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New efficient synthesis of 1,2,4-trisubstituted imidazoles and imidazo[1,2-*c*]quinazolines by a tandem aza-Wittig/electrocyclic ring-closure process

Yi-Bo Nie, Zhuan Duan, Ming-Wu Ding *

Key Laboratory of Pesticide & Chemical Biology of Ministry of Education, Central China Normal University, LuoYu Road 100, Wuhan 430079, PR China

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ABSTRACT

A series of 1,2,4-trisubstituted imidazoles **5** were synthesized efficiently by a tandem aza-Wittig/1,5-electrocyclic ring-closure reaction of vinyliminophosphoranes **3** with aldehydes. Reactions of **5s**,**t** with triphenylphosphine produced iminophosphoranes **7**. A tandem aza-Wittig reaction of iminophosphorane **7** with isocyanate generated imidazo[1,2-c]quinazolines **9** in high yields.

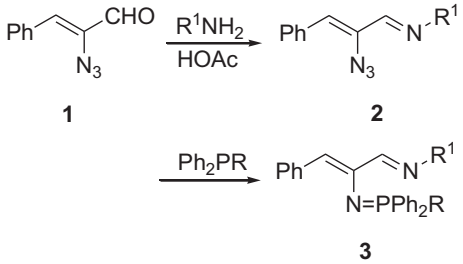
1. Introduction

Imidazoles are important heterocycles bearing good biological and pharmaceutical activities and have attracted the attention of synthetic chemists for many years.[1] A wide variety of imidazole derivatives have been used as antitumor agents,[2] heme oxygenase inhibitors,[3] B-Raf kinase inhibitors,[4] plant growth regulators,[5] and pesticides.[6] The imidazole ring system is also a component of some natural products, such as isonaamine A, dorimidazole A, and preclathridine A.[7] The structural diversity and complexity of naturally occurring imidazoles have generated much interest in the development of efficient methods for their synthesis. There are many methods reported for the synthesis of imidazoles,[8] however, only a few were known for the synthesis of 1,2,4-trisubstituted imidazoles. For example, some 1,2,4-trisubstituted imidazoles were recently prepared from the reaction of *N*-alkyl-*N*-(β-keto)amide with NH_4OAc,[9] the cyclization of some thioamides obtained from amino acid esters,[10] and the palladium-catalyzed cyclization of the *O*-pentafluorobenzoylamidoximes.[11]

The aza-Wittig reactions of iminophosphoranes have received increasing attention in view of their utility in the synthesis of nitrogen-containing heterocyclic compounds.[12] The carbodiimides or aldimines, obtained efficiently by aza-Wittig reaction of iminophosphoranes with isocyanates or aldehydes under mild neutral condition, can be used as synthetic intermediates of heterocycles by tandem processes involving aza-Wittig/intramolecular electrocyclic ring closure. This tandem process has been utilized previously in synthesis of many heterocycles, such as pyridines,[13] isoquinolines,[14] benzo[*b*]thieno[2,3-*b*]pyridines,[15] pyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine,[16] pyrido[1,2-*c*]pyrimidine,[17] quinazolines,[18] and imidazo[1,5-*a*]pyridines.[19] We have recently been interested in the synthesis of various heterocycles through aza-Wittig reactions.[20] Here we wish to report a new efficient synthesis of 1,2,4-trisubstituted imidazoles and imidazo[1,2-*c*]quinazolines via the tandem aza-Wittig/electrocyclic ring-closure process, from easily accessible starting materials.

2. Results and discussion

The α-azidocinnamaldehyde **1**, obtained from the reaction of α,β-dibromocinnamaldehyde with sodium azide,[21] reacted with amine in the presence of acetic acid to give the azide **2** in 79–92% yields. Further Staudinger reaction of azides **2** with triphenylphosphine (R=Ph) or methyldiphenylphosphine (R=Me) at room temperature produced iminophosphorane **3** in high yields (Scheme 1).



Scheme 1. Preparation of vinyliminophosphoranes **3**.

Initially, we selected the triphenyliminophosphorane **3a** and benzaldehyde as the reactants (Scheme 2, Table 1). When the triphenyliminophosphorane **3a** and benzaldehyde was stirred in ethanol at room temperature for 24 h, no product was detected by TLC detection (Table 1, entry 1). However, imidazole derivative **5a**

* Corresponding author. Tel.: +86 27 63158845; fax: +86 27 67862041; e-mail address: ding5229@yahoo.com.cn (M.-W. Ding).

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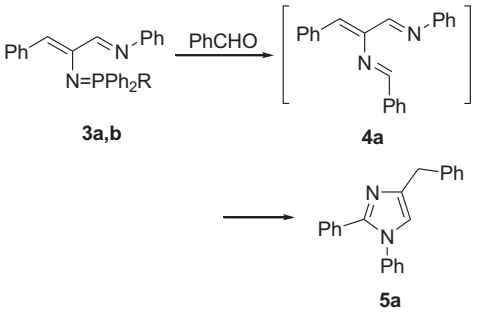
was directly obtained as the reaction was carried out at 50 °C or 80 °C for 24 h with 29% or 62% yields (Table 1, entries 2 and 3). The expected aza-Wittig product **4a** might produced but cyclized quickly to give imidazole **5a** under the reaction condition. When more reactive methyldiphenyl iminophosphorane **3b** was used as the reactant, the reaction took place even at room temperature for 24 h and the imidazole **5a** was obtained in 72% yield (Table 1, entry 4). At higher temperature (80 °C), the same reaction occurred smoothly to give **5a** in 85% yield with only 3 h (Table 1, entry 5).



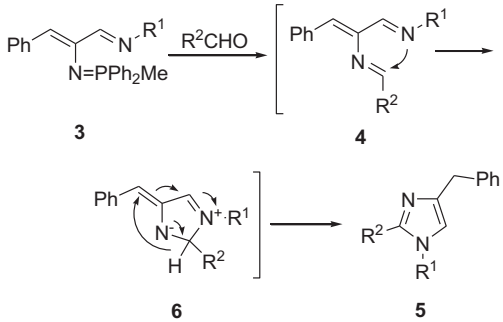
Scheme 2. Preparation of compounds **5a**.

Table 1
Optimization of the reaction conditions

Entry	R	Condition	Yield[a] (%)
1	Ph	rt/24 h	0
2	Ph	50 °C/24 h	29
3	Ph	80 °C/24 h	62
4	Me	rt/24 h	72
5	Me	80 °C/3 h	85

[a] Isolated yields of **5a** based on iminophosphorane **3**.

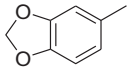
With the optimized condition, various methyldiphenyl iminophosphorane **3** and aldehydes were employed for the reaction (Scheme 3). All reactions proceeded smoothly to give the corresponding imidazoles **5** (Table 2) in 58–91% yields. When various aromatic or aliphatic aldehydes were used, the reaction produced imidazoles **5** in moderate to good yields at 80 °C for 3–5 h. However, as the thermal labile 2-azidobenzaldehyde was utilized, the best yields of the products **5s**,**t** were obtained when the reaction was carried out at room temperature (Table 2). The formation of the imidazoles **5** can be rationalized in terms of an initial aza-Wittig reaction to give the imine **4**, which undergoes 1,5-electrocyclic ring-closure to give **5** through intermediate **6**.[19,22]



Scheme 3. Preparation of imidazoles **5**.

