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Ligand-free, $PdCl_2(PPh_3)_2$ catalyzed, microwave-assisted Suzuki coupling of 1-chloro-3-phenylisoquinoline in the synthesis of diversified 1,3-disubstituted isoquinolines

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Abstract An efficient ligand-free, microwave-assisted, Pd-catalyzed, Suzuki coupling of 1-chloro-3-phenylisoquinoline and boronic acids, in the presence of sodium carbonate base and 1,4-dioxane solvent, is reported for the synthesis of diversified 1,3-disubstituted isoquinolines.

Keywords Suzuki coupling · Ligand-free · 1,3-disubstituted isoquinolines · $PdCl_2(PPh_3)_2$ · Boronic acids

Introduction

The 2010 Nobel prize in chemistry was awarded to Prof. Suzuki for his discovery and development of the Suzuki coupling reaction of an aryl- or vinyl-boronic acid with an aryl-, vinyl-, or alkyl-halide catalyzed by palladium. It is widely used to synthesize poly-olefins, styrenes, and substituted biphenyls. A variety of catalysts and development of the method in this reaction have broadened the applications and the scope of the reaction. The Suzuki cross-coupling reaction is an extremely versatile methodology for the generation of carbon–carbon bonds [1–3]. This reaction has paved a way for the synthetic chemist to develop an efficient

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methodology in organic synthesis and also in the total synthesis of targeted compounds.

The reaction was first reported by Akira Suzuki and his group in 1979 [4, 5]. The Suzuki reaction has found a wide application in modern synthetic organic chemistry for the preparation of biaryl compounds [6–9]. Over the years, the Suzuki cross-coupling has been developed further to include the reaction between boronic acids, boronate esters, or organoboranes and organic halides or pseudohalides [10]. There are many advantages of the reaction, e.g., mild reaction conditions, commercial availability of the environmentally safe boronic acids, easy removal of inorganic byproducts, stability of boronic acids towards heat, air, and moisture, and tolerance to a wide variety of functional groups [11]. Byproducts which can be formed are coupling products of phosphine-bound aryls and self-coupled products. It is necessary to have a base present during the reaction, since it will be able to form borates which are more electron-rich than the boronic acid, thereby, facilitating the transmetallation step [12]. The most commonly used base is Na_2CO_3, but it is often ineffective with sterically hindered substrates. Instead, $Ba(OH)_2$ and K_3PO_4 can be used in such reactions in order to obtain good yields [13, 14]. The addition of ligands, which stabilize the metal catalyst, has made it possible to couple aryl chlorides [15] and hindered substrates, which has presented problems in the past [16].

1,3-disubstituted isoquinoline skeleton is an integral part of many naturally occurring substances and pharmaceutically important compounds [17–19]. 1,3-disubstituted isoquinolines have resulted in them being used as building blocks [20] in pharmaceutical compounds [21], as chiral ligands for the transition metal catalysts [22], and their iridium complexes in organic light-emitting diodes (OLEDs) [23]. A number of methods have been developed for the synthesis of 1,3-disubstituted isoquinolines, including palladium-catalyzed cross-coupling of iodine-mediated electrophilic cyclization of 2-alkynylbenzaldoximes [24], copper catalyzed tandem synthesis of [1, 2, 3] triazolo [5,1-a]isoquinolines [25], irradiation of 1-methoxy-2-azabuta-1,3-dienes in neutral medium [26], isobenzofuran-nitrile Diels–Alder reaction [27], light-induced iminyl radical cyclization of acyloximes [28], and silver [29] and gold [30] catalyzed cyclization of 2-alkynyl benzyl azides. Disubstituted isoquinolines are endowed with an extensive range of biological activities [31]. Moreover, they display potent thrombin inhibitory activity and antibacterial activity against Gram-positive bacteria [32].

In our continued interest on isoquinolines and heterocyclics [33–48], the present study involved the Suzuki coupling, in order to explore an efficient catalytic system in the synthesis of diversified 1,3-disubstituted isoquinolines. The optimization envisaged that the use of $PdCl_2(PPh_3)_2$ catalyst, Na_2CO_3 base, and 1,4-dioxane solvent under aqueous-free microwave irradiation conditions offered greater efficiency in the synthesis of 1,3-disubstituted isoquinolines.

