol, methanol, acetonitrile, and CH_2Cl_2. Results showed that the highest yields (93 %) were obtained using ethanol compared to 89 % in methanol, 91 % in acetonitrile, and 54 % in dichloromethane indicating that the reaction was markedly affected by the nature of the solvent. The best results were obtained applying stirring and heating under reflux for 30 min in the presence of catalytic amount of $UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$ in ethanol (Table 1). This optimal protocol was applied to a variety of arene carbaldehydes and the results are summarized in Table 2.

In all these cases, $UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$ catalyzed the condensation reaction proceeding smoothly and resulting in excellent yield of the corresponding products. The reaction was fairly general, clean, efficient, and easy to work-up. In this method, formation of 2,4,5-triaryl-1*H*-imidazoles proceeds well with substituted aromatic aldehydes without the need of any strong acid. Various substituted aromatic aldehydes with electron donating and electron withdrawing groups were used in the cyclocondensation forming 2,4,5-triaryl-1*H*-imidazoles in high yields. Various functional groups were found to be compatible with the reaction conditions.

Structures of new 2,4,5-triaryl-1*H*-imidazoles were characterized by their IR, ^{1}H NMR, ^{13}C NMR, and mass spectra (Table 3), whereas the known compounds were identified by comparing their spectroscopic data and melting points with reported literature values.

The following reaction mechanism was proposed for the $UO_2(NO_3)_2 \cdot 6H_2O$ catalyzed reaction of arene carbaldehyde, ammonium acetate, and benzil (Fig. 1). In the first step, the catalyst probably facilitates the formation of a diamine intermediate A by increasing the electrophilicity of the carbonyl group. The intermediate A, condenses with benzil in the presence of the catalyst to result in another intermediate B, which in turn rearranges to the trisubstituted imidazole by a [1,5]-hydrogen shift.

Table 2. Reaction times (t) and isolated yields of $UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$ catalyzed synthesis[a] of 2,4,5-triaryl-1*H*-imidazoles and some of their characteristics[b]



Compd.	R	t/min	Yield/%	Color	M.p./°C	R_t/min
Ia	Phenyl	30	93	pale yellow	274–276[c]	3.11
Ib	3-Bromophenyl	90	86	white	326–328[d]	3.39
Ic	3-Nitrophenyl	120	89	bright yellow	>360[e]	3.10
Id	3-Methylphenyl	90	87	white	296–298	3.23
Ie	4-Dimethylaminophenyl	60	92	yellow	262–264[f]	3.07
If	4-Ethylphenyl	60	91	white	240–242	3.26
Ig	4-Ethoxyphenyl	60	93	white	218–220	3.12
Ih	4-Methylphenyl	60	89	pale yellow	228–230[g]	3.18
Ii	3-Ethoxy-4-hydroxyphenyl	90	88	white	258–260	2.86
Ij	2,4-Dichlorophenyl	90	90	white	174–176[h]	3.18
Ik	3,4-Dimethoxyphenyl	120	92	white	220–222[i]	3.01
Il	Styryl	180	94	reddish brown	210–212[j]	3.21
Im	3-Pyridyl	180	86	white	244–246	3.02
In	2-Thienyl	180	96	white	260–262[k]	3.01

a) Reactants and conditions: benzil (1 mmol), aldehyde (1.2 mmol), NH_4OAc (4 mmol), 10 mole % of $UO_2(NO_3)_2 \cdot 6H_2O$ per 0.05 g of Al_2O_3; *b*) HPLC (MeOH): retention time (R_t); *c*) 276–278 °C reported by Shelke et al. (2009); *d*) 305–310 °C reported by Giordano and Belli (1975); *e*) >360 °C reported by Xia and Lu (2007); 316–318 °C reported by Song et al. (2010); *f*) 263–264 °C reported by Xia and Lu (2007); 259–260 °C reported by Zhou et al. (2010), 256–259 °C reported by Samai et al. (2009); *g*) 227–228 °C reported by Shen et al. (2008); *h*) 175–177 °C reported by Xia and Lu (2007), 177–178 °C reported by Song et al. (2010), 175–178 °C reported by Samai et al. (2009); *i*) 220–221 °C reported by Shelke et al. (2009), 214–215 °C reported by Li et al. (2010), 216–218 °C reported by Zhou et al. (2005); *j*) 216–217 °C reported by Blokhin et al. (1979); *k*) 260–262 °C reported by Shelke et al. (2009), 265–267 °C reported by Li et al. (2010), 253–255 °C reported by Jadhav et al. (2008).