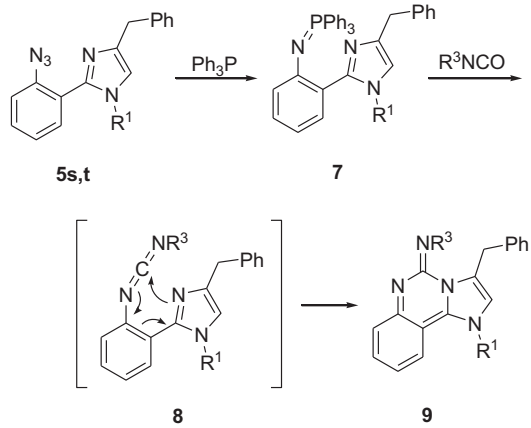
The obtained 2-(2-azidophenyl)imidazoles **5s**,**t** were further treated with triphenylphosphine, and the iminophosphorane **7** was obtained in high yield via Staudinger reaction (Scheme 4). When solutions of iminophosphoranes **7** in dry methylene dichloride

Table 2
Preparation of imidazoles **5** from methyldiphenyl iminophosphorane **3** (R=Me)

	R^1	R^2	Condition	Yield[a] (%)
5a	Ph	4-Cl-C_6H_4	80 °C/3 h	85
5b	Ph	4-F-C_6H_4	80 °C/3 h	82
5c	Ph	Furan-2-yl	80 °C/4 h	72
5d	Ph	*n*-C_3H_7	80 °C/5 h	63
5e	Ph	3-NO_2–C_6H_4	80 °C/3 h	58
5f	Ph	4-CH_3O–C_6H_4	80 °C/4 h	81
5g	Ph	Ph	80 °C/3 h	83
5h	Ph	2-CH_3O–C_6H_4	80 °C/4 h	80
5i	Benzyl	4-Cl–C_6H_4	80 °C/3 h	84
5j	4-Cl–C_6H_4	4-Cl–C_6H_4	80 °C/3 h	91
5k	4-Cl–C_6H_4	2,4-2Cl–Ph	80 °C/3 h	87
5l	4-Cl–C_6H_4		80 °C/4 h	75
5m	4-Cl–C_6H_4	4-NO_2–C_6H_4	80 °C/3 h	69
5n	4-Cl–C_6H_4	Ph	80 °C/3 h	82
5o	4-Cl–C_6H_4	4-CH_3O–C_6H_4	80 °C/4 h	81
5p	4-Cl–C_6H_4	4-Br–C_6H_4	80 °C/3 h	83
5q	4-Cl–C_6H_4	4-F–C_6H_4	80 °C/3 h	82
5r	2-CH_3–C_6H_4	4-Cl–C_6H_4	80 °C/3 h	76
5s	4-Cl–C_6H_4	2-N_3–C_6H_4	rt/24 h	65
5t	Ph	2-N_3–C_6H_4	rt/24 h	60

[a] Isolated yields based on iminophosphorane **3** (R=Me).

were further treated with aromatic isocyanate at room temperature, the color of the reaction mixture quickly turned red, and imidazo[1,2-*c*]quinazolines **9** were isolated as orange to red crystalline solids in good yields (Table 3, Scheme 4). Presumably, the conversion of **7** into **9** involves initial aza-Wittig reaction between the iminophosphorane **7** and the isocyanate to give a carbodiimide **8** as highly reactive intermediate, which easily undergoes 1,6-electrocyclic ring closure to give the imidazo[1,2-*c*]quinazolines **9**. It is noteworthy that the reaction can be easily carried out at room temperature under mild neutral condition.



Scheme 4. Preparation of imidazo[1,2-*c*]quinazolines **9**.

Table 3
Preparation of imidazo[1,2-*c*]quinazolines **9**

	R^1	R^3	Yield[a] (%)
9a	4-Cl–C_6H_4	4-Cl–C_6H_4	93
9b	4-Cl–C_6H_4	4-CH_3–C_6H_4	84
9c	Ph	4-Cl–C_6H_4	84
9d	Ph	4-CH_3–C_6H_4	83
9e	Ph	3-CH_3–C_6H_4	90
9f	4-Cl–C_6H_4	3-CH_3–C_6H_4	92
9g	4-Cl–C_6H_4	Ph	85
9h	4-Cl–C_6H_4	*i*-Pr	91
9i	Ph	4-F–C_6H_4	81
9j	Ph	Ph	82

[a] Isolated yields of **9** based on iminophosphorane **7**.

3. Conclusion

We have developed a new and efficient synthesis of unreported 1,2,4-substituted imidazoles and imidazo[1,2-*c*]quinazolines via aza-Wittig/electrocyclic ring-closure reaction from vinyl-iminophosphorane. This method utilizes easily accessible starting material and allows mild reaction conditions, straightforward product isolation and good yields. It has the potential in synthesis of various 1,2,4-trisubstituted or fused imidazoles, which are of considerable interest as potential biological active compounds or pharmaceuticals.

4. Experimental

4.1. General

Melting points were determined using an X-4 model apparatus and were uncorrected. MS were measured on a Finnigan Trace MS spectrometer. IR was recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. NMR was recorded in $CDCl_3$ or DMSO-d_6 on a Varian Mercury 400 or 600 spectrometer and resonances relative to TMS. Elementary analyses were taken on a Vario EL III elementary analysis instrument.

4.2. Synthesis of azides 2

*4.2.1. (2-Azido-3-phenylallylidene)benzenamine (**2a**).* α-Azido-cinnamaldehyde **1** (0.35 g, 2 mmol) was added to a solution of aniline (0.19 g, 2 mmol) in methanol (15 mL) with two drops of acetic acid. The reaction mixture was stirred at ambient temperature for 3–4 h until a solid precipitated. The solid formed was filtered off and recrystallized from ethanol/petroleum ether (1:1) to give 0.44 g (89%) of azide **2a** as light yellow solid. Mp: 85–87 °C, IR (KBr, cm^{-1}): 2140, 1637, 1592, 1497, 1458, 1421, 1368, 1332, 1309, 1276, 1187, 1086, 976, 784, 713. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.13 (s, 1H, N=CH), 7.84 (d, *J*=6.6 Hz, 2H, Ar–H), 7.40–7.20 (m, 8H, Ar–H), 6.17 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 156.4, 149.7, 134.1, 132.9, 130.0, 129.8, 129.1, 128.8, 128.4, 128.2, 126.5, 120.9. Anal. Calcd for $C_{15}H_{12}N_4$: C, 72.56; H, 4.87; N, 22.57. Found: C, 72.36; H, 4.98; N, 22.71.

*4.2.2. (2-Azido-3-phenylallylidene)-1-phenylmethanamine (**2b**).* Operation as above with phenylmethanamine (0.21 g, 2 mmol), compound **2b** (0.41 g, 79%) was also isolated as light yellow solid. Mp: 158–160 °C, IR (KBr, cm^{-1}): 3063, 3028, 2110, 1681, 1636, 1494, 1450, 1394, 1340, 1300, 1262, 1048, 1028, 877, 731. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.77 (d, *J*=7.2 Hz, 2H, Ar–H), 7.37–7.20 (m, 8H, Ar–H), 6.74 (s, 1H, =CH), 3.99 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 158.8, 138.9, 134.2, 132.7, 129.8, 129.7, 128.5, 128.4, 127.7, 127.0, 126.2, 64.0. Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 72.98; H, 5.51; N, 21.12.

*4.2.3. (2-Azido-3-phenylallylidene)-4-chloroaniline (**2c**).* Operation as above with 4-chloroaniline (0.26 g, 2 mmol), compound **2c** (0.52 g, 92%) was also isolated as light yellow solid. Mp: 111–113 °C, IR (KBr, cm^{-1}): 2161, 2112, 1611, 1483, 1446, 1392, 1354, 1260, 1165, 1090, 1009, 829, 760, 693. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.09 (s, 1H, N=CH), 7.83 (d, *J*=7.8 Hz, 2H, Ar–H), 7.41–7.13 (m, 7H, Ar–H), 6.18 (s, 1H, =CH). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 156.7, 148.1, 134.0, 132.8, 132.2, 130.0, 129.3, 129.0, 128.8, 128.5, 122.3. Anal. Calcd for $C_{15}H_{11}ClN_4$: C, 63.72; H, 3.92; N, 19.82. Found: C, 63.57; H, 3.78; N, 20.02.

