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Multicomponent green synthesis, spectroscopic and structural investigation of multi-substituted imidazoles. Part 1

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Abstract: Ten 1,2,4,5-tetra-substituted imidazole derivatives have been synthesized with a 2-hydroxyethy substituent at the 1-nitrogen atom and potentially electron releasing hydroxy-, methoxy-, dimethylamino- or nitro substituents in various positions on the benzene ring located on the 2-carbon atom. The prototypical derivative with an unsubstituted phenyl ring at the 2-position is also reported. The compounds are obtained in excellent yields (average 86 %) via a four-component cyclocondensation reaction of benzil, ethanolamine, and the appropriate aromatic carbaldehyde together with ammonium acetate. The reaction uses a novel ionic liquid catalyst, DEAHS (diethyl ammonium hydrogen sulfate), under solvent-free conditions and a green synthetic protocol. The key advantages of this process are high yield, shorter reaction times and ease of work-up. Furthermore, the products can be purified by a non-chromatographic method and the catalyst is re-usable. All of these newly synthesized compounds have been characterized from spectral data; the X-ray structures of three representative molecules are also detailed.

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1 Introduction

Imidazoles are an important class of heterocycles being the core fragment of numerous natural products and biological systems [1]. In general, compounds incorporating imidazole moieties play important roles in biochemical processes and display significant pharmacological properties [2]. Various substituted imidazole derivatives have also been found to have important biological functions acting as anti-helminthic, analgesic, antibacterial, antifungal, antiviral, tuberculostatic, cytostatic, and anti-inflammatory agents [3].

Multicomponent reactions (MCRs) have excited a great deal of interest among chemists and pharmacists due to their outstanding status in modern organic synthesis and medicinal chemistry. MCRs are one-pot processes bringing together three or more reaction components with high atom economy and good selectivity [4, 5]. Developing new MCRs [6] and improving known multi-component reactions are areas of considerable current interest and MCR processes leading to imidazole derivatives are no exception. The presence of imidazole rings in so many biologically important natural products and pharmacologically active compounds has spawned a diverse array of synthetic approaches to the production of these heterocycles [7], the majority being classical methods [8–10]. In particular, tetrasubstituted imidazoles and their derivatives have been synthesized by several methods [11–14]. In addition, such syntheses are usually carried out in polar organic solvents such as ethanol, methanol, acetic acid, DMF and DMSO and involve complex isolation requirements, side products and tedious recovery procedures. Despite intensive efforts to improve these syntheses, only a handful of general methods exist for the construction of tetrasubstituted imidazoles. These include reactions

catalyzed by silica gel or Zeolite HY [15], silica gel-$NaHSO_4$ [16], molecular iodine [17], $K_5CoW_{12}O_{40}\cdot 3H_2O$ [18], heteropolyacids [19] and $HClO_4$-SiO_2 [20]. BF_3, as a strong Lewis acid, has also been used in both small and large scale reactions as an acid catalyst [21]. All of these processes generate waste containing both catalyst and solvent, which must be recovered, treated and disposed of. The toxicity and volatile nature of many organic solvents, particularly chlorinated hydrocarbons, which are widely used in huge amounts for organic reactions, have posed a serious threat to the environment [22]. Thus, the design of solvent-free catalytic reactions has received tremendous attention in recent times in the area of green synthesis [23, 24].

Ionic liquid (IL) technology offers a new and environmentally benign approach toward modern synthetic chemistry. Ionic liquids have interesting advantages such as extremely low vapor pressure, excellent thermal stability, reusability and the ability to dissolve many organic and inorganic substrates [25]. Ionic liquids have been successfully employed as solvents and catalysts for a variety of reactions [26–29] which promise widespread applications in both small and large scale organic syntheses. In a continuation of our efforts to develop Lewis and Brønsted acid catalyzed synthetic methodologies [30–33] and further to our study of the synthesis of bio-active molecules [34–36] we report herein a simple and environmentally friendly MCR technique for the synthesis of potentially bio-active tetrasubstituted imidazole compounds (Scheme 1) in high yields using the novel Brønsted acidic ionic liquid, diethyl ammonium hydrogen sulfate (DEAHS) as a catalyst for the first time.