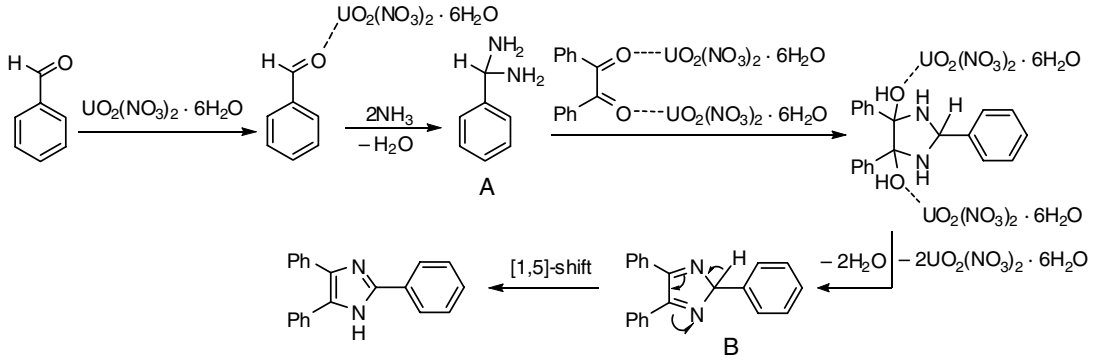


Fig. 1. Probable mechanism of the uranyl nitrate-catalyzed formation of 2,4,5-triaryl-1*H*-imidazoles.

UV analysis

The reaction progress with benzaldehyde, benzil, and uranyl nitrate was monitored by electronic absorption spectra. Benzaldehyde and benzil have their absorption maxima in an ethanol solution at 297 nm and 298 nm, respectively, whereas $UO_2(NO_3)_2 \cdot 6H_2O$ has absorption maximum at 250 nm under similar conditions. The spectral response of benzaldehyde plus catalyst as well as benzil plus catalyst in an ethanol solution showed absorption maxima at 293 nm and 287 nm, respectively, at room temperature. A hypsochormic shift of 4 nm from 297 nm to 293 nm and that of 11 nm from 298 nm to 287 nm observed for benzaldehyde and benzil suggests that the complexation between benzaldehyde, benzil, and $UO_2(NO_3)_2 \cdot 6H_2O$ took place.

Antibacterial activity

Results of the in vitro assays of antibacterial activity (MIC values) of compounds *Ia–In* are given in Table 4.

According to the preliminary antibacterial screening by the well diffusion method, compounds *Ia–In* were found to be active against all three standard bacterial strains studied: *E. coli*, *P. aeruginosa*, and *S. aureus*. Compounds *Ic*, *Il–Im*, and *In* showed good

