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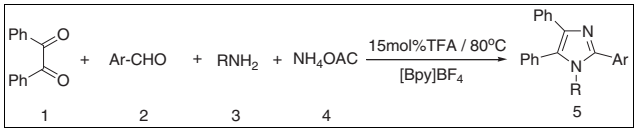

The four-component condensation of benzil, aromatic aldehyde, primary amine, and ammonium acetate catalyzed by TFA in ionic liquid [Bpy]BF_4 at 80°C provided 1,2,4,5-tetrasubstituted imidazoles in moderate to high yields.

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INTRODUCTION

The development of a simple, efficient, and environmentally synthetic method for widely used organic compounds from readily available reagents is one of the major challenges for the chemists' world [1]. With a wide range of applications, imidazoles are receiving growing attention in recent years [2]. Compounds containing imidazole moiety have many pharmacological properties and play important roles in biochemical processes [3]. In addition with different substitutions, imidazoles have variable biological activities such as anti-allergic activity [4], anti-inflammatory activity [5], and analgesic activity [6]. Besides being known as inhibitors of p38MAP kinase [7], various substituted imidazoles also act as therapeutic agents [8], plant growth regulators [9], and glucagon receptors [10]. Moreover, a recent report indicates that synthetic imidazoles are potent inhibitors of protein–protein interactions [11]. So, it is much in demand to find simple and efficient methods for their synthesis.

In the last decades, many methods have been developed for the synthesis of tetra-substituted imidazoles: (a) four-component condensation of a 1,2-diketone, aldehyde, primary amine, and ammonium acetate using BF_3–SiO_2 [12], silica gel–$NaHSO_4$ [13], $HClO_4$–SiO_2 [14], $K_5CoW_{12}O_{40}\cdot 3H_2O$ [15], $InCl_3\cdot 3H_2O$–MeOH [16], L–proline–MeOH [17], I_2–EtOH [18], HPA–EtOH [19], zeolite–HY–$Cu(NO_3)_2$ [20], MCM-41 or *p*-TsOH [21], 1-butyl-3-methylimidazolium bromide [22], and Brønsted acidic ionic liquid [23] as catalyst; (b) hetero-Cope rearrangement [3]; (c) condensation of 1,2-diketone with an aryl nitrile and primary amine under microwave irradiation [25]; and (d) reaction of mesoionic 1,3-oxazolium-5-olates with *N*-(arylmethylene) benzenesulfonamides [26].

However, some methods suffer disadvantages such as tedious workup, low yields, longer reaction time, or using hazard organic solvents [27]. Hence, the development of clean, high yielding, and environmental benign approaches is still desirable and much in demand.

In this article, we report an efficient and simple strategy to construct the framework of 1,2,4,5-tetrasubstituted imidazole. The procedure involved the mixing of commercially available benzil (**1**), aromatic aldehyde (**2**), primary amine (**3**), and ammonium acetate (**4**) in ionic liquid [Bpy]BF_4 at 80°C catalyzed by TFA (Scheme 1).

RESULTS AND DISCUSSION

Initially, to optimize reaction condition, some catalysts were screened first when benzil, *p*-fluorobenzaldehyde, *p*-fluoraniline, and ammonium acetate were chosen as substrates (Table 1). It was shown that 15 mol% of TFA is the suitable one (entry **8**), which may attribute to its suitable acidity, for the ones with stronger or weaker acidity have no advantages in this reaction. Consequently, all further studies were conducted using 15 mol% of TFA as catalyst.

Having established the best catalyst, the effect of solvents and temperature on the model reaction was subsequently investigated (Table 2). Among the tested solvents such as ethanol, THF, DMF, acetone, H_2O, chloroform, [Bmim]Br, [Bpy]Br, and [Bpy]BF_4, [Bpy]BF_4 gave the highest yield (entry **11**). It was observed that the suitable temperature was 80°C.

So, the mixture of benzil (**1**), aromatic aldehyde (**2**), amine (**3**), ammonium acetate (**4**), and [Bpy]BF_4 was stirred in the presence of 15 mol% of TFA at 80°C for 1.5–3 h to give the corresponding compounds (**5**) (Table 3). In all the cases, 1,2,4,5-tetrasubstituted imidazoles have been obtained in moderate to high yields in short times (1.5–3 h). It was important to note that the process tolerates both electron-donating groups such as hydroxyl (entry **5k**) and alkoxyl

Scheme 1. One-pot synthesis of 1,2,4,5-tetrasubstituted imidazole.

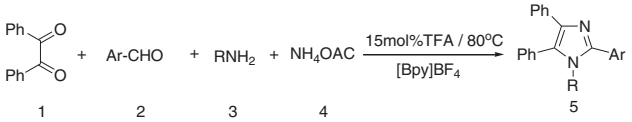


Table 1

The influence of catalysts on the yield of **5x**.