Results and discussion

In our continued interest of isoquinolines and heterocyclics [33–48], in the present letter, the coupling of a series of boronic acid and 1-chloroisoquinoline in the

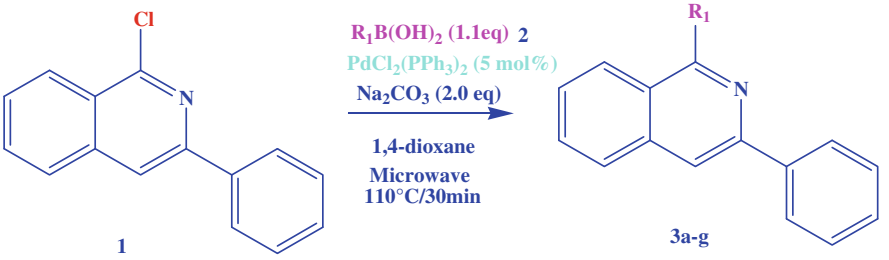
synthesis of 1,3-disubstituted isoquinoline through ligand-free Suzuki coupling is reported. The reaction of 1-chloro-3-phenylisoquinoline **1** and boronic acids **2** in 1,4-dioxane in the presence of $PdCl_2(PPh_3)_2$ catalyst and sodium carbonate base under microwave irradiation at 150 W at 110 °C for 30 min afforded 1,3-disubstituted isoquinolines **3** in excellent yields and high purity (Scheme 1; Table 1).

The optimization of the reaction conditions was carried out by choosing the Suzuki coupling of 1-chloro-3-phenylisoquinoline **1** and 4-pyridylboronic acid **2a** as the model reaction. The development of optimized conditions included the screening of various catalysts in the presence of sodium carbonate base, the effect of ligands, and the effect of bases (Tables 2–4). As shown in Table 2, the reaction proceeds well in the presence of $PdCl_2(PPh_3)_2$ catalyst (entry 4), with an excellent product yield. However, $Pd(PPh_3)_4$ and palladium acetate/X-Phos catalysts produced lower yields (Table 2, entries 5 and 6); the rest of the catalysts were found to be less effective.

The influence of phosphine ligands in the reaction was then explored by choosing the Suzuki coupling of 1-chloro-3-phenylisoquinoline **1** with phenylboronic acid **2c** as a model reaction (Scheme 2). The reaction results indicated that a major quantity of byproduct 3-phenyl isoquinoline-1-ol **4c** was formed in the presence of phosphine ligand, with a lesser amount of required product **3c**.

Further, to optimize this reaction condition, variation of the amount of ligand load and aqueous-free conditions were investigated, which suggested the result as indicated in Table 3, entries 1–6. From the results, it is clear that the phosphine ligand and palladium acetate catalytic system is not a suitable catalyst system for the desired product **3c**; however, they are fruitful in achieving the undesired product, 3-phenyl isoquinoline-1-ol **4c**.

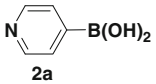
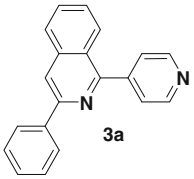
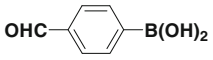
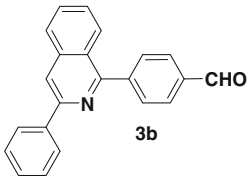
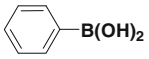
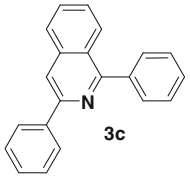
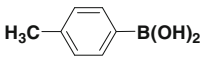
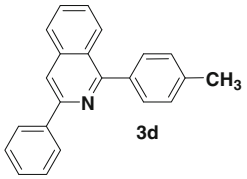
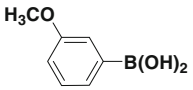
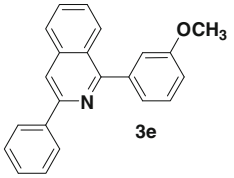
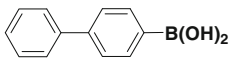
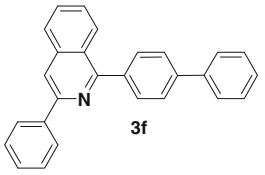
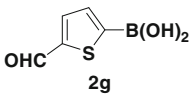
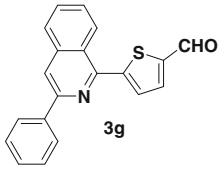
Further investigations were made to explore the influence of bases on the Suzuki reaction of **1** and **2a** (Table 4). Among the bases tested, sodium carbonate (Table 4, entry 6) proved to be an excellent base at 110 °C in 1,4-dioxane solvent under microwave irradiation conditions, while sodium bicarbonate, potassium carbonate, and cesium carbonate are found to be moderately effective (entries 1, 3, and 5,