*4.2.4. (2-Azido-3-phenylallylidene)-2-methylaniline (**2d**).* Operation as above with *o*-toluidine (0.21 g, 2 mmol), compound **2d** (0.43 g, 83%) was also isolated as light yellow solid. Mp: 141–143 °C, IR (KBr, cm^{-1}): 2157, 2109, 1612, 1588, 1447, 1386, 1353, 1261, 1100, 758, 694; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.09 (s, 1H, N=CH), 7.85 (d, *J*=6.6 Hz, 2H, Ar–H), 7.41–6.96 (m, 7H, Ar–H), 6.18 (s, 1H, =CH), 2.38 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 155.8, 148.8, 134.1, 133.5, 133.4, 130.5, 130.0, 129.8, 128.8, 128.4, 127.9, 126.6, 116.9, 18.3. Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 72.98; H, 5.51; N, 21.62.

4.3. Synthesis of iminophosphoranes 3

*4.3.1. N-(3-Phenyl-2-((triphenylphosphoranylidene)amino) allylidene)aniline (**3a**).* A solution of triphenylphosphine (0.52 g, 2 mmol) in dry methylene dichloride (10 mL) was added dropwise at room temperature to a well-stirred solution of azide **2a** (0.50 g, 2 mmol) in dry methylene dichloride (10 mL). The reaction mixture was stirred at room temperature for 4 h; then the solvent was removed under reduced pressure. The residue was recrystallized from ethanol/petroleum ether (1:2) to give iminophosphoranes **3a** (0.88 g, 91%) as yellow solid. Mp: 151–153 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.25 (d, *J*=7.2 Hz, 2H, Ar–H), 7.76–6.98 (m, 22H, Ar–H and N=CH), 6.19 (d, *J*=7.8 Hz, 2H, Ar–H), 6.02 (d, *J*=7.2 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 161.0, 150.4, 145.6, 138.8, 135.2, 134.5, 132.6, 132.1, 131.9, 130.3, 128.9, 128.5, 127.8, 125.5, 124.6, 123.2, 120.0. Anal. Calcd for $C_{33}H_{27}N_2P$: C, 82.14; H, 5.64; N, 5.81. Found: C, 82.38; H, 5.79; N, 5.62.

*4.3.2. N-(2-((Methyldiphenylphosphoranylidene)amino)-3-phenylallylidene)aniline (**3b**).* A solution of methyldiphenylphosphine (0.40 g, 2 mmol) in dry methylene dichloride (10 mL) was added dropwise at room temperature to a well-stirred solution of azide **2a** (0.50 g, 2 mmol) in dry methylene dichloride (10 mL). The reaction mixture was stirred at room temperature for 4 h, then the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with petroleum ether/diethyl ether (6:1, v/v) as eluent to give **3b** (0.72 g, 86%) as yellow solid. Mp: 144–145 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.25 (d, *J*=7.8 Hz, 2H, Ar–H), 7.80–7.05 (m, 17H, Ar–H and N=CH), 6.48 (d, *J*=7.8 Hz, 2H, Ar–H), 6.01 (d, *J*=7.8 Hz, 1H, =CH), 2.30 (d, $^2J_{P-H}$=13.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.1, 150.8, 145.9, 138.8, 136.5, 135.8, 130.4, 130.3, 129.2, 128.9, 128.7, 128.2, 127.8, 125.5, 124.8, 123.2, 123.1, 120.2, 19.5, 19.1. Anal. Calcd for $C_{28}H_{25}N_2P$: C, 79.98; H, 5.99; N, 6.66. Found: C, 79.89; H, 6.07; N, 6.96.

*4.3.3. 4-Chloro-N-(2-((methyldiphenylphosphoranylidene) amino)-3-phenylallylidene)aniline (**3c**).* Operation as above with azide **2c** (0.56 g, 2 mmol), compound **3c** (0.84 g, 92%) was also isolated as light yellow solid. Mp: 54–56 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.24 (d, *J*=7.8 Hz, 2H, Ar–H), 7.78–7.13 (m, 16H, Ar–H and N=CH), 6.39 (d, *J*=8.4 Hz, 2H, Ar–H), 6.01 (d, *J*=7.2 Hz, 1H, =CH), 2.28 (d, $^2J_{P-H}$=12.6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 162.5, 149.3, 145.8, 138.7, 136.4, 135.7, 130.4, 130.3, 130.2, 129.0, 128.9, 128.8, 128.3, 128.2, 127.9, 125.8, 124.0, 123.8, 121.5, 19.5, 19.0. Anal. Calcd for $C_{28}H_{24}ClN_2P$: C, 73.92; H, 5.32; N, 6.16. Found: C, 73.79; H, 5.41; N, 6.07.

*4.3.4. 2-Methyl-N-(2-((methyldiphenylphosphoranylidene) amino)-3-phenylallylidene)aniline (**3d**).* Operation as above with azide **2d** (0.52 g, 2 mmol), compound **3d** (0.78 g, 90%) was also isolated as light yellow solid. Mp: 38–40 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.23 (d, *J*=7.8 Hz, 2H, Ar–H), 7.76–6.93 (m, 16H, Ar–H and N=CH), 6.17 (d, *J*=7.8 Hz, 1H, Ar–H), 5.98 (d, *J*=7.2 Hz, 1H, =CH), 2.31 (d, $^2J_{P-H}$=13.2 Hz, 3H, CH_3), 1.64 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 163.7, 151.4, 145.7, 138.7, 136.0, 135.4, 130.6, 130.4, 129.9, 129.2, 128.9, 128.3, 128.2, 127.8, 126.2, 125.6, 124.1, 123.6, 123.4, 119.0, 19.5, 19.0, 17.3. Anal. Calcd for $C_{29}H_{27}N_2P$: C, 80.16; H, 6.26; N, 6.45. Found: C, 80.31; H, 6.15; N, 6.72.

4.4. Synthesis of imidazoles 5

*4.4.1. 4-Benzyl-2-(4-chlorophenyl)-1-phenyl-1H-imidazole (**5a**).* 4-Chlorobenzaldehyde (0.28 g, 2 mmol) was added to a solution of iminophosphorane **3b** (0.69 g, 2 mmol) in ethanol (15 mL). The solution was then heated at reflux for 3 h. After the reaction was completed, the solvent was evaporated and the residue was purified by column chromatography to give **5a** (0.59 g, 85%) as white solid. Mp: 171–173 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.39–7.14 (m, 14H, Ar–H), 6.69 (s, 1H, imidazole-5-H), 4.04 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 144.8, 142.4, 139.5, 138.1, 134.1, 129.7, 129.4, 128.9, 128.6, 128.3, 128.2, 128.0, 126.1, 125.6, 120.0, 34.9. MS (EI, 70 eV) *m*/*z*: 344 (M^+, 46), 214 (100), 206 (14), 103 (14), 94 (10), 77 (45). Anal. Calcd for $C_{22}H_{17}ClN_2$: C, 76.63; H, 4.97; N, 8.12. Found: C, 76.48; H, 5.17; N, 8.40.

*4.4.2. 4-Benzyl-2-(4-fluorophenyl)-1-phenyl-1H-imidazole (**5b**).* Operation as above with 4-fluorobenzaldehyde (0.25 g, 2 mmol), compound **5b** (0.54 g, 82%) was also isolated as white solid. Mp: 83–85 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.38–6.93 (m, 14H, Ar–H), 6.68 (s, 1H, imidazole-5-H), 4.04 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 163.2, 161.6, 145.0, 142.2, 139.6, 138.2, 130.4, 129.2, 128.9, 128.3, 127.8, 126.4, 126.0, 125.5, 119.7, 115.1, 115.0, 34.9. MS (EI, 70 eV) *m*/*z*: 328 (M^+, 50), 208 (14), 198 (100), 180 (10), 104 (10), 94 (23), 77 (46). Anal. Calcd for $C_{22}H_{17}FN_2$: C, 80.47; H, 5.22; N, 8.53. Found: C, 80.64; H, 5.07; N, 8.82.