Entry	Catalyst	Catalyst (mol%)	Isolated yield (%)
1	HCl	15	NP
2	H_2SO_4	15	NP
3	HCOOH	15	Nr
4	SSA	15	NP
5	CH_3COOH	15	Nr
6	CF_3COOH	5	30
7	CF_3COOH	10	55
8	CF_3COOH	15	87
9	CF_3COOH	20	87
10	CF_3COOH	25	86

Reaction condition: benzil (1 mmol), *p*-fluorobenzaldehyde (1 mmol), *p*-fluoraniline (1 mmol), and ammonium acetate (5 mmol) in ionic liquid [Bpy]BF_4 (2 mL) at 80°C for 2 h. NP, no desired products; Nr, no reaction; SSA, silica sulfuric acid.

Table 2

The influence of solvents and temperature on the synthesis of **5x**.

Entry	Solvent	T(°C)	Isolated yield (%)
1	C_2H_5OH	80	10
2	THF	80	Nr
3	DMF	80	Nr
4	CH_3COCH_3	80	Nr
6	H_2O	80	Nr
7	$CHCl_3$	80	Nr
8	[Bmim]Br	80	56
9	[Bpy]Br	80	61
10	[Bmim]BF_4	80	74
11	[Bpy]BF_4	80	87
12	[Bpy]BF_4	90	87
13	[Bpy]BF_4	100	86
14	[Bpy]BF_4	70	65
15	[Bpy]BF_4	60	54
16	[Bpy]BF_4	r.t.	0

Reaction condition: benzil (1 mmol), *p*-fluorobenzaldehyde (1 mmol), *p*-fluoraniline (1 mmol), and ammonium acetate (5 mmol) in [Bpy]BF_4 (2 mL) for 2 h catalyzed by 15 mol% of TFA. Nr, no reaction.

group (entry **5e**) and electron-withdrawing substituents (such as halide groups) on the aldehyde and amine. The groups on the meta-position of the amine has produced low to moderate yields of the corresponding imidazoles and took longer reaction time, which illustrated that the steric hindrance may have a certain impact on the reaction. On the other hand, the cyclohexylamine gave the lower yield, which may be due to its lower activity and bigger steric hindrance.

The probable mechanism was shown in Scheme 2. The first step involved the acid-catalyzed reaction of amine (**3**) with aromatic aldehyde (**2**), which acted as the source of methylene to give imine (**A**) as the first key intermediate. The addition of (**A**) to nucleophiles NH_3 then gave the intermediate (**B**). Subsequently, the intermediate (**B**) condensed with the activated benzil to form the intermediate (**D**). Then, the dehydration and rearranging of (**D**) and (**E**) via [1,5] sigmatropic shift to give the final imidazoles (**F**).

In summary, we described a simple and convenient method for the synthesis of 1,2,4,5-tetrasubstituted imidazoles in [Bpy]BF_4 at 80°C in the presence of TFA. Both aromatic aldehyde and aliphatic aldehyde can be used as substrates. In addition, the method has many advantages such as facile operations, the wide application of substrate, convenient post-processing, and short reaction times (1.5–3 h).

EXPERIMENTAL

All reagents were purchased from commercial sources and used without further purification. NMR spectra were recorded on a Bruker Avance DMX400 (Hitachi, Japan) spectrometer in $CDCl_3$ with TMS as an internal standard. Infrared spectra were recorded on Bruker FTIR-Tensor 27 spectrometer expressed in cm^{-1} (KBr). Mass was determined by using a Bruker Micro TOF-MS high-resolution mass spectrometer. TLC analysis was performed with glass-backed plates precoated with silica gel and examined under UV (254 nm).

Synthesis of 1,2,4,5-tetrasubstituted imidazoles. The mixture of benzil (1 mmol), aromatic aldehyde (1 mmol), primary amine (1 mmol), and ammonium acetate (5 mmol) was taken in a 50-mL round-bottom flask containing 15 mol% of TFA and [Bpy]BF_4 (2 mL) and stirred at 80°C for the given time. After completion of reaction (monitored by TLC), it was diluted with water (15–20 mL); the precipitate was filtered, washed with water to neutral and dried, then crystallized from 95% ethanol to give the pure product.

We found that when more than one equivalent ammonium acetate was used, the reaction will show better results. Thus, the molar ratio of benzil to ammonium acetate was kept at 1:5.

Spectral data for new compounds.

1-(4-Chlorophenyl)-2,4,5-triphenyl-1H-imidazole (5a). mp 198–199°C; IR (KBr) ν: 3053, 2911, 1600, 1513, 1493, 1444, 1396, 1370, 1272, 1139, 1090, 1074, 1019, 959, 843, 770, 754, 705, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.19 (t, J = 7.2 Hz, 1H, Ar H), 7.24–7.35 (m, 12H, Ar H), 7.39–7.41 (m, 4H, Ar H), 7.50 (d, J = 7.6 Hz, 2H, Ar H); HRMS: Calcd for $C_{27}H_{19}Cl\,N_2$ $[M+H]^+$; found (expected): 407.1548 (407.1316).