Table 3. Spectral data of compounds *Ia–In*

Compound	Spectral data[a]
Ia	IR, $\tilde{\nu}$/cm^{-1}: 3423 (NH), 3038 (ArC—H), 1601 (C═C), 1582 (C═N) ^{1}H NMR ($CDCl_3$), δ: 7.32–7.66 (m, 13H, ArH), 7.92 (d, 2H, J = 7.8 Hz, ArH-2, ArH-6), 9.29 (s, 1H, NH) HRMS (EI), m/z (found/calc.): 296.1343/296.1313 (M^+, $C_{21}H_{16}N_2$)
Ib	IR, $\tilde{\nu}$/cm^{-1}: 3420 (NH), 3063 (ArC—H), 1601 (C═C), 1583 (C═N) ^{1}H NMR (DMSO-d_6), δ: 7.24 and 7.31 (2t, 3H, J = 7.5 Hz, 2 × ArH-4, ArH-4′), 7.38–7.57 (m, 9H, ArH), 8.07 (d, 1H, J = 8.5 Hz, ArH-6′), 8.28 (s, 1H, ArH-2′), 12.83 (s, 1H, NH) ESI-MS, m/z 375 $[M + H]^+$ HRMS (EI): m/z (found/calc.): 374.0409/374.0419 (M^+, $C_{21}H_{15}BrN_2$)
Ic	IR, $\tilde{\nu}$/cm^{-1}: 3420 (NH), 3056 (ArC—H), 1601 (C═C), 1583 (C═N), 1522 and 1348 (NO_2)[b,c,d] ^{1}H NMR (DMSO-d_6), δ: 7.24–7.57 (m, 10H, ArH), 7.78 (t, 1H, J = 8.0 Hz, ArH-5′), 8.22 (dd, 1H, J = 2.3 Hz, ArH-6′), 8.51 (d, 1H, J = 7.8 Hz, ArH-4′), 8.96 (t, 1H, J = 2.0 Hz, ArH-2′), 13.11 (s, 1H, NH)[b,c,d] HRMS (EI): m/z (found/calc.): 341.1190/341.1164 (M^+, $C_{21}H_{15}N_3O_2$)
Id	IR, $\tilde{\nu}$/cm^{-1}: 3442 (NH), 3059 (ArC—H), 2966 (CH), 1595 (C═N)[e] ^{1}H NMR (DMSO-d_6), δ: 2.38 (s, 3H, CH_3), 7.19–7.54 (m, 12H, ArH), 7.86 (d, 1H, J = 7.5 Hz, ArH-6′), 7.91 (s, 1H, ArH-2′), 12.65 (s, 1H, NH) ESI-MS, m/z 311 $[M + H]^+$ HRMS (EI): m/z (found/calc.): 310.1465/310.1470 (M^+, $C_{22}H_{18}N_2$)
Ie	IR, $\tilde{\nu}$/cm^{-1}: 3386 (NH), 3053 (ArC—H), 2910 (CH_3), 1649 (C═C), 1612 (C═N), 1384 (C—N)[d] ^{1}H NMR ($CDCl_3$), δ: 2.99 (s, 6H, $N(CH_3)_2$), 6.72 (d, 2H, J = 8.6 Hz, ArH-3′,5′), 7.23–7.33 (m, 6H, 2 × ArH-3,4,5), 7.52 (d, 4H, J = 7.5 Hz, 2 × ArH-2), 7.79 (d, 2H, J = 8.6 Hz, ArH-2′,6′), 9.72 (s, 1H, NH)[d] HRMS (EI): m/z (found/calc.): 339.1811/339.1735 (M^+, $C_{23}H_{21}N_3$)
If	IR, $\tilde{\nu}$/cm^{-1}: 3440 (NH), 3062 (ArC—H), 2963 (CH), 1594 (C═C), 1579 (C═N) ^{1}H NMR ($CDCl_3$), δ: 1.27 (t, 3H, J = 7.5 Hz, CH_3), 2.70 (q, 2H, J = 7.5 Hz, CH_2), 7.27–7.55 (m, 12H, ArH), 7.83 (d, 2H, J = 8.1 Hz, ArH-2′,6′), 9.38 (brs, 1H, NH)[b] ^{13}C NMR ($CDCl_3$), δ: 15.85, 28.43, 125.72, 126.91, 127.53, 128.15, 128.41, 128.50, 128.62, 128.88, 129.09, 131.64, 135.74, 137.43, 144.42, 146.14[b] ESI-MS, m/z 325 $[M + H]^+$
Ig	IR, $\tilde{\nu}$/cm^{-1}: 3420 (NH), 3031 (ArC—H), 2978 (CH), 1613 (C═C), 1578 (C═N) ^{1}H NMR ($CDCl_3$), δ: 1.45 (t, 3H, J = 6.9 Hz, CH_3), 4.08 (d, 2H, J = 6.9 Hz, CH_2), 6.97 (d, 2H, J = 8.4 Hz, ArH-3′,5′), 7.26–7.65 (m, 10H, ArH), 7.83 (d, 2H, J = 8.4 Hz, ArH-2′,6′), 9.23 (br s, 1H, NH) ^{13}C NMR ($CDCl_3$), δ: 14.63, 63.11, 114.50, 122.98, 126.34, 126.68, 127.02, 127.56, 128.11, 128.31, 128.56, 136.72, 145.62, 149.71, 158.68 ESI-MS, m/z 341 $[M + H]^+$
