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ACID, METAL AND PEROXIDE-FREE SYNTHESIS OF 2,4,5-TRISUBSTITUTED IMIDAZOLES COMMENCING FROM INTERNAL ALKENES USING AN IODINE/DMSO SYSTEM

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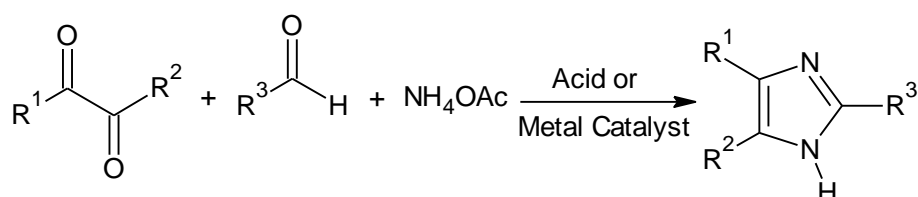
Abstract – An efficient acid, metal and peroxide-free synthesis of 2,4,5-trisubstituted imidazoles commencing from internal alkenes and aldehydes using an inexpensive and eco-friendly iodine/DMSO system has been reported. This simple methodology affords a plethora of 2,4,5-trisubstituted imidazoles in moderate to good yields under mild reaction conditions. Based on preliminary control studies, a reasonable mechanism to the target imidazole is proposed.

Oxidations play a vital role in academia and industry as it assists in the creation of new, complex molecules or the modification of existing ones.¹ Given the importance of this transformation, the demand for novel, environmentally benign, and cost-effective oxidation methods have steadily increased.² Within this context, the oxidation of alkenes, in particular, continues to be of importance as it is used to prepare epoxides,³ carbonyls,⁴ and 1,2-diols.⁵ Additionally, the conversion of internal alkenes to α -diketones is of interest to organic chemists as it allows for the generation of synthetically useful compounds such as quinoxalines and spirocycles.⁶ Hence, a multitude of synthetic routes have been devised for the conversion of internal alkenes to α -diketones and selected examples include the use of potassium permanganate in acetic anhydride⁷ and ruthenium-catalyzed hydrogen abstraction.⁸

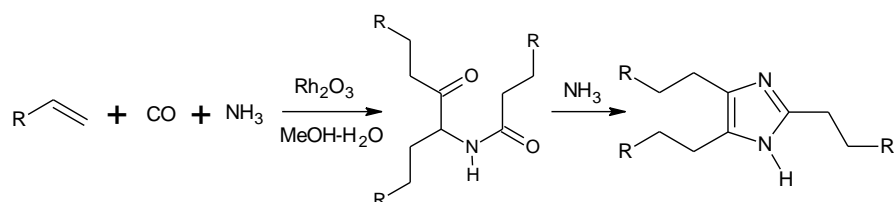
2,4,5-Trisubstituted imidazoles are important heterocyclic compounds as they display interesting biological^{9,10} and synthetic applications.¹¹ The traditional route towards these fascinating molecules involves the multicomponent reaction of a α -diketone, aldehyde and ammonium acetate in the presence of a metal or acid catalyst (Scheme 1a) such as acetic acid,¹² ytterbium triflate,¹³ and $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 4\text{H}_2\text{O}$,¹⁴ to name but a few. Surprisingly, there are limited synthetic routes towards 2,4,5-trisubstituted imidazoles commencing from alkenes and one of the earliest reports involves the use of a rhodium oxide catalyst and ammonia in a methanol-water mixture in the presence of carbon monoxide (Scheme 1b).¹⁵ The challenges associated with this approach include the use of an expensive rhodium catalyst, employment of toxic carbon

monoxide, formation of side-products, substrate scope limitations as well as poor yields. Approximately four decades later, a singular example of a 2,4,5-trisubstituted imidazole synthesis using a ketoiodination/cyclization methodology from internal alkenes was reported (Scheme 1c).¹⁶ The limitations of this method include the use of a laborious work-up procedure and the use of heat and shock-sensitive 2-iodoxybenzoic acid (IBX). More recently, Yang and co-workers reported the synthesis of α -diketones using an internal alkene *via* a bifunctional iron nanocomposite catalyst, *tert*-butyl hydroperoxide (TBHP) and tetrabutylammonium iodide (TBAI) in an acetonitrile-water medium (Scheme 1d).¹⁷ The authors highlighted the utility of the synthesized α -diketone by extending their study to the preparation of 2,4,5-triphenyl-1*H*-imidazole. Despite the novelty of this approach, the use of a transition-metal complex which is not commercially available and has to be prepared by a tedious approach as well as the use of potentially dangerous hydroperoxides detracts from this methodology.

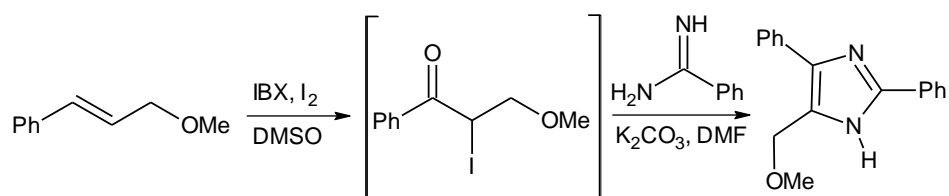
a.] Traditional Synthesis



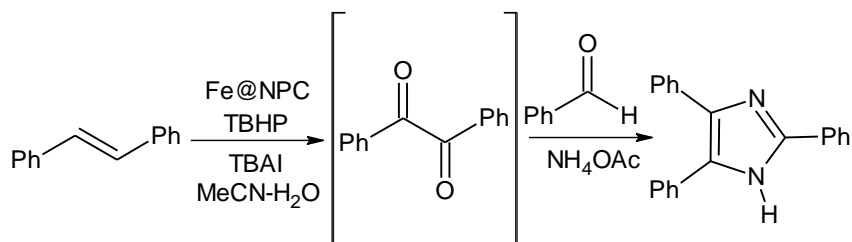
b.] *J. Org. Chem.*, 1971, 36, 3927.