2-(4-Bromophenyl)-1-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole(5b). mp 210–212°C; IR (KBr) ν: 3063, 2954, 1601, 1564, 1491, 1441, 1411, 1370, 1319, 1272, 1180, 1169, 1137, 1089, 1073, 1017, 1006, 983, 960, 915, 841, 832, 786, 772, 752, 726, 712, 676, 650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.18 (t, J = 6.8 Hz, 1H, Ar H), 7.24–7.34 (m, 13H, Ar H), 7.39–7.41 (m, 2H, Ar H), 7.51 (d, J = 7.6 Hz, 2H, Ar H); HRMS: Calcd for $C_{27}H_{18}BrClN_2$ $[M+H]^+$; found (expected): 485.0640 (485.0421).

1-(4-Chlorophenyl)-2-(3,4,5-trimethoxyphenyl)-4,5-diphenyl-1H-imidazole (5c). mp 192–194°C; IR (KBr) ν: 3029, 2927,

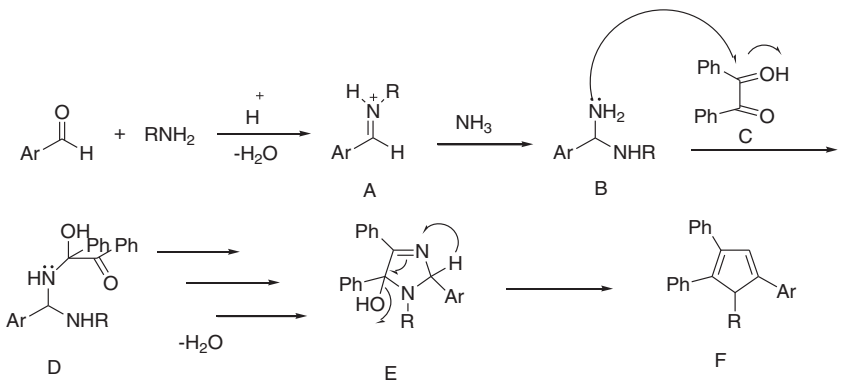
Table 3

Synthesis of tetrasubstituted imidazoles 5 in ionic liquid.

Entry	Ar	R	*t* (h)	Isolated yield (%)	Lit. yield (%)
5a	C_6H_5	4-ClC_6H_4	2	87	
5b	4-BrC_6H_4	4-ClC_6H_4	2	89	
5c	3,4,5-$(CH_3O)_2C_6H_3$	4-ClC_6H_4	2	86	
5d	4-IC_6H_4	4-ClC_6H_4	1.5	90	
5e	4-$CH_3OC_6H_4$	4-ClC_6H_4	2	85	
5f	4-$CH_3OC_6H_4$	C_6H_5	2	88	
5g	4-FC_6H_4	C_6H_5	2	87	
5h	4-IC_6H_4	C_6H_5	1.5	88	
5i	4-ClC_6H_4	C_6H_5	2	89	80 [28]
5j	C_6H_5	C_6H_5	2	87	75 [28]
5k	4-OHC_6H_4	C_6H_5	2	81	78 [17]
5l	4-BrC_6H_4	C_6H_5	2	85	73 [28]
5m	4-BrC_6H_4	$PhCH_2$	2	87	
5n	4-IC_6H_4	$PhCH_2$	1.5	88	
5o	3,4,5-$(CH_3O)_3C_6H_2$	$PhCH_2$	2	87	89 [27]
5p	C_6H_5	$PhCH_2$	2	82	79 [16]
5q	4-FC_6H_4	4-$CH_3OC_6H_4$	2	86	
5r	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$	2	84	
5s	C_6H_5	4-$CH_3OC_6H_4$	2	82	
5 t	3,4,5-$(CH_3O)_3C_6H_2$	4-$CH_3OC_6H_4$	2	85	
5u	C_6H_5	4-BrC_6H_4	2	83	
5v	4-FC_6H_4	4-BrC_6H_4	1.5	85	
5w	4-FC_6H_4	4-$CH_3C_6H_4$	1.5	86	
5x	4-FC_6H_4	4-FC_6H_4	2	87	
5y	4-$CH_3OC_6H_4$	3-ClC_6H_4	2	78	
5z	4-IC_6H_4	3-ClC_6H_4	2	83	
5aa	4-FC_6H_4	3-ClC_6H_4	3	80	
5bb	C_6H_5	3-ClC_6H_4	3	75	
5cc	4-FC_6H_4	3-BrC_6H_4	3	70	
5dd	4-$CH_3OC_6H_4$	3-BrC_6H_4	3	65	
5ee	4-FC_6H_4	3-$CH_3C_6H_4$	3	62	
5ff	3,4,5-$(CH_3O)_3C_6H_2$	CH_3	2	86	
5gg	4-FC_6H_4	CH_3	2	85	
5hh	4-ClC_6H_4	cyclohexyl	3	56	

Reaction condition: benzil (1 mmol), aromatic aldehyde (1 mmol), amine (1 mmol), and ammonium acetate (5 mmol) in $[Bpy]BF_4$ (2 mL) at 80°C catalyzed by TFA.