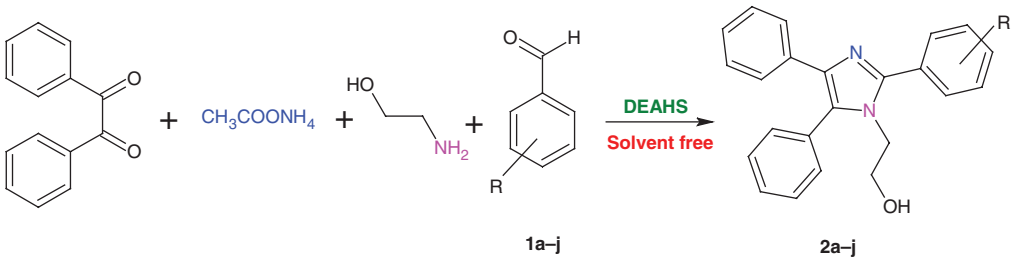
Because of the pharmaceutical potential of these products, the structures of three representative derivatives have been determined by X-ray crystallography and are reported here. Structures of 2,4,5-triphenyl-substituted imidazole compounds are reasonably common with 214 hits in the Cambridge Structural Database (CSD) [37], including the archetypal lophine (2,4,5-triphenyl-1*H*-imidazole) [38]. This number drops to 180 if coordination complexes of the imidazole derivatives are excluded. However, only five structures of 2,4,5-triphenyl-substituted imidazole derivative with a alcohol substituents on the imidazole sp^3-N atom have been reported. One of these [39] is compound **2e** in this paper, with details of the spectroscopic identification of this molecule included here for completeness and comparison with the other, similar derivatives. Two other related compounds have 2-hydroxypropyl substituents [40, 41], with 3-phenylpropan-1-ol substituents on the sp^3-N atom in the two other similar compounds [42, 43]. Interestingly, only ten other structures in the database have alkyl chains of two or more C atoms on the 1-nitrogen atom of the imidazole [44–52], with simple aliphatic chains predominating and with no other alcohol derivatives.

2 Results and discussion

2.1 Synthetic procedures

In order to determine the most appropriate reaction conditions and to evaluate the catalytic efficiency of the ionic liquid diethyl ammonium hydrogen sulfate (DEAHS) [53], an initial model study was carried out on the synthesis of 1,2,4,5-tetrasubstituted imidazoles. Among the tested solvents were methanol, ethanol, DMF and DMSO; a solvent-free system was also investigated. Condensation of benzil, benzaldehyde, ethanolamine, and ammonium acetate to form 2-(2,4,5-triphenyl-1*H*-imidazol-1-yl)ethanol (**2a**) was found to be significantly more facile under solvent-free conditions and proceeded to give the highest yield in a relatively very short time, Table 1.

Additionally, we sought to evaluate the generality of this process for the synthesis of a broad range of derivatives with a variety of substituents on the phenyl ring at the 2-position of the imidazole ring, Scheme 1. Thus, reactions of benzil (10 mmol), with various aromatic



Scheme 1: Synthesis of **2a–2j**, R = H, **2a**, 2-OH, **2b**, 4-OH, **2c**, 3-OCH_3, **2d**, 4-OCH_3, **2e**, 2,4-OCH_3, **2f**, 3,4-OCH_3, **2g**, 2,5-OCH_3, **2h**, 4-$(CH_3)_2N$, **2i** and4-NO_2, **2j**.

Table 1: Synthesis of 2-(2,4,5-triphenyl-1*H*-imidazol-1-yl)ethanol (**2a**) using diethylammonium hydrogen sulfate (DEAHS) catalyst (0.3 equiv) in different solvents.

Solvent	*T* (°C)	Time	Yield (%)
Methanol	67	3 h	40
Ethanol	78	3 h	45
Acetonitrile	67	3 h	35
DMF	100	2 h	55
DMSO	100	2 h	60
Solvent-free conditions	100	20 min	98

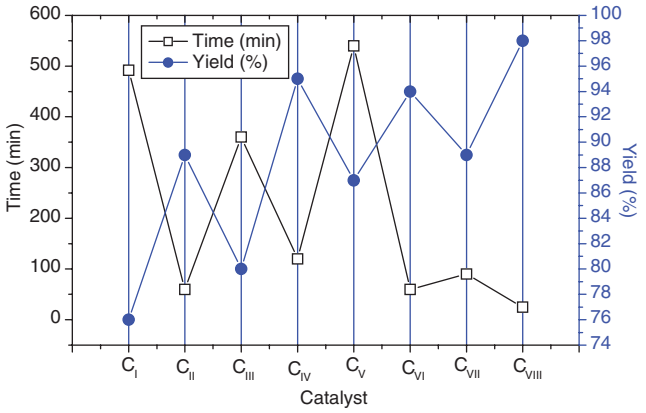


Fig. 1: Dependence of the yield and time of reaction on the catalyst type.

aldehydes (10 mmol) bearing electron releasing groups (such as hydroxyl, mono- and di-methoxy, or dimethyl amino substituents), ethanolamine (11 mmol) and ammonium acetate (10 mmol), were carried out in the presence of diethylammonium hydrogen sulfate (0.5 g, 3 mmol) as catalyst (Table 1). The yields of all the products so obtained were very good to excellent. Furthermore, the reactions proceeded without the formation of any side products, such as 2,4,5-trisubstituted imidazoles, which are normally observed as an impediment to efficient synthesis under the influence of other strong acids [19, 20]. An earlier report of the preparation of (**2a**) used a similar preparative route, but with L-proline triflate as the catalyst [54].