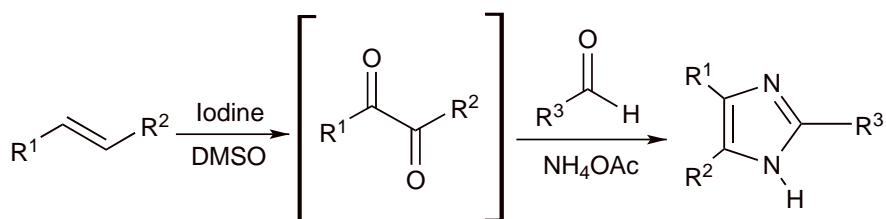
c.] *Org. Biomol. Chem.*, 2012, 10, 1093.



d.] *ACS Catal.*, 2020, 10, 4617.



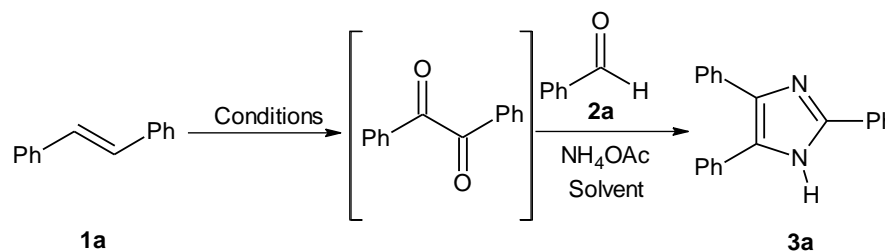
e.] This work (acid, metal and peroxide free synthesis)



Scheme 1. Different synthetic routes towards 2,4,5-trisubstituted imidazoles

Recently, the iodine/DMSO system has emerged as a powerful tool in chemistry as it exhibits diverse applications in organic synthesis¹⁸ and previously, we have reported the efficient synthesis of 2,4,5-trisubstituted imidazoles from α -methylene ketones,¹⁹ and internal alkynes^{20,21} using this system. Given the challenges highlighted above for imidazole synthesis commencing from alkenes, herein we report a simple route towards the construction of these fascinating molecules using an acid, metal and peroxide-free approach (Scheme 1e).

Our study commenced by examining a one-pot reaction between *trans*-stilbene **1a**, benzaldehyde **2a**, and ammonium acetate in DMSO for 1 hour in the presence of 1 equivalent molecular iodine. Unfortunately, the desired product **3a** was not detected and only starting material was recovered (Table 1, entry 1). Next, we repeated the experiment except the reaction time was increased to 24 hours, however, the desired product was still not detected (Table 1, entry 2). Based on these observations, we turned our attention towards a one-pot, two-step process where *trans*-stilbene **1a** was reacted with molecular iodine in DMSO for 24 hours at 155 °C, thereafter, benzaldehyde **2a** and ammonium acetate were added, and the mixture was further refluxed for 1 hour. Under these conditions, the desired product was obtained in a moderate but encouraging isolated yield of 37% (Table 1, entry 3). The syntheses of 2,4,5-trisubstituted imidazoles are

Table 1. Optimization of reaction conditions for the formation of 2,4,5-triphenylimidazole from *trans*-stilbene^a

Entry	Conditions	Solvent	Yield (%) ^b
1 ^c	I ₂ /DMSO	–	N. R
2 ^d	I ₂ /DMSO	–	N. R
3	I ₂ /DMSO	–	37
4	I ₂ /DMSO	DMF	42
5	I ₂ /DMSO	hexane	Trace
6	I ₂ /DMSO	PhMe	22
7	I ₂ /DMSO	EtOH	48
8 ^e	I ₂ /DMSO	<i>n</i> -BuOH	62
9 ^f	I ₂ /DMSO	<i>n</i> -BuOH	65
10	I ₂ /DMSO	<i>n</i> -BuOH	85
11 ^g	I ₂ /DMSO	<i>n</i> -BuOH	58
12 ^h	I ₂ /DMSO	<i>n</i> -BuOH	38
13 ⁱ	I ₂ /DMSO	<i>n</i> -BuOH	N. R
14 ^j	I ₂ /DMSO	<i>n</i> -BuOH	18
15 ^k	I ₂ /DMSO	<i>n</i> -BuOH	N. R
16 ^l	I ₂ /PhMe	<i>n</i> -BuOH	N. R
17 ^m	I ₂ /H ₂ O	<i>n</i> -BuOH	N. R
18 ⁿ	I ₂ /MeCN	<i>n</i> -BuOH	Trace
19 ^o	DMSO	<i>n</i> -BuOH	N. R
20	I ₂ O ₅ /DMSO	<i>n</i> -BuOH	N. R
21	3-iodobenzoic acid/ DMSO	<i>n</i> -BuOH	Trace
22 ^p	I ₂ /DMSO	<i>n</i> -BuOH	N. R
23 ^q	I ₂ /DMSO	<i>n</i> -BuOH	N. R

^a Reaction conditions: Step 1: **1a** (0.5 mmol), I₂ (1 equiv.) / DMSO (0.5 mL), 20 h, 155 °C. Step 2: **2a** (0.5 mmol), NH₄OAc (10 equiv.), Solvent (2 mL), reflux, 1 h. ^b Isolated yield. ^c One pot, one step for 1 h. ^d One pot, one step for 24 h. ^e I₂ (1 equiv.) / DMSO (0.5 mL). ^f I₂ (1 equiv.) / DMSO (1 mL). ^g I₂ (1.5 equiv.) / DMSO (0.5 mL). ^h I₂ (1.5 equiv.) / DMSO (1.5 mL). ⁱ I₂ (2 equiv.) / DMSO (2 mL). ^j Step 1 for 24 h, 115 °C.