R_1= 4-pyridyl, 4-formylphenyl, phenyl, *p*-tolyl, 3-methoxyphenyl, 4-biphenyl, thiophene-2-carbonyl

Scheme 1 Synthesis of 1,3-disubstituted isoquinolines

Table 1 Suzuki coupling of 1-chloro-3-phenylisoquinolines **1** and boronic acids **2**[a]

Entry	Boronic acids **2**	Product **3**	Yield[b] (%)
1	 **2a**	 **3a**	90
2	 **2b**	 **3b**	73
3	 **2c**	 **3c**	82
4	 **2d**	 **3d**	87
5	 **2e**	 **3e**	72
6	 **2f**	 **3f**	65
7	 **2g**	 **3g**	78

[a] Reaction conditions: **1** (0.1 mmol), **2** (0.11 mmol), $PdCl_2(PPh_3)_2$ (5 mol%), Na_2CO_3 (2.0 eq), 1,4-dioxane (4 mL) microwave irradiated at 150 W at 110 °C for 30 min

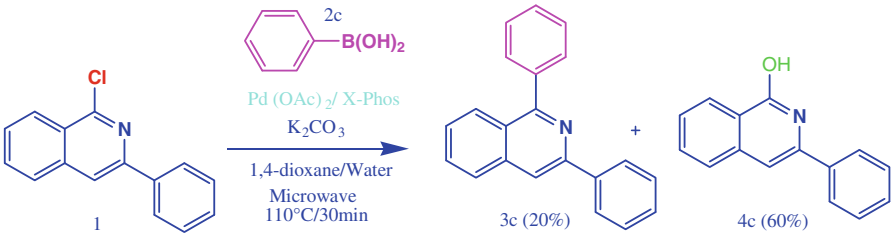
[b] Isolated yield

Table 2 Effect of catalysts in the Suzuki coupling of **1** with boronic acid **2a**

Entry	Catalyst	Base	Water	Yield[a] (%)
1	$Pd(PPh_3)_4$	Na_2CO_3	–	55
2	$PdCl_2(dppf)_2$	Na_2CO_3	–	30
3	$Pd_2(dba)_3$	Na_2CO_3	–	25
4	$PdCl_2(PPh_3)_2$	Na_2CO_3	–	90
5	$Pd(OAc)_2$/(X-Phos, 0.1 eq)	K_2CO_3	0.1 mL	20
6	$Pd(OAc)_2$/(ruphos, 0.1 eq)	K_2CO_3	0.1 mL	22

Reaction conditions: **1** (0.1 mmol), **2** (0.11 mmol), catalyst (5 mol %), base (2.0 eq), 1,4-dioxane (4 mL), microwave irradiated at 150 W at 110 °C for 30 min

[a] Isolated yield



Scheme 2 Suzuki coupling of 1-chloro-3-phenylisoquinoline **1** with phenylboronic acid **2c**

Table 3 Effect of phosphine ligands in the Suzuki reaction of **1** with boronic acid **2c**

Entry	Ligand	Water (mL)	K_2CO_3 (eq)	Product **3c** (%)	Byproduct **4c** (%)
1	X-phos (0.5 eq)	0.1	2.0	20	60
2	Ruphos (0.5 eq)	0.1	2.0	22	65
3	X-phos (0.1 eq)	0.1	2.0	18	60
4	X-phos (0.1 eq)	–	2.0	–	62
5	X-phos (0.1 eq)	0.1	–	–	20
6	X-phos (0.1 eq)	–	–	–	15

Reaction conditions: **1** (0.1 mmol), **2c** (0.11 mmol), $PdCl_2(PPh_3)_2$ (5 mol%), base, 1,4-dioxane (4 mL) microwave irradiated at 150 W at 110 °C for 30 min

respectively). The rest of the bases were found to be less effective (entries 2 and 4). The influence of the amount of base was also investigated, and the result indicated that lower the amount of base could yield loss of product **3a** (Table 4, entries 7 and 8) and that 2.0 eq of base is necessary for effective conversion (Table 4, entries 9 and 10). With the optimized result in hand, various 1,3-disubstituted isoquinolines were synthesized and the results are reported (as shown in Scheme 1; Table 1). The desired products **3a–g**, were obtained in high yield (65–90%) and purity. The purified products were characterized by different spectral techniques, including ^1H, ^{13}C, LC-MS, IR, and CHNS analysis. The proposed mechanism of the reaction is depicted in Scheme 3. The mechanism of the Suzuki reaction involved the oxidative

addition of aryl halide to palladium in the formation of organo-palladium species; meanwhile, the boron atom of boronic acid gets activated by the base, which enhances the polarization of the organic ligand, and facilitates transmetallation and, finally, reductive elimination to give rise to the final isoquinolines.