The yield and reaction time for the formation of **2a** has been recorded using different catalysts as listed in Table 2 and the results represented graphically in Fig. 1. While it is obvious that reaction temperatures will have a significant effect on reaction times, the data in Table 1 clearly confirm that DEAHS is indeed a highly efficient catalyst in terms of both yield and reaction time when compared to other type of catalysts that have been used.

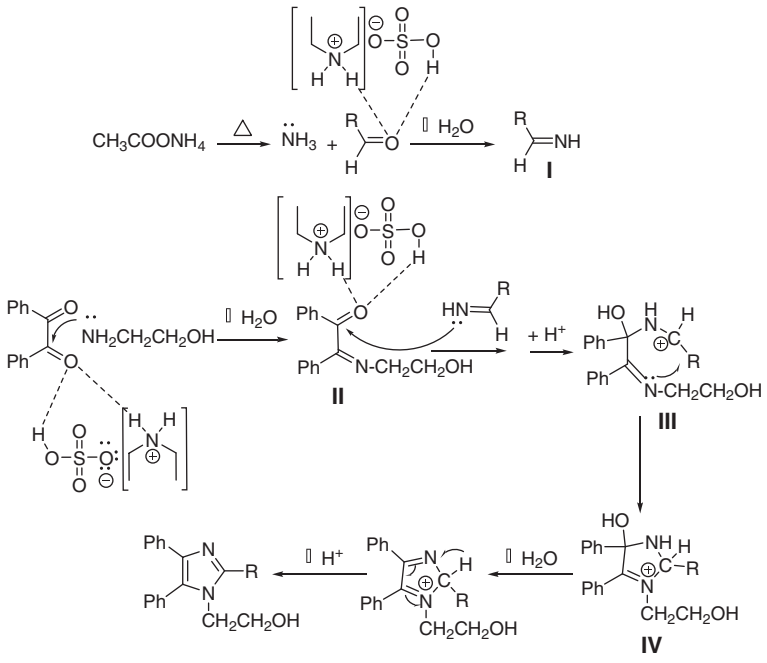
Hydrogen bond formation between the carbonyl group of the starting aldehyde and the catalyst DEAHS makes the carbonyl very susceptible to nucleophilic attack by an ammonia molecule generated from the ammonium acetate starting material. The resulting intermediate readily loses a water molecule to produce the imine **I** (Scheme 2). Similarly the catalyst promotes an additional condensation reaction of one of the carbonyl groups from benzil with the aminoethanol reactant to furnish the imine **II**. DEAHS also catalyzes nucleophilic attack by the imine **I** on the second carbonyl group in imine **II** followed by protonation to form the intermediate cation **III**. This in turn undergoes an intramolecular cyclization to give the unstable cyclic cation **IV** which eliminates water and then loses a proton to yield the target products **2a**–**2j**. All products were fully characterized by spectroscopic methods such as IR, ^{1}H NMR, ^{13}C NMR and the structures of **2a**, **2c** and **2j** were determined by X-ray crystallography (see below).

2.2 Spectroscopic properties

The IR spectra of all of the compounds showed definitive broad bands in the frequency range 3568–3144 cm^{-1} for the

Table 2: Comparison of the efficiency (yield and reaction time) of various catalysts with diethyl ammonium hydrogen sulfate in the synthesis of the 2-(2,4,5-triphenyl-1*H*-imidazol-1-yl)ethanol, **2a**.

No	Catalyst	Conditions	Time (min)	Yield (%)	Refs.
C_{I}	$InCl_3 \cdot 3H_2O$	MeOH, r. t.	492	76	[12]
C_{II}	KH_2PO_4	Reflux in EtOH	60	89	[55]
C_{III}	$Yb(OPf)_3$	$C_{10}F_{18}$, 80 °C	360	80	[1]
C_{IV}	$Zr(acac)_4$	Reflux in EtOH	120	95	[56]
C_{V}	L-proline	Methanol, 60 °C	540	87	[57]
C_{VI}	$[Hbim]BF_4$	100 °C	60	94	[58]
C_{VII}	$NiCl_2 \cdot 6H_2O$-Al_2O_3	Reflux in EtOH	90	89	[59]
C_{VIII}	$Et_2NH_2^+ HSO_4^-$ (DEAHS)	100 °C	20	98	this work



Scheme 2: General mechanism for the multi-component synthesis.