Scheme 2



1600, 1523, 1514, 1479, 1446, 1420, 1387, 1369, 1222, 1158, 1139, 1108, 1072, 1017, 959, 917, 839, 816, 772, 737, 720, 698, 660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.66 (s, 6H, 2 × OCH_3), 3.84 (s, 3H, OCH_3), 6.63 (s, 2H, Ar H), 7.01 (d, J = 8.8 Hz, 2H, Ar H), 7.12–7.14 (m, 2H, Ar H), 7.20–7.30 (m, 8H, Ar H), 7.58 (d, J = 7.2 Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.89, 146.69, 138.36, 135.96, 134.24, 134.16, 131.11, 130.63, 130.31, 129.77, 129.36, 128.27, 128.22, 127.40, 126.81, 125.47, 106.39, 60.91, 55.91, 30.93; HRMS: Calcd for $C_{30}H_{25}ClN_2O_3$ $[M+H]^+$; found (expected): 497.1770 (497.1633).

1-(4-Chlorophenyl)-2-(4-iodophenyl)-4,5-diphenyl-1H-imidazole (5d). mp 221–223°C; IR (KBr) ν: 3062, 1590, 1524, 1511, 1501, 1479, 1444, 1419, 1370, 1234, 1179, 1157, 1140, 1097, 1074, 1027, 843, 788, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.96 (d, J = 8.4 Hz, 2H, Ar H), 7.10–7.16 (m, 4H, Ar H), 7.20–7.29 (m, 8H, Ar H), 7.56 (d, J = 7.2 Hz, 2H, Ar H), 7.61 (d, J = 8.4 Hz, 2H, Ar H).

1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (5e). mp 176–177°C; IR (KBr) ν: 3060, 1600, 1499, 1480, 1446, 1416, 1356, 1325, 1300, 1121, 1089, 1070, 1012, 974, 953, 835, 758, 729, 720, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.80 (s, 3H, OCH_3), 6.80 (d, J = 8.8 Hz, 2H, Ar H), 6.96 (d, J = 8.8 Hz, 2H, Ar H), 7.10–7.12 (m, 2H, Ar H), 7.19–7.26 (m, 8H, Ar H), 7.34 (d, J = 8.8 Hz, 2H, Ar H), 7.57 (d, J = 7.2 Hz, 2H, Ar H); HRMS: Calcd for $C_{28}H_{21}ClN_2O$ $[M+H]^+$; found (expected): 437.1652 (437.1421).

2-(4-Methoxyphenyl)-1,4,5-triphenyl-1H-imidazole (5f). mp 168–169°C; IR (KBr) ν: 3061, 2957, 2934, 2905, 2837, 1608, 1577, 1528,1495, 1481, 1441, 1421, 1387, 1368, 1307, 1294, 1252, 1182, 1154, 1113, 1071, 1025, 958, 916, 840, 781, 764, 735, 720, 700, 657, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.73 (s, 3H, OCH_3), 6.85 (d, J = 8.0 Hz, 2H, Ar H), 7.15–7.35 (m, 15H, Ar H), 7.49 (d, J = 8.0 Hz, 2H, Ar H).

2-(4-Fluorophenyl)-1,4,5-triphenyl-1H-imidazole (5g). mp 192–194°C; IR (KBr) ν: 3049, 1597, 1522, 1494, 1446, 1418, 1387, 1371, 1225, 1156, 1139, 1098, 1071, 1026, 1016, 959, 918, 839, 789, 777, 764, 734, 696, 659, 609 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.93 (t, J = 8.4 Hz, 2H, Ar H), 7.02–7.04 (m, 2H, Ar H), 7.11–7.13 (m, 2H, Ar H), 7.17–7.30 (m, 9H, Ar H), 7.39–7.42 (m, 2H, Ar H), 7.58 (d, J = 8.0 Hz, 2H, Ar H); HRMS: Calcd for $C_{27}H_{19}Cl\ N_2$ $[M+H]^+$; found (expected): 391.1819 (391.1611).

2-(4-Iodophenyl)-1,4,5-triphenyl-1H-imidazole (5h). mp 218–220°C; IR (KBr) ν: 3049, 1596, 1523, 1494, 1446, 1419, 1388, 1371, 1225, 1159, 1072, 960, 839, 789, 764, 735, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.03 (d, J = 7.2 Hz, 2H, Ar H), 7.10–7.13 (m, 2H, Ar H), 7.16 (d, J = 8.4 Hz, 2H, Ar H), 7.20–7.25 (m, 5H, Ar H), 7.28–7.31 (m, 4H, Ar H), 7.57 (d, J = 8.4 Hz, 4H, Ar H); HRMS: Calcd for $C_{27}H_{19}I\ N_2$ $[M+H]^+$; found (expected): 499.0871 (499.0672).

1-Benzyl-2-(4-bromophenyl)-4,5-diphenyl-1H-imidazole (5m). mp 171–172°C; IR (KBr) ν: 3057, 2925, 1592, 1573, 1517, 1500, 1458, 1435, 1381, 1327, 1276, 1238, 1208, 1171, 1117, 1103, 1028, 1011, 882, 856, 830, 755, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 5.01 (s, 2H, CH_2), 6.80–6.82 (m, 2H, Ar H), 7.15 (d, J = 6.8 Hz, 1H, Ar H), 7.19–7.23 (m, 7H, Ar H), 7.30–7.36 (m, 3H, Ar H), 7.51 (s, 4H, Ar H), 7.55 (d, J = 7.6 Hz, 2H, Ar H).