In conclusion, an efficient, experimentally simple, ligand-free, Pd-catalyzed, microwave-assisted, Suzuki coupling in the presence of sodium carbonate and 1,4-dioxane system for diversified 1,3-disubstituted isoquinolines has been established. The highlights of this catalytic system include high catalytic activity, ready availability of catalyst, and aqueous-free reaction conditions.

Experimental section

All reagents were purchased from Sigma-Aldrich, India, and used without further purification. All boronic acids were purchased from Sigma-Aldrich, India, and used as received. IR spectra were recorded using Avatar 330 equipped with a DTGS detector. The NMR was recorded on a Bruker Spectrospin Avance DPX400 Ultrashield (400 MHz) spectrometer instrument. Mass spectra were obtained using Agilent mass spectrometry 1200 series. Microwave irradiation was performed in 8-mL vials. The Biotage microwave equipment operating with a frequency of 20 kHz and output power 0–150 W was utilized for the study. The CHNS analyses were carried out on a Vario Micro elemental analyzer. Melting points were checked on an open capillary tube in Elchem microprocessor-based DT apparatus and the values are uncorrected.

General procedure for the synthesis of 1,3-disubstituted isoquinolines **(3a–g)**

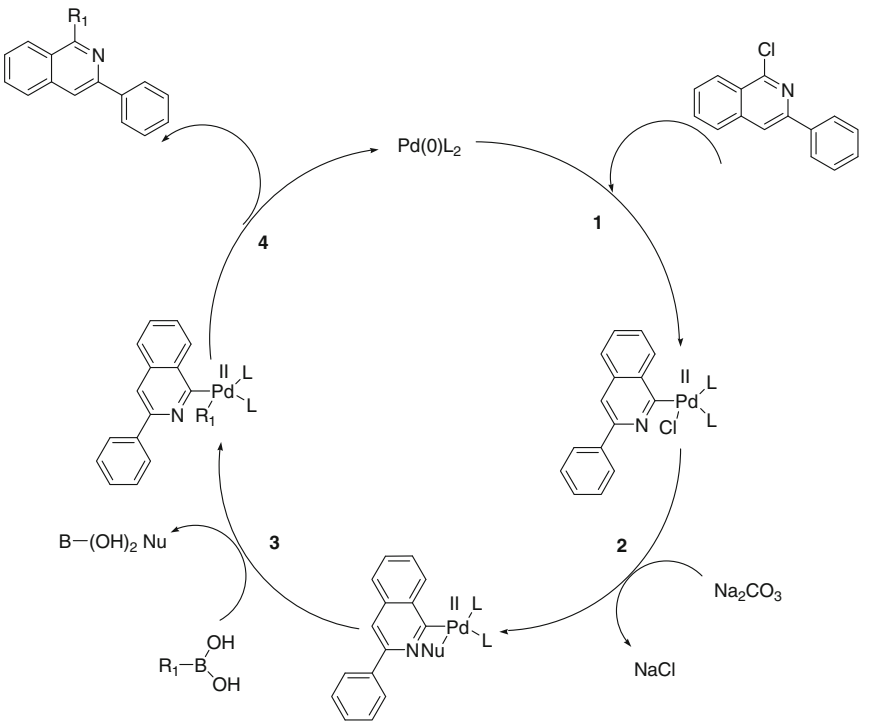
A mixture of 1-chloro-3-phenylisoquinoline **1**, (0.1 mmol) boronic acids **2**, (0.11 mmol) sodium carbonate (2.0 eq), and 1,4-dioxane (4 mL) was degassed

Table 4 Effect of bases in the Suzuki reaction of **1** with boronic acid **2a**

Entry	Base	Amount of base (eq)	Yield[a] (%)
1	$NaHCO_3$	2.0	65
2	NaO^tBut	1.1	20
3	K_2CO_3	1.5	60
4	NaOH	1.0	40
5	Cs_2CO_3	2.0	65
6	Na_2CO_3	2.0	90
7	Na_2CO_3	1.0	55
8	Na_2CO_3	1.5	75
9	Na_2CO_3	2.5	90
10	Na_2CO_3	3.0	90