^k Step 1 at 80 °C. ^l Step 1 reflux. ^m Step 1 reflux. ⁿ Step1 reflux. ^o Absence of Molecular Iodine. ^p NH₄OAc (5 equiv.). ^q NH₄OAc (3 equiv.) N. R: No reaction.

known to be solvent-specific,^{22,23} and a range of organic solvents were examined (DMF, hexane and toluene), however, in all cases, trace to moderate yields were observed (Table 1, entries 4 – 6). Ethanol is known to favour the three-component imidazole reaction,^{24,25} however, in this case, (Table 1, entry 7) the target imidazole was formed in a moderate yield of 48%. Recently, *n*-butanol has been reported as the best solvent for a multicomponent coupling reaction between an α -diketone, aldehyde and ammonia which produced 2,4,5-trisubstituted imidazoles in excellent yields.²⁶ Inspired by this result, the use of *n*-butanol as a solvent, in the current synthesis, produced the desired imidazole in an improved yield of 62% (Table 1, entry 8).

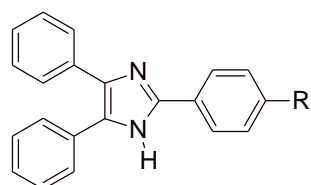
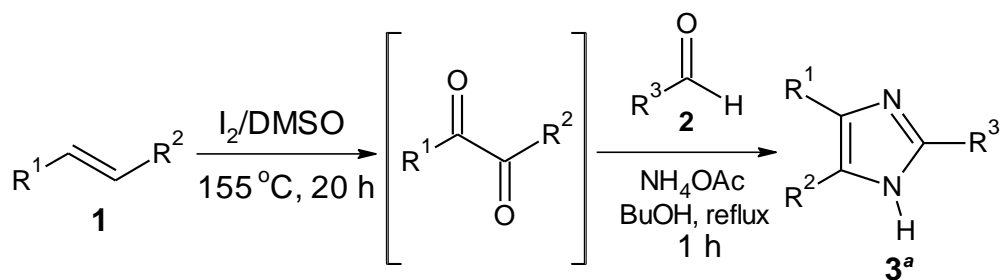
To find the optimal catalyst loading for this reaction, the iodine quantity and DMSO volumes were varied. When the volume of DMSO was increased to 1 mL, it afforded the 2,4,5-trisubstituted imidazole in an isolated yield of 65% (Table 1, entry 9). Increasing the molecular iodine quantity to 1.25 equivalents and decreasing the DMSO volume to 0.5 mL resulted in the formation of the desired product **3a** in a good, isolated yield of 85% (Table 1, entry 10). Using 1.5 equivalents of molecular iodine in 0.5 mL DMSO decreased the amount of the desired product to 58% (Table 1, entry 11) while increasing the volume of DMSO to 1.5 mL decreased the desired product even further to 38% (Table 1, entry 12). Increasing both the iodine quantity to 2 equivalents and DMSO volume to 2 mL resulted in no product formation and the recovery of the starting materials (Table 1, entry 13). It was clear that the amount of iodine and DMSO affects the reaction and may be due to DMSO playing multiple roles in the system.

We then attempted to decrease the temperature to 115 °C for the first step but this change resulted in a diminished isolated yield of 18% (Table 1, entry 14). Further decrease in temperature to 80 °C resulted in no product formation and only the starting material was recovered (Table 1, entry 15). To determine if DMSO is the ideal coupling partner for iodine, we examined toluene (PhMe), acetonitrile (MeCN), and water as potential iodine coupling partners. No product was obtained in toluene and water (Table 1, entries 16 and 17), whereas only trace amounts were obtained in acetonitrile (Table 1, entry 18) signifying the critical role of DMSO.

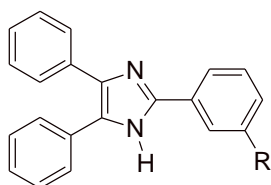
When molecular iodine was omitted, no reaction occurred (Table 1, entry 19) implying that iodine is essential for this reaction. Other non-metal, iodine-containing catalysts were also examined to determine if indeed molecular iodine is the best iodine source. When iodopentoxide (I₂O₅) was used, no product was obtained (Table 1, entry 20) while the use of 3-iodobenzoic acid afforded the desired product in trace amounts (Table 1, entry 21) suggesting that molecular iodine is the best iodine source for this system. In

previous imidazole syntheses, fluctuating amounts of ammonium acetate have been used^{27,28} and we varied its amount by using 5 and 3 equivalents, however, under these conditions, no product was obtained (Table 1, entries 22 and 23). Therefore, the conditions described in Table 1, entry 10, were found to be the optimal as it allowed for maximum formation of the desired product.