1-Benzyl-2-(4-iodophenyl)-4,5-diphenyl-1H-imidazole (5n). mp 182–183°C; IR (KBr) ν: 3059, 3025, 2939, 1599, 1557, 1478, 1446, 1410, 1359, 1324, 1299, 1256, 1120, 1070, 1061, 1029, 1004, 972, 952, 917, 828, 775, 760, 737, 724, 714, 694, 666, 633, 617 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 5.08 (s, 2H, CH_2), 6.80–6.82 (m, 2H, Ar H), 7.13–7.22 (m, 8H, Ar H), 7.29–7.36 (m, 3H, Ar H), 7.38 (d, J = 8.0 Hz, 2H, Ar H), 7.55 (d, J = 8.0 Hz, 2H, Ar H), 7.72 (d, J = 8.4 Hz, 2H, Ar H).

2-(4-Fluorophenyl)-1-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (5q). mp 194–196°C; IR (KBr) ν: 3063, 2966, 2931, 2837, 1603, 1512, 1480, 1461, 1442, 1422, 1390, 1373, 1298, 1251, 1180, 1169, 1159, 1137, 1107, 1072, 1030, 960, 913, 840, 817, 776, 724, 714, 697, 656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.79 (s, 3H, OCH_3), 6.79 (d, J = 8.8 Hz, 2H, Ar H), 6.93–7.03 (m, 4H, Ar H), 7.10–7.13 (m, 2H, Ar H), 7.17–7.20 (m, 1H, Ar H), 7.22–7.26 (m, 5H, Ar H), 7.35 (d, J = 8.4 Hz, 2H, Ar H), 7.58 (d, J = 7.2 Hz, 2H, Ar H).

1,2-Bis(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (5r). mp 201–203°C; IR (KBr) ν: 3052, 2934, 2854, 1599, 1567, 1548, 1529, 1512, 1499, 1479, 1465, 1441, 1409, 1381, 1360, 1335, 1288, 1179, 1121, 1093, 1074, 1014, 993, 956, 929, 901, 839, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.78 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.77 (t, J = 8.4 Hz, 4H, Ar H), 6.96 (d, J = 8.8 Hz, 2H, Ar H), 7.11–7.24 (m, 8H, Ar H), 7.39 (d, J = 8.4 Hz, 2H, Ar H), 7.59 (d, J = 7.2 Hz, 2H, Ar H).

1-(4-Methoxyphenyl)-2,4,5-triphenyl-1H-imidazole (5s). mp 175–177°C; IR (KBr) ν: 3051, 2961, 2836, 1602, 1510, 1479, 1462, 1444, 1398, 1294, 1247, 1178, 1169, 1106, 1072, 1029, 841, 771, 712, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.77 (s, 3H, OCH_3), 6.76 (d, J = 8.8 Hz, 2H, Ar H), 6.96 (d, J = 10.4 Hz, 2H, Ar H), 7.12–7.25 (m, 6H, Ar H), 7.30–7.36 (m, 2H, Ar H), 7.41–7.47 (m, 3H, Ar H), 7.55–7.60 (m, 3H, Ar H), 7.98 (d, J = 7.6 Hz, 1H, Ar H).

2-(3,4,5-Trimethoxyphenyl)-1-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (5t). mp 207–208°C; IR (KBr) ν: 3011, 2933, 2839, 1603, 1582, 1511, 1483, 1440, 1413, 1337, 1295, 1250, 1181, 1167, 1123, 1075, 1028, 1007, 965, 921, 869, 840, 778, 738, 724, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.65 (s, 6H, 2 × OCH_3), 3.77 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 6.69 (s, 2H, Ar H), 6.79 (d, J = 8.8 Hz, 2H, Ar H), 7.01 (d, J = 8.8 Hz, 2H, Ar H), 7.13–7.26 (m, 8H, Ar H), 7.59 (d, J = 7.2 Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.26, 155.47, 152.75, 146.74, 138.13, 136.78, 131.15, 130.71, 129.59, 128.38, 128.16, 127.40, 126.61, 114.30, 106.26, 60.88, 55.91, 55.50, 30.93; HRMS: Calcd for $C_{31}H_{28}N_2\ O_4$ $[M+H]^+$; found (expected): 493.2349 (493.2128).

1-(4-Bromophenyl)-2,4,5-triphenyl-1H-imidazole (5u). mp 196–197°C; IR (KBr) ν: 3038, 1600, 1488, 1461, 1443, 1396, 1323, 1202, 1128, 1071, 1027, 1016, 965, 915, 840, 766, 734, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.90 (d, J = 8.4 Hz, 1H, Ar H), 7.12 (d, J = 8.0 Hz, 1H, Ar H), 7.20–7.23(m, 1H, Ar H), 7.31–7.49 (m, 13H, Ar H), 7.57(d, J = 8.0 Hz, 2H, Ar H), 7.93 (d, J = 8.4 Hz, 1H, Ar H).