Reaction conditions: **1** (0.1 mmol), **2c** (0.11 mmol), catalyst, base, 1,4-dioxane (4 mL) microwave irradiated at 150 W at 110 °C for 30 min

[a] Isolated yield



L= PPh_3

R_1= 4-pyridyl, 4-formylphenyl, phenyl, *p*-tolyl, 3-methoxyphenyl, 4-biphenyl, thiophene-2-carbonyl

Scheme 3 Mechanism of reaction

twice using nitrogen gas. Then, $PdCl_2(PPh_3)_2$ (5.0 mol%) was added and again degassed twice and microwave irradiated at 150 W at 110 °C for 30 min. The reaction was monitored by TLC. After completion of the reaction, the resulting solution was filtered off using celite pad (to remove catalyst) and the filtrate was concentrated in vacuo. The crude product was subjected to silica-gel (230–400 mesh) flash column chromatography using hexane-ethyl acetate (90:10) eluent to afford the pure products (Table 1). The compounds were confirmed by FTIR, ^{1}H NMR, ^{13}C NMR, CHNS, and MS techniques. The analysis data of **3a–g** are given below.

3a: Yellow solid: mp 87–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.83–8.82 (d, 2H, *J* 5.6), 8.21–8.18 (d, 2H, *J* 8.4), 8.14 (s, 1H), 8.07–8.05 (d, 1H, *J* 8.4), 7.98–7.96 (d, 1H, *J* 8.4), 7.74–7.71 (m, 3H), 7.58–7.49 (m, 3H), 7.44–7.41 (t, 1H, *J* 7.2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.58, 150.45, 149.91, 147.34, 139.11, 137.84, 130.44, 128.82, 128.75, 127.74, 127.51, 127.01, 126.53, 125.36, 124.80, 116.67; IR (ν cm^{-1}) 3029.3, 2918.5, 2850.3, 2283.4, 2167.1, 2132.1, 2027.9, 1988.0, 1951.9, 1716.3, 1615.9, 1588.7, 1562.9, 1539.0, 1492.6, 1447.5, 1408.5, 1379.0, 1333.5,

1211.5, 1176.5, 1137.8, 1067.8, 1026.4, 977.8, 881.0, 856.3, 828.4, 761.6, 680.6, 643.2, 621.0, 594.3, 564.1, 516.8; LC-MS: *m/e* 283.2, $C_{20}H_{14}N_2$ requires Mol. Wt.: 282.12. Elemental analysis, calculated: C, 85.08; H, 5.00; N, 9.92%. Found: C, 85.09; H, 5.03; N, 9.95%.

3b: Yellow solid: mp 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.18 (s, 1H), 8.54 (s, 1H), 8.29–8.27 (d, 2H, *J* 8.4), 8.18–8.14 (m, 3H), 8.03–8.01 (d, 3H, *J* 8.0), 7.87–7.83 (t, 1H, *J* 7.6), 7.69–7.65 (t, 1H, *J* 8.0), 7.57–7.53 (t, 2H, *J* 7.2), 7.48–7.44 (t, 1H, *J* 7.2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.00, 150.16, 137.96, 136.33, 130.99, 130.62, 129.68, 128.81, 127.69, 127.52, 127.16, 126.99, 125.61, 116.73; IR (ν cm^{-1}) 3368.4, 3034.4, 2919.2, 2850.4, 2724.4, 2185.3, 2131.6, 2029.1, 1934.3, 1693.1, 1598.2, 1550.4, 1490.6, 1439.9, 1376.6, 1329.7, 1300.1, 1258.8, 1202.5, 1168.8, 1070.8, 1019.8, 970.0, 880.1, 823.3, 761.1, 679.7, 646.5, 589.6, 512.6; LC-MS: *m/e* 310.2, $C_{22}H_{15}NO$ requires Mol. Wt.: 309.12. Elemental analysis, calculated: C, 85.41; H, 4.89; N, 4.53; O, 5.17%. Found: C, 85.46; H, 4.93; N, 4.50%.