Ih	IR, $\tilde{\nu}$/cm^{-1}: 3406 (NH), 3028 (ArC—H), 2862 (CH), 1601 (C═C), 1542 (C═N)[c,d] ^{1}H NMR ($CDCl_3$), δ: 2.39 (s, 3H, CH_3), 7.23–7.52 (m, 12H, ArH), 7.78 (d, 2H, J = 6.6 Hz, ArH-2′,6′), 9.45 (s, 1H, NH)[c,d,f] HRMS (EI): m/z (found/calc.): 310.1500/310.1470 (M^+, $C_{22}H_{18}N_2$)
Ii	IR, $\tilde{\nu}$/cm^{-1}: 3512 (OH), 3420 (NH), 3059 (ArC—H), 2977 (CH), 1604 (C═C), 1543 (C═N) ^{1}H NMR ($CDCl_3$), δ: 1.48 (t, 3H, J = 6.9 Hz, CH_3), 4.22 (q, 2H, J = 6.9 Hz, CH_2), 5.86 (s, 1H, OH), 6.98 (d, 1H, J = 8.4 Hz, ArH-5′), 7.22–7.61 (m, 12H, ArH), 9.28 (br s, 1H, NH) ^{13}C NMR ($CDCl_3$), δ: 15.25, 64.49, 111.19, 116.18, 118.90, 122.41, 127.50, 128.00, 128.58, 128.84, 129.09, 135.89, 137.14, 146.50, 147.28, 147.80 ESI-MS, m/z 357 $[M + H]^+$
Ij	IR, $\tilde{\nu}$/cm^{-1}: 3439 (NH), 3067 (ArC—H), 2862 (CH), 1595 (C═C), 1552 (C═N)[d,g] ^{1}H NMR ($CDCl_3$), δ: 7.25–7.53 (m, 12H, ArH), 8.41 (d, 1H, J = 8.5 Hz, ArH-2′), 10.21 (brs, 1H, NH)[d,g] HRMS (EI): m/z (found/calc.): 364.0587/364.0534 (M^+, $C_{21}H_{14}Cl_2N_2$)
Ik	IR, $\tilde{\nu}$/cm^{-1}: 3426 (NH), 3057 (ArC—H), 2959 (CH), 1591 (C═C), 1542 (C═N)[h,i] ^{1}H NMR ($CDCl_3$), δ: 3.89 and 3.92 (2s, 6H, CH_3), 6.90 (d, 1H, J = 8.5 Hz, ArH-5′), 7.27–7.38 (m, 7H, ArH), 7.54 (m, 4H, 2 × ArH-3,5), 7.59 (d, 1H, J = 2.0 Hz, ArH-6′), 9.87 (s, 1H, NH)[h,i] HRMS (EI): m/z (found/calc.): 356.1610/356.1525 (M^+, $C_{23}H_{20}N_2O_2$)
Il	IR, $\tilde{\nu}$/cm^{-1}: 3423 (NH), 3026 (ArC—H), 2959 (CH), 1670 (HC═CH), 1596 (C═C), 1580 (C═N) ^{1}H NMR ($CDCl_3$), δ: 6.69 (dd, 2H, J = 10.4 Hz, HC═CH), 7.39–7.65 (m, 11H, ArH), 7.95 (d, 4H, J = 9.6 Hz, 2 × ArH-2,6), 9.68 (d, 1H, J = 10.4 Hz, NH)
Im	IR, $\tilde{\nu}$/cm^{-1}: 3384 (NH), 3053 (ArC—H), 1603 (C═C), 1577 (C═N) ^{1}H NMR (DMSO-d_6), δ: 7.24–7.65 (m, 11H, ArH), 8.39 (tt, 1H, J = 2.0 Hz, H-2 in pyridyl), 8.57 (dd, 1H, J = 2.0 Hz, J = 1.5 Hz, H-4 in pyridyl), 9.26 (d, 1H, J = 1.5 Hz, H-6 in pyridyl), 12.91 (s, 1H, NH) HRMS (EI): m/z (found/calc.): 297.1317/297.1266 (M^+, $C_{20}H_{15}N_3$)
In	IR, $\tilde{\nu}$/cm^{-1}: 3410 (NH), 3037 (ArC—H), 1601 (C═C), 1587 (C═N)[h] ^{1}H NMR (DMSO-d_6), δ: 7.15 (t, 1H, J = 4.3 Hz, H-4 in thienyl), 7.21–7.52 (m, 10H, ArH), 7.56 (dd, 1H, J = 1.0 Hz, H-5 in thienyl), 7.69 (dd, 1H, J = 1.0 Hz, J = 1.5 Hz, H-3 in thienyl), 12.78 (s, 1H, NH)[h,j] ESI-MS, m/z 303 $[M + H]^{+h}$