1-(4-Bromophenyl)-2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole (5v). mp 203–204°C; IR (KBr) ν: 3042, 2963, 2838, 1598, 1578, 1517, 1499, 1458, 1436, 1411, 1378, 1327, 1290, 1249, 1171, 1115, 1104, 1091, 1030, 1009, 901, 879, 854, 827, 794, 758, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.89 (d, J = 8.4 Hz, 2H, Ar H), 6.97 (t, J = 8.4 Hz, 2H, Ar H), 7.10–7.12 (m, 2H, Ar H), 7.18–7.25 (m, 4H, Ar H), 7.28–7.31 (m, 2H, Ar H), 7.38–7.41 (m, 4H, Ar H), 7.57 (d, J = 7.2 Hz, 2H, Ar H).

2-(4-Fluorophenyl)-4,5-diphenyl-1-p-tolyl-1H-imidazole (5w). mp 182–184°C; IR (KBr) ν: 3047, 2963, 2911, 1600, 1592, 1579, 1563, 1498, 1459, 1435, 1414, 1378, 1327, 1274, 1238, 1144, 1089, 1028, 1007, 963, 868, 799, 788, 749, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 2.32 (s, 3H, CH_3), 6.89–6.96 (m, 4H, Ar H), 7.05 (d, J = 8.0 Hz, 2H, Ar H), 7.12 (d, J = 7.2 Hz, 2H, Ar H), 7.17–7.26 (m, 6H, Ar H), 7.39–7.43 (m, 2H, Ar H), 7.57 (d, J = 7.6 Hz, 2H, Ar H).

1,2-Bis(4-fluorophenyl)-4,5-diphenyl-1H-imidazole (5x). mp 196–197°C; IR (KBr) ν: 3056, 1602, 1523 1509, 1480, 1446, 1414, 1387, 1370, 1325, 1223, 1154, 1128, 1096, 1073, 1026, 1015, 959, 917, 839, 774, 737, 720, 697, 658, 623 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.94–7.03 (m, 6H, Ar H), 7.11–7.13 (m, 2H, Ar H), 7.18–7.25 (m, 4H, Ar H), 7.27–7.28 (m, 2H, Ar H), 7.39–7.42 (m, 2H, Ar H), 7.57 (d, J = 7.2 Hz, 2H,

Ar H); HRMS: Calcd for $C_{27}H_{18}F_2N_2$ $[M+H]^+$; found (expected): 409.1794 (409.1517).

1-(3-Chlorophenyl)-2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole(5y). mp 202–203°C; IR (KBr) ν: 3059, 1590, 1574, 1500, 1477, 1443, 1428, 1391, 1372, 1322, 1181, 1139, 1073, 1026, 961, 919, 802, 777, 721, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.79 (s, 3H, OCH_3), 6.80 (d, $J = 8.8$ Hz, 2H, Ar H), 6.93(d, $J = 8.0$ Hz, 1H, Ar H), 7.04 (s, 1H, Ar H), 7.11–7.26 (m, 10H, Ar H), 7.36 (d, $J = 8.8$ Hz, 2H, Ar H), 7.58 (d, $J = 7.6$ Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.82, 146.89, 138.46, 138.26, 134.32, 131.14, 130.46, 130.34, 129.97, 128.69, 128.51, 128.17, 127.37, 126.85, 126.67, 122.78, 113.75, 55.27, 30.93.

1-(3-Chlorophenyl)-2-(4-iodophenyl)-4,5-diphenyl-1H-imidazole (5z). mp 193–194°C; IR (KBr) ν: 3061, 1589, 1499, 1478, 1443, 1432, 1406, 1300, 1183, 1140, 1095, 1074, 1058, 1028, 1007, 992, 960, 830, 806, 788, 774, 735, 720, 697, 655 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.94 (d, $J = 7.6$ Hz, 1H, Ar H), 7.05 (s, 1H, Ar H), 7.12 (d, $J = 7.2$ Hz, 2H, Ar H), 7.17 (d, $J = 8.4$ Hz, 2H, Ar H), 7.20–7.31 (m, 8H, Ar H), 7.57 (d, $J = 7.2$ Hz, 2H, Ar H), 7.62 (d, $J = 8.4$ Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.87, 138.78, 137.48, 134.48, 134.03, 131.09, 130.47, 130.17, 129.76, 128.60, 128.35, 128.23, 127.34, 126.87, 94.72, 30.93.

1-(3-Chlorophenyl)-2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole (5aa). mp 193–194°C; IR (KBr) ν: 3062, 1590, 1524, 1511, 1501, 1479, 1444, 1419, 1370, 1234, 1179, 1157, 1140, 1097, 1074, 1027, 843, 788, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.92–7.00 (m, 3H, Ar H), 7.04 (s, 1H, Ar H), 7.11–7.14 (m, 2H, Ar H), 7.21–7.30 (m, 8H, Ar H), 7.40–7.44 (m, 2H, Ar H), 7.58 (d, $J = 7.2$ Hz, 2H, Ar H); HRMS: Calcd for $C_{27}H_{18}ClF\ N_2$ $[M+H]^+$; found (expected): 425.1440 (425.1222).