*4.4.3. 4-Benzyl-2-(furan-2-yl)-1-phenyl-1H-imidazole (**5c**).* Operation as above with furan-2-carbaldehyde (0.19 g, 2 mmol), compound **5c** (0.43 g, 72%) was also isolated as white solid. Mp: 82–84 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.42–7.21 (m, 11H, Ar–H), 6.60 (s, 1H, imidazole-5-H), 6.28–5.99 (m, 2H, Ar–H), 4.05 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 144.6, 142.6, 142.5, 139.6, 138.6, 137.9, 129.2, 128.9, 128.6, 128.3, 126.3, 126.1, 119.5, 110.9, 108.9, 34.9. MS (EI, 70 eV) *m*/*z*: 300 (M^+, 60), 208 (16), 170 (100), 102 (8) 94 (19), 77 (46). Anal. Calcd for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33. Found: C, 80.25; H, 5.63; N, 9.42.

*4.4.4. 4-Benzyl-1-phenyl-2-propyl-1H-imidazole (**5d**).* Operation as above with butyraldehyde (0.15 g, 2 mmol), compound **5d** (0.35 g, 63%) was also isolated as light yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.43–7.20 (m, 10H, Ar–H), 6.49 (s, 1H, imidazole-5-H), 3.97 (s, 2H, CH_2), 2.60 (t, J=7.8 Hz, 2H, CH_2), 1.68–1.62 (m, 2H, CH_2), 0.87 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 148.0, 140.7, 139.9, 137.9, 129.3, 128.9, 128.3, 128.0, 126.0, 125.8, 117.5, 34.9, 29.0, 21.8, 13.8. MS (EI, 70 eV) *m*/*z*: 276 (M^+, 44), 248 (100), 206 (12), 172 (20), 146 (52), 103 (22), 91 (27), 77 (53). Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.14. Found: C, 82.86; H, 7.35; N, 10.02.

*4.4.5. 4-Benzyl-2-(3-nitrophenyl)-1-phenyl-1H-imidazole (**5e**).* Operation as above with 3-nitrobenzaldehyde (0.30 g, 2 mmol), compound **5e** (0.41 g, 58%) was also isolated as light yellow solid. Mp: 104–105 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.22 (s, 1H, Ar–H), 8.11 (d, J=6.6 Hz, 1H, Ar–H), 7.75 (d, J=6.6 Hz, 1H, Ar–H), 7.41–7.19 (m, 11H, Ar–H), 6.77 (s, 1H, imidazole-5-H), 4.06 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 147.9, 143.4, 142.9, 139.4, 137.7, 134.0, 131.8, 129.7, 129.1, 128.9, 128.6, 128.4, 126.2, 125.7, 123.1, 122.7, 120.9, 34.9. MS (EI, 70 eV) *m*/*z*: 355 (M^+, 43), 309 (6), 225 (100), 206 (10), 179 (17), 103 (13), 91 (8), 77 (35). Anal. Calcd for $C_{22}H_{17}N_3O$: C, 74.35; H, 4.82; N, 11.82. Found: C, 74.13; H, 5.04; N, 12.05.

*4.4.6. 4-Benzyl-2-(4-methoxyphenyl)-1-phenyl-1H-imidazole (**5f**).* Operation as above with 4-methoxybenzaldehyde (0.27 g, 2 mmol), compound **5f** (0.55 g, 81%) was also isolated as white solid. Mp: 112–114 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.39–7.15 (m, 12H, Ar–H), 6.77 (d, J=9.0 Hz, 2H, Ar–H), 6.64 (s, 1H, imidazole-5-H), 4.05 (s, 2H, CH_2), 3.77 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.4, 145.9, 141.9, 139.7, 138.5, 129.9, 129.2, 129.0, 128.3, 127.6, 126.0, 125.6, 122.8, 119.3, 113.4, 55.0, 35.0. MS (EI, 70 eV) *m*/*z*: 340 (M^+, 69), 249 (38), 210 (100), 146 (17), 130 (16), 103 (16), 91 (15), 77 (60). Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.37; H, 6.08; N, 8.41.

*4.4.7. 4-Benzyl-1,2-diphenyl-1H-imidazole (**5g**).* Operation as above with benzaldehyde (0.21 g, 2 mmol), compound **5g** (0.51 g, 83%) was also isolated as white solid. Mp: 120–122 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.40–7.16 (m, 15H, Ar–H), 6.69 (s, 1H, imidazole-5-H), 4.06 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 146.0, 142.3, 139.7, 138.4, 130.2, 129.2, 129.0, 128.6, 128.3, 128.1, 128.0, 125.7, 125.5, 119.8, 119.7, 35.0. MS (EI, 70 eV) *m*/*z*: 310 (M^+, 47), 206 (12), 180 (100), 103 (12), 77 (38). Anal. Calcd for $C_{22}H_{18}N_2$: C, 85.13; H, 5.85; N, 9.03. Found: C, 85.34; H, 5.65; N, 9.32.

*4.4.8. 4-Benzyl-2-(2-methoxyphenyl)-1-phenyl-1H-imidazole (**5h**).* Operation as above with 2-methoxybenzaldehyde (0.27 g, 2 mmol), compound **5h** (0.54 g, 80%) was also isolated as light yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60–6.99 (m, 13H, Ar–H), 6.74 (s, 1H, imidazole-5-H), 6.69 (d, J=8.4 Hz, 1H, Ar–H), 4.06 (s, 2H, CH_2), 3.24 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 156.5, 144.1, 142.3, 140.0, 139.2, 131.9, 130.5, 129.1, 128.7, 128.4, 126.8, 126.1, 123.7, 120.7, 120.4, 118.2, 110.8, 54.5, 35.2. MS (EI, 70 eV) *m*/*z*: 340 (M^+, 100), 309 (27), 248 (12), 210 (44), 206 (16), 130 (16), 104 (16), 91 (35), 77 (60). Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 81.36; H, 6.13; N, 8.57.

*4.4.9. 1,4-Dibenzyl-2-(4-chlorophenyl)-1H-imidazole (**5i**).* A solution of methyldiphenylphosphine (0.40 g, 2 mmol) in dry methylene dichloride (10 mL) was added dropwise at room temperature to a well-stirred solution of azide **2b** (0.52 g, 2 mmol) in dry methylene dichloride (10 mL). After stirring for 4 h, the solvent was removed under reduced pressure. Then 4-chlorobenzaldehyde (0.28 g, 2 mmol) and 15 mL ethanol was added to the mixture. The solution was then heated at reflux for 3 h. The solvent was evaporated and the residue was purified by column chromatography to give compound **5i** (0.60 g, 84%) as white solid. Mp: 115–117 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.47–7.03 (m, 14H, Ar–H), 6.56 (s, 1H, imidazole-5-H), 5.10 (s, 2H, CH_2), 3.99 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 146.4, 142.1, 139.8, 136.7, 134.6, 129.8, 128.8, 128.7, 128.6, 128.2, 127.7, 126.1, 125.9, 118.6, 50.0, 35.0. MS (EI, 70 eV) *m*/*z*: 358 (M^+, 23), 248 (7), 208 (8), 103 (12), 91 (100). Anal. Calcd for $C_{23}H_{19}ClN_2$: C, 76.98; H, 5.34; N, 7.81. Found: C, 76.86; H, 5.52; N, 8.09.

*4.4.10. 4-Benzyl-1,2-bis(4-chlorophenyl)-1H-imidazole (**5j**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 4-chlorobenzaldehyde (0.28 g, 2 mmol), compound **5j** (0.69 g, 91%) was also isolated as white solid. Mp: 106–108 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.37–7.23 (m, 11H, Ar–H), 7.08 (d, J=8.4 Hz, 2H, Ar–H), 6.66 (s, 1H, imidazole-5-H), 4.03 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 144.8, 142.7, 139.4, 136.6, 134.3, 133.7, 129.7, 129.5, 128.8, 128.4, 128.3, 126.7, 126.1, 119.7, 34.9. MS (EI, 70 eV) *m*/*z*: 380 (M^+, 28), 250 (53), 248 (100), 111 (15), 77 (12), 40(27). Anal. Calcd for $C_{22}H_{16}Cl_2N_2$: C, 69.67; H, 4.25; N, 7.39. Found: C, 69.57; H, 4.59; N, 7.22.