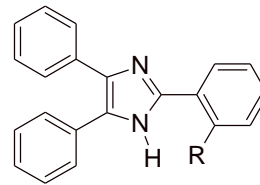
With the optimized conditions in hand, the substrate scope for substituted internal alkenes against various aromatic aldehydes was explored and the results are depicted in Scheme 2. The varying of benzaldehyde derivatives substituted at the *para*-position afforded 2,4,5-trisubstituted imidazoles in good yields of 83 and 87% (Scheme 2, entries 3b and 3c). Varying the benzaldehyde derivatives that are *meta*-substituted with electron-withdrawing groups afforded the imidazoles in good yields of 73% – 75% (Scheme 2, entries 3d – 3f). Moderate yields of 61% – 66% were obtained when *ortho*-substituted benzaldehyde derivatives bearing electron-donating groups were used (Scheme 2, entries 3g and 3h). Encouraged by these results, a bulky aldehyde, 2-naphthaldehyde, was employed which afforded the 2-(naphthalen-2-yl)-4,5-diphenyl-1*H*-imidazole in a good yield of 79% (Scheme 2, entry 3i). To diversify our scope, a five-membered ring aldehyde bearing a heteroatom (2-thiophenecarboxaldehyde) was employed which afforded the corresponding imidazole in 43% isolated yield (Scheme 2, entry 3j). The use of an aliphatic aldehyde such as hexanal was not successful and only starting material was recovered (Scheme 2, entry 3k) while cyclohexane-2-carboxaldehyde afforded the desired product in trace amounts (Table 2, entry 3l). This is in accordance with the literature, as aliphatic aldehydes are often problematic in imidazole synthesis and normally result in poor yields of corresponding imidazoles.²⁹ The use of diverse alkenes, but-2-ene, and *trans*- β -methylstyrene were found to be incompatible with this system as they resulted in no product formation and the recovery of the starting materials. (Scheme 2, entries 3m and 3n respectively). To expand this scope, the use of 4-bromostilbene as a starting material and benzaldehyde afforded the corresponding imidazole as a mixture of tautomers in a good yield of 74% (Scheme 2, entry 3o) while the use of a *para*-substituted bromobenzaldehyde afforded the corresponding imidazole in a good yield of 78%, also as a mixture of tautomers (Table 2, entry 3p).



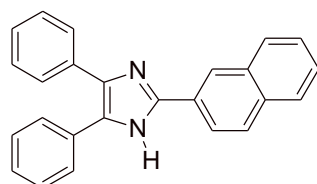
3a, R = H, 85%
3b, R = Cl, 83%
3c, R = Br, 87%



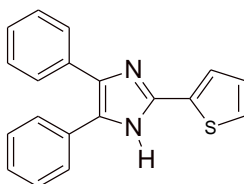
3d, R = NO₂, 73%
3e, R = Br, 75%
3f, R = Cl, 73%



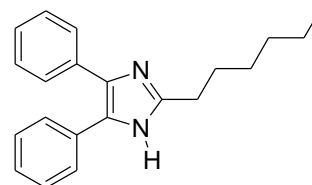
3g, R = OMe, 66%
3h, R = Me, 61%



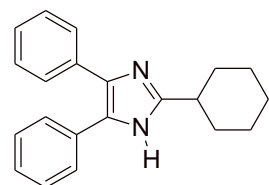
3i, 79%



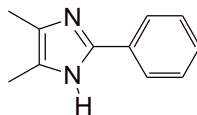
3j, 43%



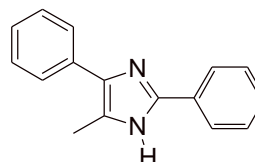
3k, 0%^b



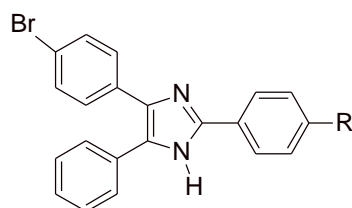
3l, Trace^c



3m, 0%^d



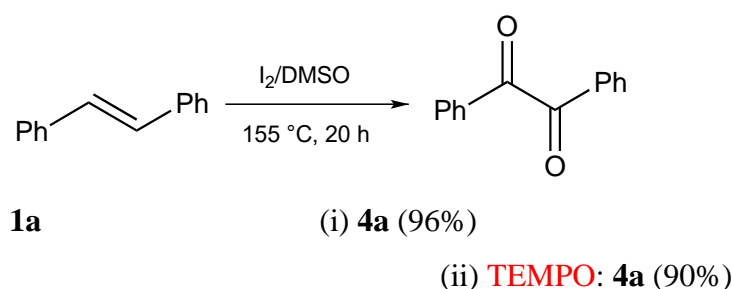
3n, 0%^d



3o, R = H, 74%^e
3p, R = Br, 78%^e

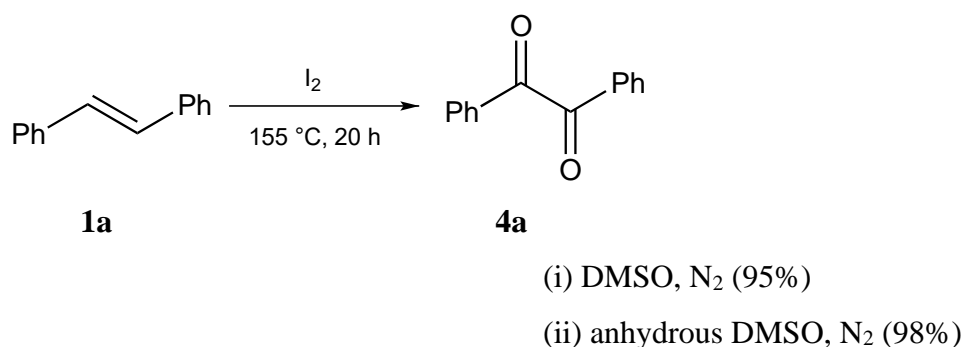
Scheme 2. Reaction conditions: Step 1: **1** (0.5 mmol), I₂ (1.25 equiv.) in DMSO (0.5 mL) at 155 °C for 20 h. Step 2: **2** (0.5 mmol), NH₄OAc (5 mmol) in *n*-BuOH (1 mL) reflux for 1 h. ^a Isolated yield. ^b Step 2 for 24 h. ^c Step 2 for 48 h. ^d Step 1 for 24 h. ^e Mixture of tautomers.