1-(3-Chlorophenyl)-2,4,5-triphenyl-1H-imidazole (5bb). mp 214–215°C; IR (KBr) ν: 3062, 1590, 1499, 1478, 1443, 1391, 1372, 1140, 1095, 1074, 1026, 961, 919, 806, 789, 776, 763, 720, 697, 654 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.94 (d, $J = 8.4$ Hz, 1H, Ar H), 7.05 (s, 1H, Ar H), 7.12–7.14 (m, 2H, Ar H), 7.17–7.31 (m, 11H, Ar H), 7.44 (d, $J = 6.4$ Hz, 2H, Ar H), 7.60 (d, $J = 7.6$ Hz, 2H, Ar H).

1-(3-Bromophenyl)-2-(4-fluorophenyl)-4,5-diphenyl-1H-imidazole (5cc). mp 191–193°C; IR (KBr) ν: 3059, 1589, 1573, 1526, 1500, 1477, 1444, 1428, 1369, 1232, 1157, 1097, 1072, 844, 780, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 6.98 (t, $J = 8.8$ Hz, 3H, Ar H), 7.12–7.30 (m, 10H, Ar H), 7.39–7.45 (m, 3H, Ar H), 7.57 (d, $J = 7.2$ Hz, 2H, Ar H); HRMS: Calcd for $C_{27}H_{18}BrFN_2$ $[M+H]^+$; found (expected): 469.0757 (469.0716).

1-(3-Bromophenyl)-2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (5dd). mp 201–202°C; IR (KBr) ν: 3062, 2955, 2931, 2831, 1611, 1590, 1576, 1531, 1502, 1477, 1443, 1421, 1381, 1305, 1293, 1248, 1176, 1112, 1064, 1028, 959, 832, 780, 735, 717, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.80 (s, 3H, OCH_3), 6.81 (d, $J = 8.8$ Hz, 2H, Ar H), 6.97 (d, $J = 8.0$ Hz, 1H, Ar H), 7.11–7.28 (m, 10H, Ar H), 7.35 (d, $J = 8.4$ Hz, 2H, Ar H), 7.42 (d, $J = 8.0$ Hz, 1H, Ar H), 7.58 (d, $J = 7.2$ Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.82, 146.88, 138.55, 138.24, 134.31, 131.54, 131.39, 131.14, 130.44, 130.20, 128.51, 128.20, 128.17, 127.37, 127.28, 126.67, 122.76, 122.29, 113.75, 55.27, 30.93.

2-(4-Fluorophenyl)-4,5-diphenyl-1-m-tolyl-1H-imidazole (5ee). mp 173–174°C; IR (KBr) ν: 3053, 3013, 2955, 2931, 2832, 1611, 1591, 1578, 1532, 1502, 1479, 1447, 1423, 1383, 1368, 1305, 1293, 1249, 1176, 1112, 1094, 1075, 1029, 993, 959, 888, 831, 788, 777, 736, 693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 2.21 (s, 3H, CH_3), 6.84 (s, 2H, Ar H), 7.07–7.26 (m, 12H, Ar H), 7.43–7.46 (m, 2H, Ar H), 7.59 (d, $J = 7.2$ Hz, 2H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.91, 161.44, 145.96, 139.23, 138.19, 136.91, 134.46, 131.12, 130.93, 130.79, 130.70, 129.15, 128.95, 128.87, 128.31, 128.17, 127.98, 127.37, 126.62, 125.48, 115.24, 115.03, 30.93, 21.19.

2-(3,4,5-Trimethoxyphenyl)-1-methyl-4,5-diphenyl-1H-imidazole (5ff). mp 218–219°C; IR (KBr) ν: 3032, 3011, 2957, 2936, 2903, 2827, 1584, 1526, 1487, 1427, 1412, 1386, 1328, 1238, 1181, 1168, 1074, 1022, 1002, 964, 937, 914, 882, 848, 837, 774, 732, 712, 699, 685, 650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.51 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 3.94 (s, 6H, $2 \times OCH_3$), 6.93 (s, 2H, Ar H), 7.13–7.23 (m, 3H, Ar H), 7.41–7.50 (m, 5H, Ar H), 7.55 (d, $J = 7.6$ Hz, 2H, Ar H).

2-(4-Fluorophenyl)-1-methyl-4,5-diphenyl-1H-imidazole (5gg). mp 169–170°C; IR (KBr) ν: 3052, 2992, 2914, 1602, 1528, 1502, 1480, 1467, 1448, 1410, 1377, 1320, 1298, 1224, 1157, 1131, 1098, 1072, 1030, 1015, 1001, 958, 922, 839, 820, 777, 749, 733, 721, 704, 649, 604 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm): 3.49 (s, 3H, CH_3), 7.15–7.23 (m, 5H, Ar H), 7.40–7.54 (m, 7H, Ar H), 7.71–7.75 (m, 2H, Ar H); HRMS: Calcd for C22H17F N2 $[M+H]^+$; found (expected): 329.1650 (329.1455).