3c: White solid: mp 165–165.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85-7.82 (d, 2H, *J* 8.31), 7.40-7.11 (m, 11H), 6.68-6.66 (d, 1H, *J* 7.59), 6.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.18, 143.88, 134.43, 133.25, 131.81, 128.68, 128.54, 128.37, 128.28, 128.22, 127.87, 127.75,127.61, 127.26, 126.05, 124.95, 124.07; IR (ν cm^{-1}) 3056.5, 2920.3, 2850.5, 1722.2, 1620.3, 1566.4, 1494.7, 1443.9, 1384.7, 1332.7, 1266.9, 1138.4, 1070.5, 1025.1, 963.7, 878.3, 848.4, 742.0, 687.7, 581.8, 557.5, 511.8; LC-MS: m/e 282.2, $C_{21}H_{15}N$ requires Mol. Wt.: 281.12. Elemental analysis, calculated: C, 89.65; H, 5.37; N, 4.98%. Found: C, 89.62; H, 5.34; N, 4.94%.

3d: White solid: mp 112–112.6 °C; ^{1}H NMR (400 MHz, CDCl3): δ 8.14–8.11(d, 3H, *J* 8.16), 8.06 (s, 1H), 7.94–7.91 (d, 1H, *J* 8.10), 7.83–7.81 (d, 2H, *J* 7.95), 7.68 (m, 1H), 7.57–7.50 (m, 4H), 7.32–7.30 (d, 2H, *J* 7.89), 2.43 (s, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 160.24, 150.18, 139.85, 138.38, 137.88, 136.74, 130.23, 130.0, 129.42, 128.56, 128.25, 125.55, 127.38, 126,95, 126.70, 125.66, 115.23, 21.28; IR (ν cm^{-1}) 3051, 2916, 2854, 2729, 2360, 1904, 1872, 1616, 1588, 1561, 1515, 1488, 1441, 1385, 1335, 1308, 1185, 1022, 975, 829, 823, 813, 766, 744, 698, 678, 643, 616; LC-MS: *m/e* 296.2, $C_{22}H_{17}N$ requires Mol. Wt.: 294.14. Elemental analysis, calculated: C, 89.46; H, 5.80; N, 4.74%. Found: C, 89.43; H, 5.77; N, 4.70%.

3e: White solid: Mp 109–110 °C; ^{1}H NMR (400 MHz, CDCl3): δ = 8.21–8.14 (m, 3H), 8.09 (s, 1H), 7.96–7.94 (d, 1H, *J* 8.13), 7.74–7.69 (t, 1H, *J* 8.1), 7.53–7.36 (m, 7H), 7.12–7.10 (d, 1H, *J* 8.10), 3.91 (s, 3H); ^{13}C NMR (100 MHz, CDCl3): δ 160.18, 159.59, 149.9, 139.11, 137.89, 130.42, 129.26, 128.7, 128.61, 127.71, 127.43, 127.22, 127.11, 125.81, 122.72, 116.26, 115.66, 114.62, 55.44; IR (ν cm^{-1}), 3063, 3032, 2992, 2960, 2918, 2851, 2829, 2361, 1951, 1923, 1662, 1617,1606, 1578, 1559, 1484, 1446, 1431, 1378, 1363, 1337, 1284, 1178, 1244, 1170, 1141, 1086, 1057, 1044, 983, 921, 894, 865, 858, 806, 799, 780, 765, 758, 690, 564; LC-MS: *m/e* 312.2, $C_{22}H_{17}NO$ requires Mol. Wt.: 311.13. Elemental analysis, calculated: C, 84.86; H, 5.50; N, 4.50; O, 5.14%. Found: C, 84.81; H, 5.47; N, 4.50%.

3f: White solid: mp 188.5–189.5 °C; ^{1}H NMR (400 MHz, DMSO d^6): δ = 8.47 (s, 1H), 8.30–8.28 (d, 2H, *J* 7.2), 8.15–8.12 (d, 2H, *J* 8.0), 7.90–7.85 (m, 4H), 7.82–7.80 (d, 3H, *J* 7.2), 7.68–7.64 (t, 1H, *J* 7.6), 7.56–7.52 (t, 4H, *J* 7.6), 7.47–7.42 (m, 2 H); ^{13}C NMR (100 MHz, DMSO d^6): δ 159.57, 149.34, 140.95, 140.14, 139.23, 138.81, 138.03, 131.02, 129.54, 129.25, 129.15, 128.21, 127.30, 127.16, 127.07, 125.07, 125.52, 116.07; IR (ν cm^{-1}), 3056, 3302, 2921, 2851., 1635, 1597, 1567, 1481, 1451, 1444, 1342, 1303, 1204, 1180, 1157, 1077, 1051, 1025, 964, 924, 815, 776, 752, 709, 693, 631; LC-MS: *m/e* 358.2, $C_{27}H_{19}N$ requires Mol. Wt.: 357.15. Elemental analysis, calculated: C, 90.72; H, 5.36; N, 3.92%. Found: C, 90.72; H, 5.36; N, 3.88%.