To gain insight into the reaction mechanism, various control experiments were carried out and firstly, *trans*-stilbene **1a** was reacted with I₂/DMSO at 155 °C for 20 hours to afford benzil **4a** an isolated yield of 96% (Scheme 3, reaction i). This result indicates that the α-diketone is indeed a key intermediate in the trisubstituted imidazole synthesis. To provide more information on the α-diketone formation, a radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO) was added to the reaction mixture under the same conditions and benzil was still formed in an isolated yield of 90% (Scheme 3, reaction ii). This suggests that the α-diketone formation does not proceed via a radical pathway.



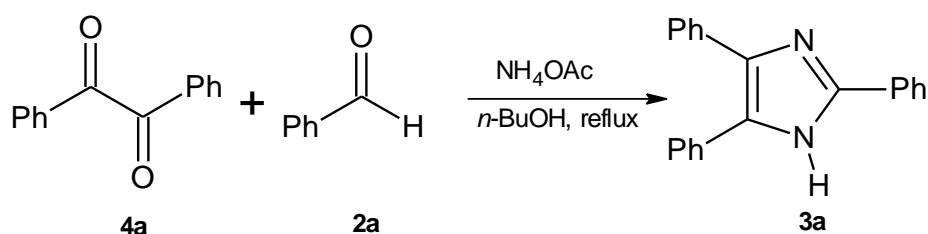
Scheme 3. Control experiments into the formation of the α-diketone

Next, we focused our attention on determining the oxygen source in the formation of the key α-diketone. Hypothetically, there are three possible sources of oxygen for the preparation of benzil from *trans*-stilbene, namely, molecular oxygen from the air, trace water in DMSO, and DMSO itself. To determine the oxygen source for this transformation, the benzil synthesis was first conducted under inert conditions and **4a** was obtained at an isolated yield of 95% (Scheme 4, reaction i), suggesting that oxygen from the air is not part of this system. Next, this oxidation reaction was then conducted under inert conditions using anhydrous DMSO, and **4a** was still obtained at an isolated yield of 98% (Scheme 4, reaction ii). This indicates trace water from the DMSO is not the source of oxygen and that DMSO is the source of oxygen in the formation of α-diketone.



Scheme 4. Control experiments into the source of the oxygen atoms in the formation of benzil

Thereafter, the coupling step was examined whereby benzil **4a**, benzaldehyde **2a**, and ammonium acetate were refluxed in *n*-butanol to form the 2,4,5-triphenylimidazole. In the presence of molecular iodine, the imidazole was formed in an isolated yield of 87% (Scheme 5, reaction i). This suggests that iodine is part of coupling process and assists in imidazole formation. Interestingly, in the absence of molecular iodine, the imidazole was still obtained in an isolated yield of 56% (Scheme 2, reaction ii). We speculate this observation is due to the reaction being catalyzed by the solvent (*n*-butanol) via hydrogen bonding as trisubstituted imidazole synthesis is known to proceed in the absence of catalyst in polar, protic solvents.³⁰ Finally, the addition of TEMPO had little impact on the reaction as the target imidazole was still formed in a yield of 85% suggesting that the coupling step does not proceed by a radical pathway.