2-(4-Chlorophenyl)-1-cyclohexyl-4,5-diphenyl-1H-imidazole (5hh). mp 193–195°C; IR (KBr) ν: 3052, 2934, 2853, 1599, 1512, 1499, 1479, 1465, 1441, 1381, 1359, 1335, 1288, 1221, 1093, 839, 693 cm^{-1}; ^1H NMR (400 MHz, CDCl3) (δ, ppm): 0.70–0.81 (m, 1H, CH_2), 0.99–1.10 (m, 2H, CH_2), 1.45–1.55 (m, 3H, CH_2), 1.63–1.66 (m, 2H, CH_2), 1.82–1.86 (m, 2H, CH_2), 3.89–3.96 (m, 1H, CH), 7.09–7.16 (m, 3H, Ar H), 7.39–7.48 (m, 9H, Ar H), 7.56 (d, $J = 7.6$ Hz, 2H, Ar H).

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REFERENCES AND NOTES

[1] Shapi, A. S.; Umesh, C. N.; Sanjay, S. P.; Thomas, D.; Rajgopal, J. L.; Kumar, V. S. Tetrahedron 2005, 61, 3539.

[2] Sharma, G. V. M.; Jyothi, Y.; Lakshmi P. S. Synth Commun 2006, 36, 2991.

[3] Saeed, B.; Mohammed, M. H.; Maryam, A. Tetrahedron Lett, 2003, 44, 1709.

[4] Misono, M. Chem Commun 2001, 13, 1141.

[5] Blank, J. W.; Durant, G. J.; Emmett, C. R. Nature 1974, 248, 65.

[6] Ucucu, U.; Karaburun, N. G.; Iskdag, I. Il Farmaco 2001, 56, 285.

[7] (a) Lee, J. C.; Laydon, J. T.; McDonnell, P. C. Nature 1994, 372, 739; (b) Takle, A. K.; Brown, M. J. B.; Davies, S. Bioorg Med Chem Lett 2006, 16, 378.

[8] Shaterian, H. R.; Ranjbar, M.; Azizi, K. Chin J Chem 2011, 29, 1635.

[9] Niknam, K.; Deris, A.; Naeimi, F.; Majleci, F. Tetrahedron Lett 2011, 52, 4642.

[10] De Laszlo, S. E.; Hacker, C.; Li, B.; Kim, D.; MacCoss, M.; Mantalo, N.; Pivnichny, J. V.; Colwell, L.; Koch, G. E.; Cascieri, M. A.; Hagmenn, W. K. Bioorg Med Chem Lett 1999, 9, 641.

[11] Vassilev, L. T.; Vu, B. T.; Graves, B.; Carvajal, D.; Podlaski, F.; Filipovic, Z.; Kong, N.; Kammlott, U.; Lukacs, C.; Klein, C.; Fotouhi, N.; Liu, E. A. Science 2004, 303, 844.

[12] Sadeghi, B.; Mirjalili, B. B. F.; Hashemi, M. M. Tetrahedron Lett 2008, 49, 2575.

[13] Karimi, A. R.; Alimohammadi, Z.; Azizian, J.; Mohammadi, A. A.; Mohammadizadeh, M. R. Catal Commun 2006, 7, 728.

[14] Kantevari, S.; Vuppalapati, S. V. N.; Biradar, D. O.; Nagarapu, L. J Mol Catal A: Chem 2007, 266, 109.

[15] Lingaiah, N.; Satyender, A.; Srinivas, K. J Mol Catal A: Chem 2007, 266, 104.

[16] Saikat, D. S.; Parasa, H.; Dilip, K. Tetrahedron Lett 2008, 49, 2216.

[17] Subhasis, S.; Ganesh, C. N.; Pallavi, S.; Singh, M. S. Tetrahedron 2009, 65, 10155.

[18] Mazaahir, K.; Poonam, M.; Vikas, B.; Rishi, K. S.; Abdul, S. E.; Mazaahir, K.; Sharmistha, D. J Mol Catal A: Chem 2007, 265, 177.

[19] Majid, M. H.; Fatemeh, D.; Fatemeh, F. B. J. Mol Catal A: Chem 2007, 263, 112.

[20] Sivakumar, K.; Kathirvel, A.; Lalitha, A. Tetrahedron Lett 2010, 51, 3018.

[21] Hekmat Shoar, R.; Rahimzadeh, G.; Derikvand, F.; Farzaneh, M. Synth Commun 2010, 40, 1270.

[22] Hassaninejad, A.; Zare, A.; Shekouhy, M.; Rad, J. A. J Comb Chem 2010, 12, 844.

[23] Davoodnia, A.; Heravi, M. M.; Safavi-Rad, Z.; Tavakoli-Hoseini, N. Synth Commun 2010, 40, 2588.

[24] Lantos, I.; Zhang, W. Y.; Shui, X.; Eggleston, D. S. J. Org Chem 1993, 58, 7092.

[25] Consonni, R.; Croce, P. D.; Ferraccioli, R.; Rosa, C. L. J Chem Res (S) 1991, 7, 188.

[26] Wang, B.; Gu, Y. L.; Luo, C.; Yang, T.; Yang, L. M.; Suo, J. S. Tetrahedron Lett 2004, 45, 3417.

[27] Telmourl, A.; Chermahini, A. N. J Mol Catal A: Chem 2011, 346, 39.