a) In NMR signal assignments, data for the substituted aryl are indicated by a prime; ArH means unresolved hydrogen atoms of all phenyls; spectral data already published: *b*) Murthy et al. (2010); *c*) Shaabani et al. (2009); *d*) Samai et al. (2009); *e*) Işikdağ and Meriç (1999); *f*) Zhou et al. (2010); *g*) Song et al. (2010); *h*) Li et al. (2010); *i*) Zhou et al. (2005); *j*) Jadhav et al. (2008).

Table 4. Antibacterial activity[a] of compounds *Ia–In*

Compound	*Staphylococcus aureus*		*Escherichia coli*		*Pseudomonas aeruginosa*	
	IZ/mm	MIC/(mg mL^{-1})	IZ/mm	MIC/(mg mL^{-1})	IZ/mm	MIC/(mg mL^{-1})
Ia	10	1.0	35	1.0	13	1.5
Ib	16	1.0	43	1.0	12	1.0
Ic	13	1.0	36	0.5	11	1.0
Id	18	1.0	46	1.0	8	0.5
Ie	16	2.0	22	2.0	16	2.0
If	11	1.0	43	1.0	10	1.0
Ig	12	2.0	18	2.0	11	2.0
Ih	12	1.0	24	2.0	9	1.0
Ii	14	1.5	18	2.0	16	2.0
Ij	9	0.5	46	1.0	11	1.0
Ik	10	0.5	22	1.0	12	1.0
Il	12	1.0	12	0.5	10	1.0
Im	11	1.0	9	0.5	15	2.0
In	14	1.5	8	0.25	13	1.0
Tetracyclin	23	1.0	26	1.0	14	1.0

a) Zone of inhibition (IZ) and minimum inhibitory concentration (MIC).