OH stretching vibration of the ethanolic OH groups of all nine compounds. The phenolic OH stretches for **2b** and **2c** could not be distinguished separately from these vibrations. In addition, C–H stretching modes were found in the range 3084–3053 cm^{-1} while the C=N stretching mode of the imidazole unit was observed in a relatively narrow range 1601–1603 cm^{-1} for **2a**–**2h** with the corresponding vibration for the dimethylamino substituted derivative **2i** appearing at 1610 cm^{-1} while that for the 4-nitro derivative **2j** appeared at 1595 cm^{-1}. The stretching vibrations of the nitro group of **2j** were observed at 1537 cm^{-1} (asymmetrical) and 1338 cm^{-1} (symmetrical). Clearly the nature of the substituent on the 2-benzene ring has a noticeable effect on the vibrational spectra.

2.3 Molecular and crystal structures of 2a, 2c and 2j

The molecular structures of the three compounds investigated by X-ray crystallography are shown in Fig. 2 (i–iii). The broad features of the three structures are sufficiently similar to be discussed together. Each molecule comprises a central imidazole ring substituted at N1 with a CH_2CH_2OH unit which generally lies almost orthogonal to the imidazole ring, Table 3. The imidazole ring also carries an aromatic ring on each C atom with a substituted benzene ring on the C2 carbon atom for all but **2a** and simple phenyl substituents on C4 and C5. The relative inclinations of these benzene rings to the central imidazole ring are also detailed in Table 3 which clearly shows that the benzene and imidazole rings are not co-planar in any of the molecules.

The C2 benzene ring substituents differentiate the three molecules, starting with the prototypical compound **2a** with a simple phenyl ring in the 2-position. 4-Hydroxy substitution is found in the C2 benzene ring of **2b**, while **2j** has a nitro substituent at the 4-position of the C21…C26 benzene rings of each of the two unique molecules. These are distinguished in the atom numbering by leading 1 and 2 characters; the two molecules differ principally in the inclination of the benzene rings at C2, C4 and C5 relative to the imidazole ring, (*vide supra*, Table 3). Also for **2j**, the planes of the nitro groups are inclined at 12.52(11)° for molecule 1 and 4.3(3)° for molecule 2 to the planes of the benzene ring to which they are bound.

3 Conclusion

We have developed a general procedure for the synthesis of tetrasubstituted imidazoles in high yield by a simple, one-pot, four-component reaction of benzil, aldehydes, ethanolamine and ammonium acetate utilizing diethylammonium hydrogen sulphate (DEAHS) as a new ionic liquid and catalyst. The reactions proceed in the absence of any solvent or additives. This protocol offers a broad

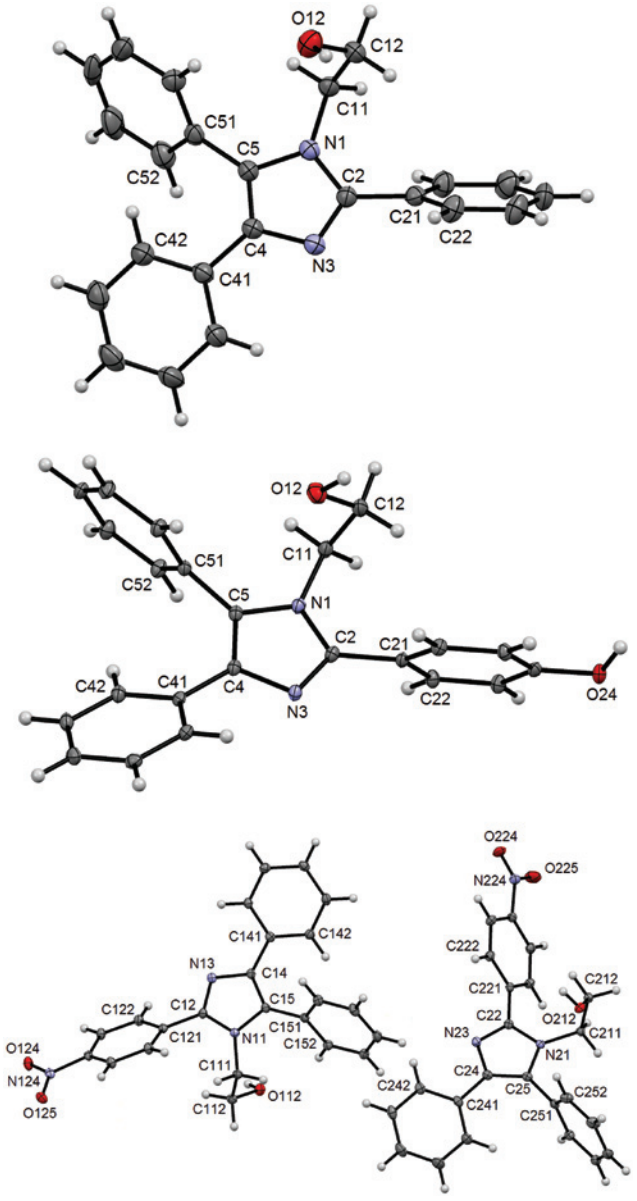


Fig. 2: The molecular structures of (i) **2a**; (ii) **2c**; (iii) the two unique molecules in the asymmetric unit of **2j** (crystallographic atom numbering and displacement ellipsoids drawn at the 50 % probability level; H atoms as spheres with arbitrary radii).