*4.4.11. 4-Benzyl-1-(4-chlorophenyl)-2-(2,4-dichlorophenyl)-1H-imidazole (**5k**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 2,4-dichlorobenzaldehyde (0.35 g, 2 mmol), compound **5k** (0.72 g, 87%) was also isolated as white solid. Mp: 124–126 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.43–7.24 (m, 10H, Ar–H), 6.98 (d, J=7.8 Hz, 2H, Ar–H), 6.77 (s, 1H, imidazole-5-H), 4.04 (s, 2H,

CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 142.8, 142.6, 139.5, 136.2, 135.9, 134.8, 133.2, 129.6, 129.3, 128.9, 128.8, 128.4, 127.2, 126.2, 125.5, 118.3, 34.9. MS (EI, 70 eV) *m*/*z*: 414 (M^+, 10), 284 (100), 240 (16), 204 (11), 138 (13), 111 (32), 103 (19), 77 (15). Anal. Calcd for $C_{22}H_{15}Cl_3N_2$: C, 63.87; H, 3.65; N, 6.77. Found: C, 64.06; H, 3.73; N, 6.92.

*4.4.12. 2-(Benzo[d][1,3]dioxol-5-yl)-4-benzyl-1-(4-chlorophenyl)-1H-imidazole (**5l**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and benzo[*d*][1,3]dioxole-5-carbaldehyde (0.30 g, 2 mmol), compound **5l** (0.58 g, 75%) was also isolated as white solid. Mp: 137–139 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.38–6.69 (m, 12H, Ar–H), 6.61 (s, 1H, imidazole-5-H), 5.94 (s, 2H, OCH_2), 4.02 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 147.8, 147.4, 145.8, 142.4, 139.6, 136.9, 133.5, 129.5, 129.0, 128.4, 126.8, 126.1, 123.9, 122.9, 119.2, 109.0, 108.1, 101.1, 35.0. MS (EI, 70 eV) *m*/*z*: 389 (M^+, 28), 258 (100), 240 (10), 204 (8), 147 (22), 111 (20), 103 (13), 91 (11), 77 (13). Anal. Calcd for $C_{23}H_{17}ClN_2O_2$: C, 71.04; H, 4.41; N, 7.20. Found: C, 71.32; H, 4.29; N, 7.45.

*4.4.13. 4-Benzyl-1-(4-chlorophenyl)-2-(4-nitrophenyl)-1H-imidazole (**5m**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 4-nitrobenzaldehyde (0.30 g, 2 mmol), compound **5m** (0.54 g, 69%) was also isolated as orange solid. Mp: 164–166 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 8.12 (d, *J*=9.0 Hz, 2H, Ar–H), 7.55 (d, *J*=9.0 Hz, 2H, Ar–H), 7.39–7.23 (m, 7H, Ar–H), 7.13 (d, *J*=9.0 Hz, 2H, Ar–H), 6.76 (s, 1H, imidazole-5-H), 4.04 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 147.0, 143.6, 143.5, 139.1, 136.3, 135.9, 134.4, 129.8, 128.8, 128.7, 128.4, 126.9, 126.2, 123.4, 121.2, 34.8. MS (EI, 70 eV) *m*/*z*: 389 (M^+, 49), 342 (8), 259 (100), 240 (10), 204 (10), 128 (9), 111 (18), 103 (17), 91 (9), 77 (11). Anal. Calcd for $C_{22}H_{16}ClN_3O_2$: C, 67.78; H, 4.14; N, 10.78. Found: C, 68.03; H, 4.32; N, 10.65.

*4.4.14. 4-Benzyl-1-(4-chlorophenyl)-2-phenyl-1H-imidazole (**5n**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and benzaldehyde (0.21 g, 2 mmol), compound **5m** (0.56 g, 82%) was also isolated as white solid. Mp: 104–106 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.39–7.22 (m, 12H, Ar–H), 7.09 (d, *J*=9.0 Hz, 2H, Ar–H), 6.66 (s, 1H, imidazole-5-H), 4.04 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 146.1, 142.6, 139.6, 136.9, 133.5, 130.0, 129.4, 129.0, 128.6, 128.4, 128.2, 126.8, 126.1, 119.5, 35.0. MS (EI, 70 eV) *m*/*z*: 344 (M^+, 43), 340 (9), 214 (100), 111 (18), 103 (16), 91 (6), 77 (12). Anal. Calcd for $C_{22}H_{17}ClN_2$: C, 76.63; H, 4.97; N, 8.12. Found: C, 76.48; H, 5.19; N, 8.33.

*4.4.15. 4-Benzyl-1-(4-chlorophenyl)-2-(4-methoxyphenyl)-1H-imidazole (**5o**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 4-methoxybenzaldehyde (0.27 g, 2 mmol), compound **5o** (0.60 g, 81%) was also isolated as white solid. Mp: 85–87 °C. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.38–7.23 (m, 9H, Ar–H), 7.09 (d, *J*=7.2 Hz, 2H, Ar–H), 6.80 (d, *J*=6.6 Hz, 2H, Ar–H), 6.61 (s, 1H, imidazole-5-H), 4.03 (s, 2H, CH_2), 3.79 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.6, 146.1, 142.4, 139.7, 137.1, 133.4, 130.0, 129.4, 129.0, 128.3, 126.8, 126.1, 122.5, 119.0, 113.6, 55.1, 35.0. MS (EI, 70 eV) *m*/*z*: 374 (M^+, 59), 244 (100), 187 (7), 111 (13), 103 (10), 91 (10), 77 (10). Anal. Calcd for $C_{23}H_{19}ClN_2O$: C, 73.69; H, 5.11; N, 7.47. Found: C, 73.87; H, 5.35; N, 7.61.

*4.4.16. 4-Benzyl-2-(4-bromophenyl)-1-(4-chlorophenyl)-1H-imidazole (**5p**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 4-bromobenzaldehyde (0.37 g, 2 mmol), compound **5p** (0.70 g, 83%) was also isolated as white solid. Mp: 99–101 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.40–7.21 (m, 11H, Ar–H), 7.08 (d, *J*=8.4 Hz, 2H, Ar–H), 6.60 (s, 1H, imidazole-5-H), 4.02 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 144.9, 142.8, 139.4, 136.6, 133.8, 131.4, 130.0, 129.6, 128.8, 128.3, 126.8, 126.1, 122.7, 119.9, 119.8, 34.9. MS (EI, 70 eV) *m*/*z*: 424 (M^+, 47), 294 (100), 240 (13), 128 (13), 111 (40), 103 (13), 77 (9). Anal. Calcd for $C_{22}H_{16}BrClN_2$: C, 62.36; H, 3.81; N, 6.61. Found: C, 62.56; H, 4.03; N, 6.85.

*4.4.17. 4-Benzyl-1-(4-chlorophenyl)-2-(4-fluorophenyl)-1H-imidazole (**5q**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 4-fluorobenzaldehyde (0.37 g, 2 mmol), compound **5q** (0.59 g, 82%) was also isolated as white solid. Mp: 79–81 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.38–7.23 (m, 9H, Ar–H), 7.08 (d, *J*=8.4 Hz, 2H, Ar–H), 6.98–6.95 (m, 2H, Ar–H), 6.66 (s, 1H, imidazole-5-H), 4.03 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.5, 161.8, 145.2, 142.6, 139.5, 136.8, 133.7, 130.4, 129.5, 128.9, 128.4, 126.8, 126.2, 119.5, 115.4, 115.2, 34.9. MS (EI, 70 eV) *m*/*z*: 362 (M^+, 43), 240 (9), 232 (100), 128 (7), 111 (18), 103 (12), 77 (9). Anal. Calcd for $C_{22}H_{16}ClFN_2$: C, 72.83; H, 4.44; N, 7.72. Found: C, 72.64; H, 4.33; N, 7.93.