3g: Yellow solid: mp 144–145 °C; ^{1}H NMR (400 MHz, CDCl3): δ = 10.06 (s, 1H), 8.56–8.54 (d, 2H, *J* 9.6), 8.31–8.29 (d, 2H, *J* 7.2), 8.19–8.16 (m, 2H), 8.08–8.07 (d, 1H, *J* 2.0), 7.90–7.87 (t, 1H, *J* 7.6), 7.80–7.76 (t, 1H, *J* 7.6), 7.60–7.56 (t, 2H, *J* 7.6), 7.50–7.46 (t, 1H, *J* 7.2); ^{13}C NMR (100 MHz, CDCl3): δ 185.33, 152.23, 151.09, 149.09, 144.71, 138.71, 138.43, 138.31, 131.48, 130.50, 129.54, 129.42, 129.32, 128.72, 126.93, 126.17, 124.69, 117.48; IR (ν cm^{-1}) 3057.2, 2924.3, 2852.0, 2030.7, 1664.7, 1619.4, 1555.0, 1495.5, 1459.6, 1369.2, 1335.9, 1283.6, 1221.9, 1056.5, 948.0, 884.7, 760.5, 690.3, 524.8; LC-MS: *m/e* 316.2, $C_{20}H_{13}NOS$ requires Mol. Wt.: 315.07. Elemental analysis, calculated: C, 76.16; H, 4.15; N, 4.44; O, 5.07; S, 10.17%. Found: C, 76.13; H, 4.13; N, 4.41; S, 10.15%.

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References

1. B. Saito, G.C. Fu, J. Am. Chem. Soc. **129**, 9602 (2007)
2. J.H. Kirchhoff, M.R. Netherton, I.D. Hill, G.C. Fu, J. Am. Chem. Soc. **124**, 13662 (2002)
3. S.D. Dreher, S.-E. Lim, D.L. Sandrock, G.A. Molander, J. Org. Chem. **74**, 3626 (2009)
4. N. Miyaura, K. Yamada, A. Suzuki, Tetrahedron Lett. **36**, 3437 (1979)
5. N. Miyaura, A. Suzuki, Chem. Rev. **95**, 2457 (1995)
6. C.M. So, C.C. Yeung, C.P. Lau, F.Y. Kwong, J. Org. Chem. **73**, 7803 (2008)
7. A. Suzuki, in *Metal-Catalyzed Cross-Coupling Reactions*, ed. by F. Diederich, P.J. Stang, vol 1 (Wiley-VCH, Weinheim, 1998), p. 49
8. A.J. Suzuki, Organomet. Chem. **576**, 147 (1999)
9. S.R. Chemler, D. Trauner, S.J. Danishefsky, Angew. Chem. Int. Ed. **40**, 4544 (2001)
10. S.P. Stanforth, Tetrahedron **54**, 263 (1998)
11. J. Deng, Y.M. Wu, Q.Y. Chen, Synthesis **16**, 2730 (2005)
12. A.O. King, N. Yasuda, Topics Organomet. Chem. **6**, 205 (2004)
13. N. Miyaura, A. Suzuki, Chem. Rev. **95**, 2457 (1995)
14. S. Kotha, K. Lahiri, D. Kashinath, Tetrahedron **58**, 9633 (2002)
15. A.F. Littke, G.C. Fu, Angew. Chem. Int. Ed. **41**, 4176 (2002)
16. T.E. Barder, S.D. Walker, J.R. Martinelli, S.L. Buchwald, J. Am. Chem. Soc. **127**, 4685 (2005)
17. Q. Huang, J.A. Hunter, R.C. Larock, Org. Lett. **3**, 2973 (2001)
18. A. Buske, S. Busemann, J. Mühlbacker, J. Schmidt, A. Porzel, G. Bringmann, G. Adam, Tetrahedran **55**, 1079 (1999)
19. G. Bringmann, J. Holenz, R. Weirich, M. Rübenacker, C. Funke, Tetrahedron **54**, 497 (1998)
20. D. Kletsas, W. Li, Z. Han, V. Papadopoulos, Biochem. Pharmacol. **67**, 1927 (2004)
21. K.W. Bentley, *The Isoquinoline Alkaloids*, vol 1 (Hardwood Academic, Amsterdam, 1998)
22. F. Durola, J.-P. Sauvage, O.S. Wenger, Chem. Commun. 171 (2006)