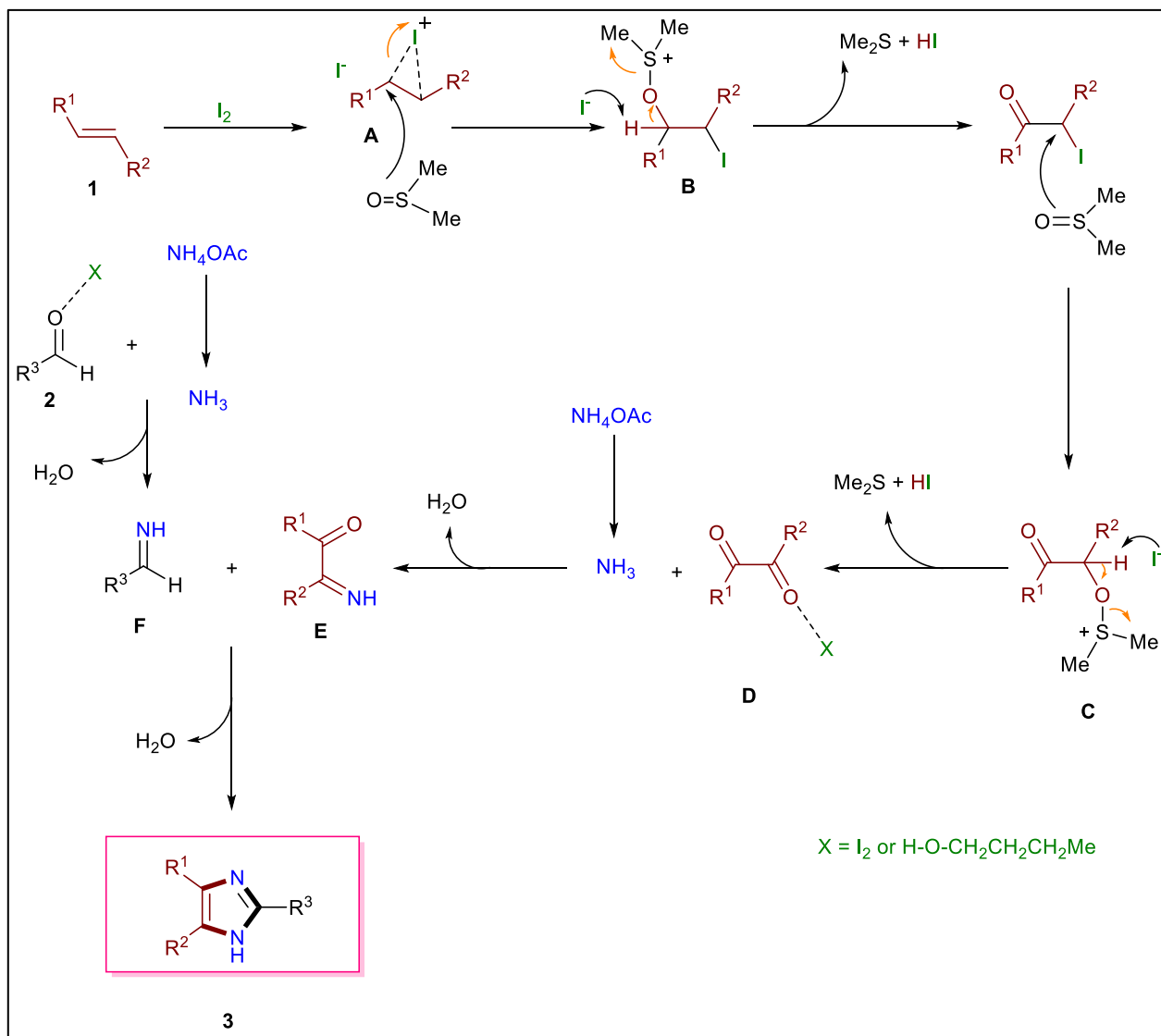
(i) I_2 (87%)

(ii) No I_2 (56%)

(iii) I_2 , TEMPO (85%)

Scheme 5. Analysis of the coupling step for the formation of 2,4,5-triphenylimidazole

Based on the results from the control experiments as well as literature reports,³¹⁻³⁵ a plausible mechanism is outlined in Scheme 6. The reaction commences with the activation of the double bond of the alkene by iodine to form iodonium intermediate **A**. Next, a molecule of DMSO attacks **A** to form intermediate **B**, whilst releasing dimethyl sulfide to generate an iodoketone. The generated iodoketone is then trapped by a molecule of DMSO to form intermediate **C**, which proceeds to form a α -diketone, while simultaneously releasing another molecule of dimethyl sulfide. Concurrently, α -diketone **D** and an aldehyde **2** are activated by either iodine or hydrogen bonding from *n*-butanol and upon reaction with ammonia forms imine intermediate **E** and **F** which undergo cyclocondensation to afford the desired 2,4,5-trisubstituted imidazole.



Scheme 6. Proposed route to 2,4,5-trisubstituted imidazoles commencing from internal alkenes

In conclusion, an innovative method using I_2 /DMSO system to prepare 2,4,5-trisubstituted imidazoles commencing from internal alkenes and aldehydes has been developed. This methodology was applied to a variety of substrates and the target imidazole derivatives were prepared in moderate to good yields. Preliminary mechanistic investigations suggested that an α -diketone is indeed a key intermediate and that the reaction is catalyzed by molecular iodine and *n*-butanol.

EXPERIMENTAL

All reagents were purchased and used without further purification. All 1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance III Spectrometer operating at either 400 or 500 MHz. Chemical shifts (δ) were reported in ppm using deuterated dimethyl sulfoxide (DMSO- d_6) residual

peak (δ 2.50) for ^1H -NMR. Chemical shifts of ^{13}C -NMR were reported relative to $\text{DMSO-}d_6$ (δ 39.51). The following abbreviations were used to describe peak splitting patterns where appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, J , were reported in Hertz units (Hz). Low-Resolution electron-spray ionization (ESI) mass spectra were recorded on a time-of-flight (TOF) micromass spectrometer. Infrared (IR) spectra were recorded on Agilent Carey 630 Spectrometer. Melting points were determined using the Kofler-hot stage melting point apparatus and are uncorrected.

Typical Procedure for the preparation of 2,4,5-trisubstituted imidazoles (3): Alkene (0.5 mmol) and iodine (0.625 mmol) were mixed in a 10 mL test tube with 0.5 mL DMSO and heated at 155 °C for 20 h. Thereafter, aldehyde (0.5 mmol), ammonium acetate (5 mmol), and *n*-butanol (1 mL) were added, and the mixture was refluxed for 1 h. After cooling, 10 mL of sodium thiosulfate/ice-cold water was added to the mixture where the crude product was precipitated, filtered, and dried in an oven. The crude precipitate was recrystallized from acetone: water (9:1) solution to yield the desired product.