scope for access to a wide spectrum of diversely substituted 1,2,4,5-tetrasubstituted imidazoles. The absence of toxic organic solvents from the entire process, multiple reusability of the catalyst, good product purity, simplicity in operation, and no requirement for chromatographic purification, shorter reaction times and high yields of products make this procedure greener, more efficient and importantly cost effective. In view of their pharmaceutical potential the molecular structures of three representative compounds were also determined by X-ray diffraction.

Table 3: Dihedral angles (deg) between the imidazole and benzene rings[a] for **2a**, **2c** and **2j**.

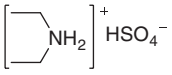
Compound	1–2	1–3	1–4
2a	53.76(19)	21.02(15)	71.31(19)
2c	72.21(7)	30.70(11)	73.82(8)
2j (molecule 1)	42.82(4)	22.91(3)	70.19(4)
2j (molecule 2)	56.10(4)	17.46(2)	89.88(4)

[a]Planes are numbered as follows: 1: N1,C2,N3,C4,C5; 2: C21…C26, 3: C41…C46; 4: C51…C56. For **2j**, atom numbers defining the planes have additional leading 1 and 2 characters for molecules 1 and 2, respectively [Fig. 2 (iii)].

4 Experimental section

All reagents were purchased from Aldrich and Merck supplier companies, and used without further purification. Melting points were determined by the open capillary method using a Gallenkamp melting point apparatus and are uncorrected. CHN microanalyses were determined using a Vario elemental analyzer (Shimadzu, Japan) at the Organic Microanalysis Unit, Faculty of Science, Cairo University, Cairo, Egypt. A SHIMADZU FT-IR-8400s spectrometer was used to record IR spectra as KBr pellets. NMR spectra were recorded on a Bruker (300 and 400 MHz) Ultra Shield NMR spectrometers with [D_6]DMSO as the solvent. Chemical shifts δ are given in ppm. The progress of the reactions and purity of the products were monitored by TLC.

4.1 Synthesis of diethyl ammonium hydrogen sulfate (DEAHS)



Diethylamine (22.2 g, 0.3 mol) was added into a 250 mL three-necked flask with a magnetic stirrer. Then 29.4 g (0.3 mol) concentrated sulfuric acid (98 %) was slowly added dropwise to the flask at room temperature then heated to 80 °C for 12 h. The product was washed with diethyl ether three times to remove traces of non-ionic material. The residue was dried under vacuum using a rotary evaporator to obtain the clear viscous product, diethyl ammonium hydrogen sulfate. Yield 98 %, pH 1.6 [53].

4.2 General method for the synthesis of 1,2,4,5-tetrasubstituted imidazoles

Benzil (10 mmol), an aldehyde (**1a**–**1j)** (10 mmol), ammonium acetate (10 mmol) and ethanolamine (11 mmol)

were added to diethylammonium hydrogen sulfate (0.5 g, 3 mmol) in an oil bath at room temperature. The resulting mixtures were heated to 100 °C for the time reported in Table 4. Reaction progress was monitored by TLC until completion after 15–35 min. The reaction mixtures were washed with water and the resulting solid products were purified in all cases by recrystallization from ethanol.

4.3 Spectroscopic properties of 2a–2j

4.3.1 2-(2,4,5-Triphenyl-1*H*-imidazol-1-yl)ethanol (2a)

M. p. 184–185 °C. – FTIR (KBr): 3265 (OH), 3061 (C–H), 2964 (C–H), 1601 (C=N) 1502 (C=C), 1456, 1181, 1096, 834, 720, 696 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.25$ (t, 2H, CH_2N), 4.07 (t, 2H, CH_2O), 5.07 (s, 1H, OH), 7.00–7.00 (m, $J = 8.8$, 2.0 Hz, 15H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.9$, 59.8, 126.6, 128.5, 129.0, 129.2, 129.3, 129.6, 130.3, 131.4, 131.6, 135.1, 137.1, 147.7. – Analysis for $C_{23}H_{20}N_2O$ (340.4): C 81.16, H 5.92, N 8.23; found C 81.20, H 6.00, N 8.25 %.