*4.4.18. 4-Benzyl-2-(4-chlorophenyl)-1-(2-methylphenyl)-1H-imidazole (**5r**).* Operation as above with iminophosphorane **3d** (0.87 g, 2 mmol) and 4-chlorobenzaldehyde (0.28 g, 2 mmol), compound **5r** (0.54 g, 76%) was also isolated as light yellow solid. Mp: 144–146 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.37–7.16 (m, 13H, Ar–H), 6.55 (s, 1H, imidazole-5-H), 4.06 (s, 2H, CH_2), 1.91 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 145.0, 142.3, 139.6, 137.5, 134.6, 133.9, 131.1, 128.9, 128.8, 128.5, 128.2, 127.2, 126.8, 125.9, 119.9, 34.9, 17.2. MS (EI, 70 eV) *m*/*z*: 358 (M^+, 62), 240 (9), 228 (100), 193 (12), 103 (15), 91 (44). Anal. Calcd for $C_{23}H_{19}ClN_2$: C, 76.98; H, 5.34; N, 7.81. Found: C, 77.21; H, 5.15; N, 7.98.

*4.4.19. 2-(2-Azidophenyl)-4-benzyl-1-(4-chlorophenyl)-1H-imidazole (**5s**).* Operation as above with iminophosphorane **3c** (0.90 g, 2 mmol) and 2-azidobenzaldehyde (0.29 g, 2 mmol) at room temperature for 24 h, compound **5s** (0.50 g, 65%) was also isolated as white solid. Mp: 109–111 °C, IR (KBr, cm^{-1}): 2132, 2103, 1578, 1462, 1399, 1299, 1189, 1095, 1012, 976, 838, 764, 705. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.47–7.00 (m, 13H, Ar–H), 6.74 (s, 1H, imidazole-5-H), 4.05 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 143.0, 142.8, 139.6, 138.7, 136.7, 133.1, 132.3, 130.7, 129.2, 129.0, 128.4, 126.2, 125.6, 124.8, 122.5, 118.6, 118.3, 35.0. MS (EI, 70 eV) *m*/*z*: 385 (M^+, 6), 357 (100), 231 (4), 178(9), 129 (11), 111 (14), 91 (28). Anal. Calcd for $C_{22}H_{16}ClN_5$: C, 68.48; H, 4.18; N, 18.15. Found: C, 68.64; H, 4.36; N, 18.43.

*4.4.20. 2-(2-Azidophenyl)-4-benzyl-1-phenyl-1H-imidazole (**5t**).* Operation as above with 2-azidobenzaldehyde (0.29 g, 2 mmol) at room temperature for 24 h, compound **5t** (0.42 g, 60%) was also isolated as light yellow oil. IR (KBr, cm^{-1}): 2127, 2097, 1600, 1497, 1452, 1298, 1027, 756, 694. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.47–7.02 (m, 14H, Ar–H), 6.78 (s, 1H, imidazole-5-H), 4.07 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 143.1, 142.6, 139.8, 138.8, 138.2, 132.4, 130.4, 129.1, 129.0, 128.4, 127.4, 126.1, 124.7, 124.4, 123.0, 118.6, 118.5, 35.1. MS (EI, 70 eV) *m*/*z*: 351 (M^+, 2), 323 (100), 246 (6), 204 (6), 103 (7), 91 (20), 77 (54). Anal. Calcd for $C_{22}H_{17}N_5$: C, 75.19; H, 4.88; N, 19.93. Found: C, 75.42; H, 4.72; N, 20.17.

4.5. Synthesis of iminophosphoranes 7

*4.5.1. 2-(4-Benzyl-1-(4-chlorophenyl)-1H-imidazol-2-yl)-N-(triphenylphosphoranylidene)aniline (**7a**).* A solution of triphenylphosphine (1.05 g, 4 mmol) in dry methylene dichloride (15 mL) was added dropwise at room temperature to a well-stirred solution of imidazole **5s** (1.54 g, 4 mmol) in dry methylene dichloride (15 mL). The reaction mixture was stirred at room temperature for 4 h; then the solvent was removed under reduced pressure. The crude product was recrystallized from ethanol/petroleum ether (1:2.5) to give **7a** (2.28 g, 92%) as yellow solid. Mp: 191–193 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.50–6.68 (m, 28H, Ar–H), 6.19 (d, *J*=9.0 Hz,

1H, Ar–H), 4.13 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.7, 148.1, 141.8, 140.6, 137.7, 132.2, 131.3, 130.9, 130.2, 129.5, 128.9, 128.2, 127.2, 126.1, 125.8, 124.6, 120.6, 116.6, 116.4, 116.3, 35.2. Anal. Calcd for $C_{40}H_{31}ClN_3P$: C, 77.47; H, 5.04; N, 6.78. Found: C, 77.68; H, 5.02; N, 6.63.

*4.5.2. 2-(4-Benzyl-1-phenyl-1H-imidazol-2-yl)-N-(triphenylphosphoranylidene)aniline (**7b**).* Operation as above with **5t** (1.40 g, 4 mmol), compound **7b** (2.08 g, 89%) was also isolated as yellow solid. Mp: 74–76 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.48–6.66 (m, 29H, Ar–H), 6.17 (d, *J*=7.8 Hz, 1H, Ar–H), 4.14 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.0, 148.1, 141.5, 140.8, 139.3, 132.4, 131.3, 131.1, 130.5, 129.2, 129.1, 128.3, 125.8, 125.7, 123.6, 120.7, 116.8, 116.5, 35.3. Anal. Calcd for $C_{40}H_{32}N_3P$: C, 82.03; H, 5.51; N, 7.17. Found: C, 81.74; H, 5.68; N, 7.35.

4.6. Synthesis of imidazo[1,2-*c*]quinazolines 9

*4.6.1. N-(3-Benzyl-1-(4-chlorophenyl)imidazo[1,2-c]quinazolin-5(1H)-ylidene)-4-chloroaniline (**9a**).* 4-Chlorophenylisocyanate (0.15 g, 1 mmol) was added dropwise to a solution of iminophosphorane **7a** (0.62 g, 1 mmol) in dry methylene dichloride (10 mL). The reaction mixture was stirred at room temperature for 0.5–1 h until a solid precipitated. The solid formed was filtered off and recrystallized from ethanol/petroleum ether (2:1) to give **9a** (0.46 g, 93%) as orange solid. Mp: 267–269 °C. ^1H NMR ($CDCl_3$, 600 MHz): δ 7.60–7.58 (m, 4H, Ar–H), 7.40–7.22 (m, 11H, Ar–H), 6.61–6.48 (m, 2H, Ar–H), 6.35 (s, 1H, imidazole-5-H), 5.04 (s, 2H, CH_2). MS (EI, 70 eV) *m*/*z*: 494 (M^+, 1), 480 (3), 207 (100), 142 (28), 132 (9), 112 (9), 103 (7), 94 (23), 77 (13). Anal. Calcd for $C_{29}H_{20}Cl_2N_4$: C, 70.31; H, 4.07; N, 11.31. Found: C, 70.12; H, 4.32; N, 11.53.

*4.6.2. N-(3-Benzyl-1-(4-chlorophenyl)imidazo[1,2-c]quinazolin-5(1H)-ylidene)-4-methylaniline (**9b**).* Operation as above with 4-methylphenylisocyanate (0.13 g, 1 mmol), compound **9b** (0.40 g, 84%) was also isolated as orange solid. Mp: 256–258 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.49–7.11 (m, 15H, Ar–H), 6.56–6.42 (m, 2H, Ar–H), 6.28 (s, 1H, imidazole-5-H), 5.01 (s, 2H, CH_2), 1.78 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.1, 146.3, 142.4, 137.5, 137.0, 134.8, 133.2, 133.0, 130.7, 129.8, 129.5, 128.9, 128.8, 128.3, 126.9, 124.8, 123.3, 122.1, 121.3, 117.5, 104.6, 35.2, 21.0. MS (EI, 70 eV) *m*/*z*: 474 (M^+, 100), 204 (5), 198 (13), 180 (7), 77 (8). Anal. Calcd for $C_{30}H_{23}ClN_4$: C, 75.86; H, 4.88; N, 11.80. Found: C, 76.08; H, 5.12; N, 12.09.