2,4,5-Triphenyl-1H-imidazole (3a, $\text{C}_{21}\text{H}_{16}\text{N}_2$, 85%):³⁶ as a white solid; mp 269-271 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 12.69 (s, 1H), 8.11-8.09 (d, $J = 7.45$ Hz, 2H), 7.55 – 7.51 (m, 4H), 7.47 – 7.40 (m, 3H), 7.38 – 7.26 (m, 6H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 146.0, 137.6, 135.7, 131.6, 129.2, 129.1, 128.9, 128.7, 128.65, 128.2, 127.6, 127.0, 126.7; $\tilde{\nu}$ (neat, cm^{-1}): 3734, 3021, 1592, 1488, 1461, 1127; ESI-MS (m/z): 295.1240 (100) [M-H^+], 296.1268 (25) [M^+].

2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole (3b, $\text{C}_{21}\text{H}_{15}\text{N}_2\text{Cl}$, 83%):^{37,38} Creamy white solid; mp 261-263 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 12.77 ppm (s, 1H), 8.12-8.10 ppm (d, $J = 8.41$ Hz, 2H), 7.57 – 7.54 (d, $J = 8.67$ Hz, 2H), 7.53 – 7.51 (m, 2H), 7.48 – 7.43 (m, 2H), 7.41 – 7.38 (m, 2H), 7.26 – 7.22 (m, 1H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 144.9, 137.8, 135.5, 133.2, 129.7, 129.2, 129.1, 129, 128.9, 128.7, 128.3, 127.6, 127; $\tilde{\nu}$ (neat, cm^{-1}) = 2638.7, 1482, 1126, 766; ESI-MS (m/z) = 329.0857 (100) [M-H^+], 331.0836 [M+H^+].

2-(4-Bromophenyl)-4,5-diphenyl-1H-imidazole (3c, $\text{C}_{21}\text{H}_{15}\text{BrN}_2$, 87%):^{39,40} mp 256-258 °C ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 12.78 (s, 1H), 8.06 – 8.03 (d, $J = 8.57$ Hz, 2H), 7.70 – 7.68 (d, $J = 8.52$ Hz, 2H), 7.53 (m, 4H), 7.48 – 7.22 (m, 6H); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 145, 137.9, 135.5, 132.1, 131.06, 130, 129.5, 129.1, 128.9, 127.6, 121.9; $\tilde{\nu}$ (neat, cm^{-1}) : 3430, 2648, 2109, 1596, 1478, 1124, 764; ESI-MS (m/z): 375.03 (100) [M+H^+], 376.04 (25) [M+2H^+].

2-(3-Nitrophenyl)-4,5-diphenyl-1H-imidazole (3d, $\text{C}_{21}\text{H}_{15}\text{O}_2\text{N}_3$, 73%):^{37,38} yellow solid; mp 315-317 °C; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 13.08 (s, 1H), 8.96 (s, 1H), 8.53 – 8.51 (d, $J = 8.01$ Hz, 1H), 8.22

– 8.19 (d, $J = 8.23$ Hz, 1H), 7.80 – 7.75 (t, $J = 8.00$ Hz, 1H), 7.57 – 7.52 (m, 4H), 7.46 – 7.33 (m, 6H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 148.8, 143.9, 138.2, 135.2, 132.3, 131.6, 131.1, 130.8, 130, 129.2, 128.9, 128.7, 127.6, 127.3, 123, 119.9; $\tilde{\nu}$ (neat, cm^{-1}): 2853, 1584, 1524, 1471, 1346, 1418, 1252, 1073; ESI-MS (m/z): 343.1117 (15) $[\text{M}+2\text{H}]^+$, 342.1087 $[\text{M}+\text{H}]^+$.

2-(3-Bromophenyl)-4,5-diphenyl-1H-imidazole (3e, $\text{C}_{21}\text{H}_{15}\text{BrN}_2$, 75%):⁴¹ Yellow solid; mp 300–301 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 12.82 (s, 1H), 8.32 (m, 1H), 8.10 – 8.09 (d, $J = 8.11$ Hz, 1H), 7.56 – 7.22 (m, 12H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 144.35, 137.92, 135.4, 133, 131.3, 131.2, 129.3, 129.1, 128.9, 128.7, 128.4, 128, 127.6, 127.1, 124.5, 122.6; $\tilde{\nu}$ (neat, cm^{-1}): 3025, 1687, 1578, 1458, 1070, 846, 695; ESI-MS (m/z): 375.0492 (100) $[\text{M}+\text{H}]^+$, 377.0478 (100), 376.0537 (30) $[\text{M}+2\text{H}]^+$.

2-(3-Chlorophenyl)-4,5-diphenyl-1H-imidazole (3f, $\text{C}_{21}\text{H}_{15}\text{ClN}_2$, 73%):⁴² white solid; mp 297–299 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 12.85 (s, 1H), 8.16 (s, 1H), 8.08 – 8.05 (d, $J = 7.89$ Hz, 1H), 7.56 – 7.29 (m, 12H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 144.5, 134.1, 132.8, 131.1, 128.9, 128.4, 128.2, 127.8, 125.1, 124.2; $\tilde{\nu}$ (neat, cm^{-1}): 3377, 1580, 1455, 1129, 767; ESI-MS (m/z): 329.1046 (100) $[\text{M}-\text{H}]^+$, 331.1026 $[\text{M}+\text{H}]^+$, 332.1050 $[\text{M}+2\text{H}]^+$.