4.3.2 2-(1-(2-hydroxyethyl)-4,5-diphenyl-1*H*-imidazol-2-yl)phenol (2b)

M. p. 287–289 °C. – FTIR (KBr): 3518 (OH), 3055 (C–H), 2985 (C–H), 2888 (C–H), 1603 (C=N) 1503 (C=C), 1452, 1169, 1067, 841, 707, 694 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.2$ (t, 2H, CH_2N), 3.95 (t, 2H, CH_2O), 4.95 (s br., 1H, CH_2OH), 6.8–7.8 (m, $J = 8.8$, 2.0 Hz, 14H, Ar-H), 10 (s br., 1H, C_6H_4OH). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.8$, 59.7, 115.8, 122.3, 126.4, 126.6, 128.5, 129.2, 129.5, 129.7, 131.0, 131.5, 131.7, 135.3, 136.6, 147.9, 158.4. – Analysis for $C_{23}H_{20}N_2O_2$ (356.4): C 77.51, H 5.66, N 7.89; found C 77.48, H 5.70, N 7.90 %.

Table 4: Reaction time, yield and physical properties of compounds **2a–2j**.

No.	R	Mol. Formula (M_r in parentheses)	M. p. (°C)	Time (min)	Yield (%)
2a	H	$C_{23}H_{20}N_2O$ (340.4)	184–185	20	98
2b	2-OH	$C_{23}H_{20}N_2O_2$ (356.4)	108–110	25	92
2c	4-OH	$C_{23}H_{20}N_2O_2$ (356.4)	287–289	15	92
2d	3-OCH_3	$C_{24}H_{22}N_2O_2$ (370.4)	160–162	35	82
2e	4-OCH_3-	$C_{24}H_{22}N_2O_2$ (370.4)	187–188	30	95
2f	2,4-CH_3O-	$C_{25}H_{25}N_2O_3$ (401.5)	175–177	30	88
2g	3,4-CH_3O-	$C_{25}H_{25}N_2O_3$ (401.5)	212–214	35	92
2h	2,5-OCH_3-	$C_{25}H_{25}N_2O_3$ (401.5)	198–200	35	92
2i	4-$(CH_3)_2N$-	$C_{25}H_{25}N_3O$ (383.5)	207–209	35	93
2j	4-NO_2-	$C_{23}H_{19}N_3O_3$ (385.4)	190–192	15	85

4.3.3 4-(1-(2-Hydroxyethyl)-4,5-diphenyl-1*H*-imidazol-2-yl)phenol (2c)

M. p. 287–289 °C. – FTIR (KBr): 3518 (OH), 3055 (C–H), 2985 (C–H), 2888 (C–H), 1603 (C=N) 1503 (C=C), 1452, 1169, 1067, 841, 707, 694 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.2$ (t, 2H, CH_2N), 3.95 (t, 2H, CH_2O), 4.95 (s br., 1H, CH_2OH), 6.8–7.8 (m, $J = 8.8$, 2.0 Hz, 14H, Ar-H), 10 (s br., 1H, C_6H_4OH). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.8$, 59.7, 115.8, 122.3, 126.4, 126.6, 128.5, 129.2, 129.5, 129.7, 131.0, 131.5, 131.7, 135.3, 136.6, 147.9, 158.4. – Analysis for $C_{23}H_{20}N_2O_2$ (356.4): C 77.51, H 5.66, N 7.89; found C 77.48, H 5.63, N 7.90 %.

4.3.4 2-(2-(3-Methoxyphenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)ethanol (2d)

M. p. 160–162 °C. – FTIR (KBr): 3334 (OH), 3064 (C–H), 2964 (C–H), 2836 (C–H), 1603 (C=N), 1502 (C=C), 1462, 1262, 1156, 1055, 873, 734, 698 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.247$ (t, 2H, CH_2N), 3.824 (s, 3H, OCH_3), 4.005 (t, 2H, CH_2O), 4.89 (s br, 1H, CH_2OH), 7.109–7.542 (m, 14H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.5$, 55.2, 59.3, 114.5, 121.3, 126.1, 126.1, 128.0, 128.9, 129.1, 129.6, 129.8, 131.0, 131.1, 132.5, 146.9, 159.2. – Analysis for $C_{24}H_{22}N_2O_2$ (370.5): C 74.56, H 5.99, N 7.60; found C 74.60, H 6.01, N 7.58 %.

4.3.5 2-(2-(4-Methoxy)-4,5-diphenyl-1*H*-imidazol-1-yl) ethanol (2e)

M. p. 187–188 °C. – FTIR (KBr): 3159 (OH), 3058 (C–H), 2965 (C–H), 2836 (C–H), 1603 (C=N), 1466 (C=C),1179, 1081, 834, 721, 695 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.25$ (t, 2H, CH_2N), 4.0 (t, 2H, CH_2O), 5.07 (s, 1H, OH), 7.03–7.7 (m, $J = 8.8$, 2.0 Hz, 14H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.8$, 55.6, 59.8, 114.4, 123.9, 126.5, 126.6, 128.5, 129,3, 129.5, 129.9, 131.0, 131.4, 131.6, 135.2, 136.8, 147.6. – Analysis for $C_{24}H_{22}N_2O_2$ (370.5): C 74.56, H 5.99, N 7.60; found C 74.65, H 6.02, N 7.57 %.