23. K.-H. Fang, L.-L. Wu, Y.-T. Huang, C.-H. Yang, I.-W. Sun, Inorg. Chim. Acta **359**, 441 (2006)
24. Z. Huo, H. Tomeba, Y. Yamamoto, Tetrahedron Lett. **49**, 5531 (2008)
25. Y.-Y. Hu, J. Hu, X.-C. Wang, L.-N. Guo, X.-Z. Shu, Y.-N. Niu, Y.-M. Liang, Tetrahedran **66**, 80 (2010)
26. P.J. Campos, M. Caro, A. Rodrĩguez, Tetrahedron Lett. **42**, 3575 (2001)
27. B.K. Ghorai, D. Jiang, J.W. Herndon, Org. Lett. **5**, 4261 (2003)
28. R. Alonso, P.J. Campos, B. Garcĩa, M.A. Rodrĩguez, Org. Lett. **8**, 3521 (2006)
29. Y.-N. Niu, Z.-Y. Yan, G.-L. Gao, H.-L. Wang, X.-Z. Shu, K.-G. Ji, Y.-M. Liang, J. Org. Chem. **74**, 2893 (2009)
30. Z. Huo, Y. Yamamoto, Tetrahedron Lett. **50**, 3651 (2009)
31. L. Xin-Hua, Z. Jing, Z. An-na, S. Bao-An, Z. Hai-Liang, B. Shan, B. Pinaki, P. Chun-Xiu, Bioorg. Med. Chem. **17**, 1207 (2009)
32. B. Heike, W. Julia, A. Christain, L. Matthias, Develop. Comp. Immun. **30**, 410 (2006)
33. K. Prabakaran, P. Manivel, F.N. Khan, Tetrahedron Lett. **51**, 4340 (2010)
34. F.N. Khan, P. Manivel, K. Prabakaran, V.R. Hathwar, Seik Weng Ng, Acta Cryst. **E65**, o2732 (2009)
35. F.N. Khan, P. Manivel, K. Prabakaran, V.R. Hathwar, Seik Weng Ng, Acta Cryst. **E66**, o488 (2010)
36. P. Manivel, S. Mohana Roopan, F. Nawaz Khan, J. Chil. Chem. Soc. **54**, 180 (2009)
37. P. Manivel, S. Mohana Roopan, F. Nawaz Khan, J. Chil. Chem. Soc. **54**, 183 (2009)
38. P. Manivel, F. Nawaz Khan, V.R. Hathwar, Phosphorus Sulfur Silicon Relat. Elem. **185**, 1932 (2010)
39. P. Manivel, F. Nawaz Khan, Phosphorus Sulfur Silicon Relat. Elem. **184**, 2910 (2009)
40. S. Mohana Roopan, T.R. Sakthi Sri, B. Ramakrishna Reddy, F. Nawaz Khan, Indian J. Heterocyclic Chem. **19**, 77 (2009)
41. S.S. Tajudeen, F.N. Khan, Synth. Commun. **37**, 3649 (2007)
42. S.M. Roopan, T. Maiyalagan, F.N. Khan, Can. J. Chem. **86**, 1019 (2008)
43. V.R. Hathwar, P. Manivel, F. Nawaz Khan, T.N.G. Row, Acta Cryst E **63**, o3707 (2007)
44. V.R. Hathwar, P. Manivel, F. Nawaz Khan, T.N.G. Row, Acta Cryst E **63**, o3707 (2007)
45. S.M. Roopan, F.R.N. Khan, Arkivoc **13**, 161 (2009)
46. S. Mohana Roopan, F. Nawaz Khan, Indian J. Heterocyclic Chem. **18**, 183 (2008)
47. P. Manivel, S. Mohana Roopan, F. Nawaz Khan, J. Chil. Chem. Soc. **53**, 1609 (2008)
48. V.R. Hathwar, P. Manivel, F. Nawaz Khan, T.N. Guru Row, Cryst. Eng. Comm. **11**, 284 (2009)