2-(2-Methoxyphenyl)-4,5-diphenyl-1H-imidazole (3g, $\text{C}_{22}\text{H}_{18}\text{ON}_2$, 66%):^{43,44} White solid; mp 207–209 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 11.88 (s, 1H), 8.08–8.05 (d, $J = 7.66$ Hz, 1H), 7.55–7.53 (d, $J = 7.45$ Hz, 2H), 7.49 – 7.47 (m, 2H), 7.45 – 7.42 (t, $J = 7.55$ Hz, 2H), 7.39 – 7.37 (m, 2H), 7.32 – 7.28 (t, $J = 7.51$ Hz, 2H), 7.23 – 7.20 (m, 1H), 7.18 – 7.16 (d, $J = 8.12$ Hz, 1H), 7.10 – 7.06 (t, $J = 7.51$ Hz, 1H), 3.93 (s, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 156.5, 143.6, 136.9, 135.8, 131.7, 130.2, 129.3, 129.08, 129.02, 128.6, 127.9, 127.6, 126.9, 121, 119.4, 112.1, 56.04; $\tilde{\nu}$ (neat, cm^{-1}): 3064, 2839, 1590, 1527, 1472, 1391; ESI-MS (m/z): 327.1439 (100) $[\text{M}+\text{H}]^+$, 349.1248 (30).

2-(2-Methylphenyl)-4,5-diphenyl-1H-imidazole (3h, $\text{C}_{22}\text{H}_{18}\text{N}_2$, 61%):^{21,45} White solid; mp 228–230 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 12.48 (s, 1H), 7.73 (m, 1H), 7.55 (m, 4H), 7.34 – 7.30 (m, 9H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 146.6, 136.7, 131.5, 130.5, 129.2, 128.8, 128.7, 127.9, 127.6, 126.9, 126.2, 21.6; $\tilde{\nu}$ (neat, cm^{-1}): 3151, 2961, 2102, 1646, 1398, 1316; ESI-MS (m/z): 311.1480 $[\text{M}+\text{H}]^+$, 312.1516 (10) $[\text{M}+2\text{H}]^+$.

2-(2-Naphthyl)-4,5-diphenyl-1H-imidazole (3i, $\text{C}_{25}\text{H}_{18}\text{N}_2$, 79%):⁴⁶ White solid; mp 274–276 °C; ^1H NMR (400 MHz, DMSO- d_6) δ 12.60 (s, 1H), 8.64 (s, 1H), 8.30 – 8.27 (d, $J = 8.60$ Hz, 1H), 8.03 – 7.94 (m, 3H), 7.60 – 7.51 (m, 6H), 7.41 – 7.30 (m, 6H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 146, 136, 133.5, 133.2, 128.9, 128.7, 128.6, 128.3, 128.2, 127.7, 127.2, 126.8, 124.2, 124; $\tilde{\nu}$ (neat, cm^{-1}): 2761.3, 1589.3, 1498, 1447, 1409, 1343, 1264, 1072; ESI-MS (m/z): 347.1555 (100), 348.1612 (30).

4,5-Diphenyl-2-(thienyl)-1H-imidazole (3j, C₁₉H₁₄N₂S, 43%):²⁶ Brown solid; mp 258-260 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.78 (s, 1H), 7.70 – 7.69 (d, *J* = 3.68 Hz, 1H), 7.56 – 7.40 (m, 8H), 7.31 (m, 2H), 7.25 – 7.16 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 142.1, 137.3, 135.3, 134.4, 131.3, 129.6, 129.2, 128.8, 128.6, 128.4, 128.3, 127.6, 127.1, 126.7, 124.2; $\tilde{\nu}$ (neat, cm⁻¹): 3381, 1650, 1002; ESI-MS (*m/z*): 301.0802 (100) [M-H]⁺, 302.0837 (25) [M⁺], 303.0798 [M+2H]⁺.

5-(4-Bromophenyl)-2,4-diphenyl-1H-imidazole (3o, C₂₁H₁₅BrN₂, 74%):¹⁹ White solid; mp 254-256 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.75 (s, 1H), 8.10 – 8.08 (d, *J* = 7.44 Hz, 2H), 7.57 – 7.37 (m, 12H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 146.3, 131.8, 130.7, 129.9, 129.2, 129.1, 128.8, 128.6, 128, 125.7; $\tilde{\nu}$ (neat, cm⁻¹): 3046, 2825, 1562, 1461, 979, 767; ESI-MS (*m/z*): 375.0597 (100) [M+H]⁺, 376.0633 (24).

2,5-Bis-(4-bromophenyl)-4-phenyl-1H-imidazole (3p, C₂₁H₁₄Br₂N₂, 78%):¹⁹ Creamy white solid; mp 253-256 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.83 (s, 1H), 8.05 – 8.03 (d, *J* = 8.62 Hz, 2H), 7.70 – 7.68 (d, *J* = 8.67 Hz, 2H), 7.53 – 7.34 (m, 9H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 145.3, 132.1, 131.8, 129.9, 129.1, 128.5, 128.1, 127.6, 122; $\tilde{\nu}$ (neat, cm⁻¹): 3063, 2828, 1601, 1477, 1069, 825, 722; ESI-MS (*m/z*): 452.9750 (100) [M+H]⁺, 450.9771 (50) [M-H]⁺, 455.9761 (15).

Benzil (4a, C₁₄H₁₀O₂, 96%):^{47,48} Yellow solid, ¹H-NMR (400 MHz, DMSO-*d*₆) δ 8.01 – 7.99 (d, *J* = 8.27 Hz, 4H), 7.7 – 7.66 (t, *J* = 7.43 Hz, 2H), 7.56 – 7.51 (t, *J* = 7.78 Hz, 4H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 194.6, 134.9, 133, 129.9, 129.

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