4.3.6 2-(2-(2,4-Dimethoxyphenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)ethanol (2f)

M. p. 175–177 °C. – FTIR (KBr): 3153 (OH), 3060 (C–H), 2980 (C–H), 2837 (C–H), 1614 (C=N) 1579 (C=C), 1454, 1258, 1153,

1072, 837, 720, 701 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.73$ (s, 6H, $2CH_3O$), 3.78 (t, 2H, CH_2N), 4.00 (t, 2H, CH_2O), 4.97 (s br, 1H, CH_2OH), 7.02–7.60 (m, 13H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.8$, 55.7, 55.7, 59.7, 111.8, 113.3, 122.1, 123.8, 126.4, 126.7, 128.3, 129.1, 129.4, 129.9, 131.5, 131.5, 134.9, 136.7, 147.9, 148.9, 149.8. – Analysis for $C_{25}H_{25}N_2O_3$ (401.5): C 74.79, H 6.28, N 6.98; found C 74.77, H 6.30, N 7.02 %.

4.3.7 2-(2-(3,4-Dimethoxyphenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)ethanol (2g)

M. p. 212–214 °C. – FTIR (KBr): 3568, 3100 (OH), 3060 (C–H), 2994 (C–H), 2885, 1601 (C=N) 1585 (C=C), 1481, 1239, 1168, 1057, 872, 725, 701 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.75$ (s, 6H, $2(CH_3O)$), 3.78 (t, 2H, CH_2N), 4.20 (t, 2H, CH_2O), 4.91 (s br, 1H, CH_2OH), 7.01–7.81 (m, 13H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.8$, 55.7, 55.7, 59.7, 111.8, 113.3, 122.1, 123.8, 126.4, 126.7, 128.3, 129.1, 129.4, 129.9, 131.4, 131.5, 134.9, 136.7, 147.9, 148.9, 149.8. – Analysis for $C_{25}H_{25}N_2O_3$ (401.5): C 74.79, H 6.28, N 6.98; found C 74.82, H 6.25, N 6.96 %.

4.3.8 2-(2-(2,5-dimethoxyphenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)ethanol (2h)

M. p. 198–200 °C. – FTIR (KBr): 3266 (OH), 3058 (C–H), 2949 (C–H), 2837 (C–H), 1603 (C=N) 1524 (C=C), 1460, 1230, 1181, 1056, 803, 727, 698 cm^{-1}. – ^1H NMR (300 MHz, [D_6] DMSO, TMS): $\delta = 3.125$ (t, 2H, CH_2N), 3.737 (t, 2H, CH_2O), 3.766 (s, 6H, $2CH_3O$), 4.716 (s br, 1H, CH_2OH), 7.043–7.538 (m, 13H, Ar-H) ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 46.7$, 56.1, 56.4, 59.8, 113.2, 116.4, 118.0, 121.5, 126.5, 126.5, 128.5, 129.3, 129.7, 131.4, 131.6, 135.4, 136.8, 145.0, 151.6, 153.5. – Analysis for $C_{25}H_{25}N_2O_3$ (401.5): C 74.79, H 6.28, N 6.98; found C 74.75, H 6.25, N 7.00 %.

4.3.9 2-(2-(4-(Dimethylamino)phenyl)-4,5-diphenyl-1*H*-imidazol-1-yl) ethanol (2i)

M. p. 207–209 °C. – FTIR (KBr): 3320, 3125 (OH), 3064 (C–H), 2970 (C–H), 2890 (C–H), 1670 (C=N) 1579 (C=C), 1450, 1245, 1174, 1098, 874, 724, 694 cm^{-1}. – ^1H NMR (300 MHz, [D_6]DMSO, TMS): $\delta = 3.95$ (s, 6H, $(CH_3)_2N$), 3.2 (t, 2H, CH_2N), 3.95 (t, 2H, CH_2O), 4.91 (s, 1H, CH_2OH), 6.78–7.65 (m, 14H, Ar-H), 10 (s br, 1H, C_6H_4OH). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 40.1$, 46.7, 59.8, 112.2, 118.9, 126.5, 128.4, 129.2, 129.5, 130.2, 131.5, 131.8, 135.4, 136.5, 148.2, 150.8. – Analysis for $C_{25}H_{25}N_3O$ (383.5): C 78.30, H 6.57, N 10.96; found C 78.32, H 6.60, N 11.00 %.