antibacterial activity against *E. coli* at MIC of 0.5 mg mL^{-1} and 0.25 mg mL^{-1}, respectively, whereas compounds *Ij–Ik* and *Id*, showed good activity (MIC = 0.5 mg mL^{-1}) against *S. aureus* and *P. aeruginosa*. Compounds *Ib–Ic*, *If*, *Ih*, *Ij–Il*, and *In* exhibited activity at MIC of 1.0 mg mL^{-1} only against *P. aeruginosa*, whereas compounds *Ia–Ib*, *Id*, and *If* exhibited significant antibacterial activity (MIC = 1.0 mg mL^{-1}) against *E. coli*. Compounds *Ic*, *Ih*, and *Il–Im* exhibited promising antibacterial activity (MIC = 1.0 mg mL^{-1}) against *S. aureus*, whereas compounds *Ij–Ik* showed MIC of 1.0 mg mL^{-1} against *E. coli*. Compounds *Ii*, *In*, and *Ia* exhibited MIC of 1.5 mg mL^{-1} against *S. aureus* and *P. aeruginosa*. Compounds *Ii*, and *Im* showed good antibacterial activity (MIC = 2.0 mg mL^{-1}) against *P. aeruginosa* and *E. coli*, whereas compounds *Ie* and *Ig* showed activity against all three organisms at MIC of 2.0 mg mL^{-1}.

Antioxidant activity

Free radical scavenging activity of compounds *Ia–In* at the 100 mg L^{-1} concentration, tested by the DPPH method is given in Table 5. The highest activity (100 %) was exhibited by compounds *Ie* and *Ii* while the lowest activity (43.18 %) was observed for compound *Ih*. Compounds *Ia–Ib*, *Id*, *If*, and *Ik* showed more than a 50 % activity compared with a standard antioxidant, butylated hydroxytoluene (BHT), at the concentration of 100 mg L^{-1}.

Antioxidant activity of compounds *Ie* and *Ii* was compared with the BHT activity at the 10 mg L^{-1}, 20 mg L^{-1}, 40 mg L^{-1}, 60 mg L^{-1}, 80 mg L^{-1}, and 100 mg L^{-1} concentrations and the results are shown in Fig. 2. The data obtained indicate that the synthesized compounds are free radical inhibitors (probably due to their ability to donate hydrogen atom).

Table 5. Antioxidant activity (AA) of compounds *Ia–In* after 30 min of incubation using the DPPH in methanol

Compound	Absorbance	AA/%
Ia	0.235	60.03
Ib	0.234	60.20
Ic	0.313	46.76
Id	0.074	87.41
Ie	0.000	100.00
If	0.027	53.40
Ig	0.295	49.83
Ih	0.344	43.18
Ii	0.000	100.00
Ij	0.319	45.75
Ik	0.274	53.40
Il	0.310	47.28
Im	0.332	43.54
In	0.319	45.75
Control	0.588	–

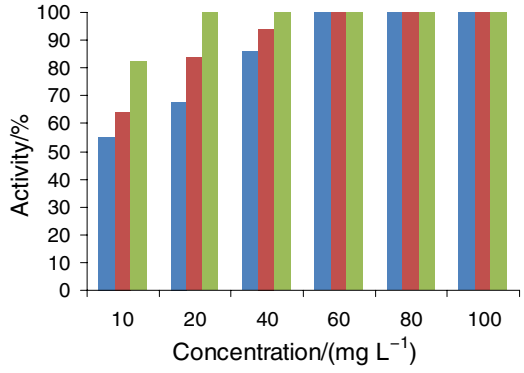


Fig. 2. Antioxidant activity of compounds *Ie* (■), *Ii* (■), and BHT (■) at different concentrations using the DPPH radical scavenging method.

Conclusions

An efficient and simple alternative method for the preparation of substituted 2,4,5-triaryl-1*H*-imidazoles under heterogeneous conditions using $UO_2(NO_3)_2 \cdot 6H_2O/Al_2O_3$ as the catalyst was investigated. Complex formation between benzaldehyde, benzil, and uranyl nitrate was confirmed by UV absorption spectra. Advantages of the presented method are its operational simplicity with good yields, shorter reaction time, low costs, and easy work-up procedure. All prepared compounds were screened for their antibacterial activity and were found to be active against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* bacterial strains. Moreover, these compounds exhibited moderate to potent antioxidant activity when using the DPPH radical scavenging method.

Acknowledgements. The authors gratefully acknowledge the management of the VIT University, Vellore, for support and providing necessary facilities.

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