*4.6.3. N-(3-Benzyl-1-phenylimidazo[1,2-c]quinazolin-5(1H)-ylidene)-4-chloroaniline (**9c**).* Operation as above with iminophosphorane **7b** (0.59 g, 1 mmol) and 4-chlorophenylisocyanate (0.15 g, 1 mmol), compound **9c** (0.39 g, 84%) was also isolated as orange solid. Mp: 251–253 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.65–7.20 (m, 16H, Ar–H), 6.56–6.42 (m, 2H, Ar–H), 6.39 (s, 1H, imidazole-5-H), 5.03 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 151.5, 148.2, 146.5, 142.3, 137.6, 136.4, 133.2, 132.6, 130.5, 129.4, 128.8, 128.6, 128.1, 127.8, 126.8, 126.5, 124.8, 124.7, 122.2, 121.8, 118.0, 105.2, 35.1. MS (EI, 70 eV) *m*/*z*: 460 (M^+, 100), 281 (6), 206 (18), 191 (12), 77 (63). Anal. Calcd for $C_{29}H_{21}ClN_4$: C, 75.56; H, 4.59; N, 12.15. Found: C, 75.79; H, 4.33; N, 12.05.

*4.6.4. N-(3-Benzyl-1-phenylimidazo[1,2-c]quinazolin-5(1H)-ylidene)-4-methylaniline (**9d**).* Operation as above with iminophosphorane **7b** (0.59 g, 1 mmol) and 4-methylphenylisocyanate (0.13 g, 1 mmol), compound **9d** (0.67 g, 83%) was also isolated as orange solid. Mp: 225–227 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.63–7.10 (m, 16H, Ar–H), 6.52–6.36 (m, 3H, Ar–H), 5.07 (s, 2H, CH_2), 2.32 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 146.5, 137.8, 136.6, 133.0, 132.7, 130.9, 130.5, 129.6, 128.9, 128.8, 126.9, 125.1, 123.4, 122.1, 121.7, 121.5, 117.3, 35.1, 21.0. MS (EI, 70 eV) *m*/*z*: 440 (M^+, 100), 222 (13), 181 (25), 104 (15), 91 (20), 77 (36). Anal. Calcd for $C_{30}H_{24}N_4$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.62; H, 5.64; N, 12.95.

*4.6.5. N-(3-Benzyl-1-phenylimidazo[1,2-c]quinazolin-5(1H)-ylidene)-3-methylaniline (**9e**).* Operation as above with iminophosphorane **7b** (0.59 g, 1 mmol) and 3-methylphenylisocyanate (0.13 g, 1 mmol), compound **9e** (0.40 g, 90%) was also isolated as red solid. Mp: 232–234 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.64–7.17 (m, 15H, Ar–H), 6.74 (d, *J*=7.2 Hz, 1H, Ar–H), 6.53 (d, *J*=8.4 Hz, 1H, Ar–H), 6.39–6.36 (m, 2H, Ar–H), 5.07 (s, 2H, CH_2), 2.34 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 152.2, 146.6, 142.6, 137.7, 136.6, 133.0, 132.8, 130.9, 130.5, 129.6, 128.8, 128.2, 126.9, 125.1, 124.2, 122.1, 121.5, 120.5, 117.4, 104.9, 35.2, 21.7. MS (EI, 70 eV) *m*/*z*: 440 (M^+, 100), 220 (5), 181 (13), 104 (12), 77 (40). Anal. Calcd for $C_{30}H_{24}N_4$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.89; H, 5.32; N, 12.61.

*4.6.6. N-(3-Benzyl-1-(4-chlorophenyl)imidazo[1,2-c]quinazolin-5(1H)-ylidene)-3-methylaniline (**9f**).* Operation as above with 3-methylphenylisocyanate (0.13 g, 1 mmol), compound **9f** (0.44 g, 92%) was also isolated as orange solid. Mp: 249–251 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.49–7.16 (m, 14H, Ar–H), 6.76 (d, *J*=7.2 Hz, 1H, Ar–H), 6.57 (d, *J*=7.8 Hz, 1H, Ar–H), 6.45–6.42 (m, 1H, Ar–H), 6.28 (s, 1H, imidazole-5-H), 5.02 (s, 2H, CH_2), 2.34 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.5, 137.8, 137.6, 137.1, 134.9, 133.3, 133.0, 130.7, 129.5, 128.8, 128.3, 128.1, 126.9, 125.0, 124.3, 122.0, 121.6, 121.4, 120.5, 117.6, 35.2, 21.7. MS (EI, 70 eV) *m*/*z*: 474 (M^+, 100), 249 (23), 211 (17), 207 (38), 198 (18), 180 (16), 116 (17), 106 (34), 96 (12). Anal. Calcd for $C_{30}H_{23}ClN_4$: C, 75.86; H, 4.88; N, 11.80. Found: C, 76.12; H, 5.07; N, 11.64.

*4.6.7. N-(3-Benzyl-1-(4-chlorophenyl)imidazo[1,2-c]quinazolin-5(1H)-ylidene)aniline (**9g**).* Operation as above with phenylisocyanate (0.12 g, 1 mmol), compound **9g** (0.39 g, 85%) was also isolated as orange solid. Mp: 264–265 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.60–7.24 (m, 15H, Ar–H), 6.95–6.45 (m, 3H, Ar–H), 6.32 (s, 1H, imidazole-5-H), 5.06 (s, 2H, CH_2). MS (EI, 70 eV) *m*/*z*: 460 (M^+, 100), 383 (9), 191 (24), 111 (25), 103 (11), 91 (16), 77 (36). Anal. Calcd for $C_{29}H_{21}ClN_4$: C, 75.56; H, 4.59; N, 12.15. Found: C, 75.46; H, 4.87; N, 12.43.

*4.6.8. N-(3-Benzyl-1-(4-chlorophenyl)imidazo[1,2-c]quinazolin-5(1H)-ylidene)propan-2-amine (**9h**).* Operation as above with 2-propylisocyanate (0.09 g, 1 mmol), compound **9h** (0.39 g, 91%) was also isolated as orange solid. Mp: 208–210 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.54–7.07 (m, 11H, Ar–H), 6.45 (d, *J*=7.8 Hz, 1H, Ar–H), 6.28 (s, 1H, imidazole-5-H), 6.25–6.23 (m, 1H, Ar–H), 4.91 (s, 2H, CH_2), 4.24–4.22 (m, 1H, CH), 1.19 (d, *J*=6.0 Hz, 6H, $2CH_3$). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 153.5, 147.0, 138.0, 136.9, 135.2, 133.2, 132.6, 130.7, 129.4, 128.7, 128.2, 126.7, 124.2, 122.2, 120.9, 115.5, 103.1, 46.2, 34.6, 24.4. MS (EI, 70 eV) *m*/*z*: 426 (M^+, 47), 411 (100), 384 (14), 370 (49), 368 (89), 343 (17). Anal. Calcd for $C_{26}H_{23}ClN_4$: C, 73.14; H, 5.43; N, 13.12. Found: C, 73.41; H, 5.36; N, 13.35.

*4.6.9. N-(3-Benzyl-1-phenylimidazo[1,2-c]quinazolin-5(1H)-ylidene)-4-fluoroaniline (**9i**).* Operation as above with iminophosphorane **7b** (0.59 g, 1 mmol) and 4-fluorophenylisocyanate (0.14 g, 1 mmol), compound **9i** (0.36 g, 81%) was also isolated as orange solid. Mp: 224–226 °C, ^1H NMR ($CDCl_3$, 600 MHz): δ 7.64–6.94 (m, 16H, Ar–H), 6.55–5.55 (m, 3H, Ar–H), 5.06 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 146.5, 142.5, 136.5, 133.2, 132.7, 131.0, 130.6, 129.5, 128.8, 126.8, 125.0, 124.5, 122.2, 121.7, 117.7, 114.7, 114.5, 105.0, 35.2. MS (EI, 70 eV) *m*/*z*: 444 (M^+, 100), 368 (7), 183 (20), 77 (34). Anal. Calcd for $C_{29}H_{21}FN_4$: C, 78.36; H, 4.76; N, 12.60. Found: C, 78.27; H, 4.92; N, 12.58.