4.3.10 2-(2-(4-Nitrophenyl)-4,5-diphenyl-1*H*-imidazol-1-yl)ethanol (2j)

M. p. 190–192 °C. – FTIR (KBr): 3144 (OH), 3084 (C–H), 2961 (C–H), 2849 (C–H), 1595 (C=N) 1524 (C=C), 1479, 1286, 1128, 1060, 875, 734, 692 cm^{-1}. – ^1H NMR (300 MHz, [D_6] DMSO, TMS): $\delta = 3.27$ (t, 2H, CH_2N), 4.08 (t, 2H, CH_2O), 5.00 (s br, 1H, CH_2OH), 7.00–8.52 (m, 14H, Ar-H). – ^{13}C NMR (300 MHz, [D_6]DMSO): $\delta = 47.5$, 59.9, 124.2, 126.7, 126.9, 128.6, 129.6, 130.3, 131.1, 131.4, 134.7, 137.9, 148.1, 145.6, 147.5. – Analysis for $C_{23}H_{19}N_3O_3$ (385.4): C 71.68, H 4.97, N 10.90; found C 71.71, H 5.00, N 10.88 %.

4.4 X-ray structure determinations

Crystallographic data for **2a**, **2c**, and **2j** are detailed in Table 5. Diffraction data for **2a** were collected at Baku Estate University on a Bruker APEXII CCD diffractometer using graphite-monochromatized MoK_α radiation ($\lambda = 0.71073$ Å). Data for **2c** and **2j** were obtained at the University of Otago on an Agilent SuperNova (Dual, Cu at zero, Atlas) diffractometer using a mirror monochromator and CuK_α radiation ($\lambda = 1.54184$ Å). The Bruker data collection was controlled by Apex2 [60] software with cell refinement and data reduction performed using Saint [60]. Multi-scan absorption corrections were applied using Sadabs [61]. For **2c** and **2j** these processes were all controlled by CrysAlisPro [62]. The structures were all solved with Shelxs [63] and refined by full-matrix least-squares on F^2 using Shelxl-2014 [64] and Titan2000 [65]. All non-hydrogen atoms were assigned anisotropic displacement parameters. The H atoms of the hydroxyl groups for all three molecules were located in difference Fourier maps and their coordinates refined with atomic displacement parameters set to $1.5 \times U_{eq}$(O). All other H atoms were positioned geometrically and refined using a riding model with d(C–H) = 0.95 Å for aromatic and 0.99 Å for CH_2 with $U_{iso} = 1.2 \times U_{eq}$(C) and 0.98 Å, $U_{iso} = 1.5 \times U_{eq}$(C) for CH_3 atoms. All molecular plots and packing diagrams were drawn using Mercury [66]. Other calculations were performed using Platon [67] and tabular material was produced using WinGX [68].

CCDC 1024500 (**2a**) 1024501 (**2b**) and 1024505 (**2j**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 5: Crystal data and numbers pertinent to data collection and structure refinement of **2a**, **2c**, and **2j**.

	2a	**2c**	**2j**
Empirical formula	$C_{23}H_{20}N_2O$	$C_{23}H_{20}N_2O_2$	$C_{23}H_{19}N_3O_3$
M_r	40.41	356.41	385.41
T, K	296(2)	100(2)	100(2)
Wavelength; λ, Å	MoK_α; 0.71073	CuK_α; 1.54184	CuK_α; 1.54184
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	$P2_1/n$	$Pca2_1$	$P2_1/c$
a, Å	8.926(2)	39.6826(8)	15.36052(11)
b, Å	14.538(4)	5.6950(12)	8.61192(6)
c, Å	14.401(4)	7.8390(19)	28.6080(2)
β, deg	104.701(4)	90	97.1582(7)
V, Å^3	1807.7(8)	1771.6(6)	3754.88(5)
Z	4	4	8
D_{calcd}, g cm^{-3}	1.251	1.336	1.364
μ, mm^{-1}	0.077	0.685	0.748
F(000), e	720	752	1616
Crystal size, mm^3	0.18 × 0.14 × 0.12	0.21 × 0.11 × 0.05	0.25 × 0.16 × 0.14
θ range, deg	2.03–25.49	4.46–76.26	3.11–76.80
Refl. total/unique/R_{int}	15263/3349/0.053	8180/2554/0.031	39758/7843/0.032
Refl. obs.with $I > 2\sigma(I)$	2543	2442	7048
Transmission max/min	0.9908/0.9862	1.0000/0.9368	1.00000/0.73475
Data/restraints/ref. param.	3349/0/238	2554/1/250	7843/0/529
Goodness-of-fit	1.188	1.086	1.043
Final $R1/wR2$ [$I > 2\sigma(I)$]	0.0997/0.2534	0.0347/0.0843	0.0347/0.0887
Final $R1/wR2$ (all data)	0.1204/0.2637	0.0375/0.0856	0.0392/0.0925
$\Delta\rho_{fin}$ (max/min), e Å^{-3}	0.37/−0.28	0.21/−0.21	0.26/−0.26
CCDC reference number	1024500	1024501	1024505

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