*4.6.10. N-(3-Benzyl-1-phenylimidazo[1,2-c]quinazolin-5(1H)-ylidene)aniline (**9j**).* Operation as above with iminophosphorane **7b** (0.59 g, 1 mmol) and phenylisocyanato (0.12 g, 1 mmol), compound

9j (0.35 g, 82%) was also isolated as orange solid. Mp: 262–264 °C, ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.69–7.25 (m, 16H, Ar–H), 6.94–6.41 (m, 3H, Ar–H), 6.37 (s, 1H, imidazole-5-H), 5.08 (s, 2H, CH_2). MS (EI, 70 eV) *m*/*z*: 426 (M^+, 100), 349 (16), 282 (9), 206 (16), 174 (17), 104 (10), 77 (60). Anal. Calcd for $C_{29}H_{22}N_4$: C, 81.66; H, 5.20; N, 13.14. Found: C, 81.85; H, 5.42; N, 13.07.

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Supplementary data

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References and notes

1. Claiborne, C. F.; Liverton, N. J.; Nguyen, K. T. *Tetrahedron Lett.* **1998**, *39*, 8939.
2. (a) Özkay, Y.; Işikdağ, İ; İncesu, Z.; Akalin, G. *Eur. J. Med. Chem.* **2010**, *45*, 3320; (b) Cui, B.; Zheng, B. L.; He, K.; Zheng, Q. Y. *J. Nat. Prod.* **2003**, *66*, 1101.
3. Vlahakis, J. Z.; Kinobe, R. T.; Bowers, R. J.; Brien, J. F.; Nakatsu, K.; Szarek, W. A. *J. Med. Chem.* **2006**, *49*, 4437.
4. Takle, A. K.; Brown, M. J. B.; Davies, S.; Dean, D. K.; Francis, G.; Gaiba, A.; Hird, A. W.; King, F. D.; Lovell, P. J.; Naylor, A.; Reith, A. D.; Steadman, J. G.; Wilson, D. M. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 378.
5. Schmierer, R.; Mildenberger, H.; Buerstell, H. German Patent 361464, 1987; *Chem. Abstr.* **1988**, *108*, 37838.
6. Maier, T.; Schmierer, R.; Bauer, K.; Bieringer, H.; Buerstell, H.; Sachse, B. U.S. Patent 4820335, 1989; *Chem. Abstr.* **1989**, *111*, 19494w.
7. (a) Carmely, S.; Ilan, M.; Kashman, Y. *Tetrahedron* **1989**, *45*, 2193; (b) Alvi, K. A.; Crews, P. *J. Nat. Prod.* **1991**, *54*, 1509; (c) Alvi, K. A.; Peters, B. M.; Hunter, L. M.; Crews, P. *Tetrahedron* **1993**, *49*, 329.
8. (a) Gulevich, A. V.; Balenkova, E. S.; Nenajdenko, V. G. *J. Org. Chem.* **2007**, *72*, 7878; (b) Sung, K.; Wu, S. H.; Chen, P. I. *Tetrahedron* **2002**, *58*, 5599; (c) Zhang, C.; Moran, E. J.; Woiwode, T. F.; Short, K. M.; Mjalli, A. M. M. *Tetrahedron Lett.* **1996**, *37*, 751; (d) Samai, S.; Nandi, G. C.; Singh, P.; Singh, M. S. *Tetrahedron* **2009**, *65*, 10155; (e) Kim, Y. M.; Lee, S.; Kim, S. H.; Kim, K. H.; Kim, J. N. *Tetrahedron Lett.* **2010**, *51*, 5922.
9. Cobb, J. M.; Grimster, N.; Khan, N.; Lai, J. Y. Q.; Payne, H. J.; Payne, L. J.; Raynham, T.; Taylor, J. *Tetrahedron Lett.* **2002**, *43*, 7557.
10. Petit, S.; Fruit, C.; Bischoff, L. *Org. Lett.* **2010**, *12*, 4928.
11. Zaman, S.; Mitsuru, K.; Abell, A. D. *Org. Lett.* **2005**, *7*, 609.
12. (a) Marsden, S. P.; McGonagle, A. E.; McKeever-Abbas, B. *Org. Lett.* **2008**, *10*, 2589; (b) Lertpibulpanya, D.; Marsden, S. P.; Rodriguez-Garcia, I.; Kilner, C. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 5000; (c) Palacios, F.; Alonso, C.; Aparicio, D.; Rubiales, G.; Santos, J. M. *Tetrahedron* **2007**, *63*, 523; (d) Alajarin, M.; Bonillo, B.; Ortin, M.-M.; Sanchez-Andrada, P.; Vidal, A.; Orenes, R.-A. *Org. Biomol. Chem.* **2010**, *8*, 4690; (e) Devarie-Baez, N. O.; Xian, M. *Org. Lett.* **2010**, *12*, 752.
13. (a) Molina, P.; Fresneda, P. M.; Alarcon, P. *Tetrahedron Lett.* **1988**, *29*, 379; (b) Barluenga, J.; Ferrero, M.; Palacios, F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2193; (c) Molina, P.; Pastor, A.; Vilaplana, M. J. *Tetrahedron* **1993**, *49*, 7769.
14. (a) Molina, P.; Tarraga, A.; Lidon, M. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1727; (b) Saito, T.; Nakane, M.; Endo, M.; Yamashita, H.; Oyamade, Y.; Motoki, S. *Chem. Lett.* **1986**, 135.
15. (a) Bonini, C.; D'Auria, M.; Funicello, M.; Romaniello, G. *Tetrahedron* **2002**, *58*, 3507; (b) Degl'Innocenti, A.; Funicello, M.; Scafato, P.; Spagnolo, P.; Zanirato, P. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2561.
16. Peinador, C.; Moreira, M. J.; Quintela, J. M. *Tetrahedron* **1994**, *50*, 6705.
17. (a) Molina, P.; Aller, E.; Lorenzo, A.; López-Cremades, P.; Rioja, I.; Ubeda, A.; Terencio, M. C.; Alcaraz, M. J. *J. Med. Chem.* **2001**, *44*, 1011; (b) Molina, P.; Lorenzo, A.; Aller, E. *Tetrahedron* **1992**, *48*, 4601.
18. (a) Bedi, P. M. S.; Kumar, V.; Mahajan, M. P. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5211; (b) Rossi, E.; Calabrese, D.; Farma, F. *Tetrahedron* **1991**, *47*, 5819.
19. Palacios, F.; Alonso, C.; Rubiales, G. *Tetrahedron* **1995**, *51*, 3683.
20. (a) Zhong, Y.; Wang, L.; Ding, M. W. *Tetrahedron* **2011**, *67*, 3714; (b) He, P.; Nie, Y. B.; Wu, J.; Ding, M. W. *Org. Biomol. Chem.* **2011**, *9*, 1429; (c) He, P.; Wu, J.; Nie, Y. B.; Ding, M. W. *Eur. J. Org. Chem.* **2010**, 1088; (d) Li, W. J.; Liu, S.; He, P.; Ding, M. W. *Tetrahedron* **2010**, *66*, 8151; (e) Huang, N. Y.; Nie, Y. B.; Ding, M. W. *Synlett* **2009**, 611; (f) Li, W. J.; Zhao, F. F.; Ding, M. W. *Synlett* **2011**, 265; (g) He, P.; Wu, J.; Nie, Y. B.; Ding, M. W. *Tetrahedron* **2009**, *65*, 8563; (h) Huang, N. Y.; Liu, M. G.; Ding, M. W. *J. Org. Chem.* **2009**, *74*, 6874.
21. (a) L'abbé, G.; Hassner, A. *J. Org. Chem.* **1971**, *36*, 258; (b) Hassner, A.; L'abbé, G.; Miller, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 981; (c) Fardelone, L. C.; Augusto, J.; Rodrigues, R.; Moran, P. J. S. *J. Mol. Catal. B: Enzym.* **2004**, *29*, 41.
22. George, M. V.; Mitra, A.; Sukumaran, K. B. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 973.