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Direct Access to 1,3,5-Trisubstituted 1*H*-1,2,4-Triazoles from *N*-Phenylbenzamidines via Copper-Catalyzed Diamination of Aryl Nitriles

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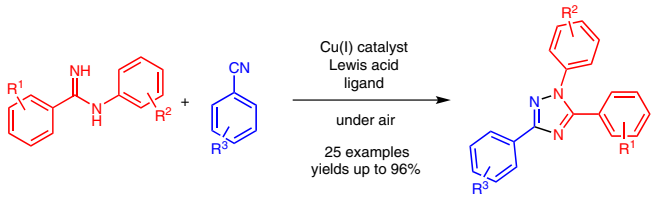

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Abstract A copper-catalyzed formation of C–N/N–N bonds using *N*-phenylbenzamidines with aryl nitriles has been developed and affords a route to 1,3,5-trisubstituted 1*H*-1,2,4-triazoles in moderate to excellent yields. The method is operationally simple and environmentally benign with a large substrate scope available and represents an economical path for numerous C–N/N–N bond formations.

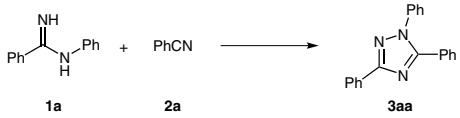
Key words amination, copper, heterocycles, ring closure, tandem reaction

1,2,4-Triazoles and their derivatives are mostly used as polymers, agricultural chemicals and pharmaceuticals.[1] General methods for their synthesis have gained booming attention.[2] Traditionally, 1,2,4-triazoles were synthesized by means of the Einhorn–Brunner reaction or the Pellizzari reaction.[1] Subsequently, they have commonly been prepared by the cyclization of substituted hydrazones with other nitrogen-containing organic compounds.[3] 1,2,4-Triazoles have also been reported as products from the reactions of amidines with carboxylic acids[4] or DMF.[5] In 2009, Ueda and Nagasawa presented a copper-catalyzed oxidative process performed by aminopyridines or amidines with nitriles.[6] However, the building blocks for triazoles often lead to disubstituted species. Certain approaches for synthesizing sterically bulky 1,3,5-trisubstituted 1,2,4-triazoles are somewhat limited, probably on account of unfavorable reaction conditions.

Copper-catalyzed tandem addition/oxidative cyclization has become one of the most focused strategies for the generation of heterocycles. Because of its low cost and low toxicity, this type of reaction is highly appealing to modern chemists.[7,8] Recently, Zhang and co-workers have raised the possibility of producing various 1,2,3-triazoles from *N*-tosylhydrazones and anilines.[9] Following the successful trials on 1,2,4-triazoles, Nagasawa's group has further contributed the synthesis of [1,2,3]triazolo[1,5-*a*]pyridines from acylpyridines.[10] Our group has also reported some facile methods for the preparation of substituted 1,2,3-triazoles by means of copper-catalyzed tandem cyclization.[11] Additionally, we discovered certain diamination processes of aldehydes,[12] as well as acetyl compounds,[13] to form different imidazole skeletons. Herein, we report the synthesis of 1,3,5-trisubstituted 1*H*-1,2,4-triazoles from readily available *N*-phenylbenzamidines and aryl nitriles. The corresponding triazoles were obtained with high regioselectivity under mild conditions. The reaction involves the spontaneous formation of a C–N bond and an N–N bond through N–H bond cleavage.

We began our observations by taking *N*-phenylbenzamidine (**1a**) and benzonitrile (**2a**) as the model substrates. The results are summarized in Table 1. Our initial attempt was carried out employing a combination of CuI (10 mol%), ZnI_2 (10 mol%) and phenanthroline (Phen) (10 mol%) in *o*-dichlorobenzene (ODCB) at 130 °C under air atmosphere; the desired product (**3aa**) was obtained in 36% yield (Table 1, entry 1). The yield dropped when the reaction was carried out at higher or lower temperature. When 2,2′-bipyridine (Bipy) (10 mol%) was used instead of phenanthroline, the yield was decreased by half (Table 1, entry 2). Other common solvents, such as DMSO and chlorobenzene, were tested; reaction in chlorobenzene gave similar results to that in ODCB solution (Table 1, entries 1, 3, 4). Considering

Table 1 Optimization of the Reaction Conditions[a]



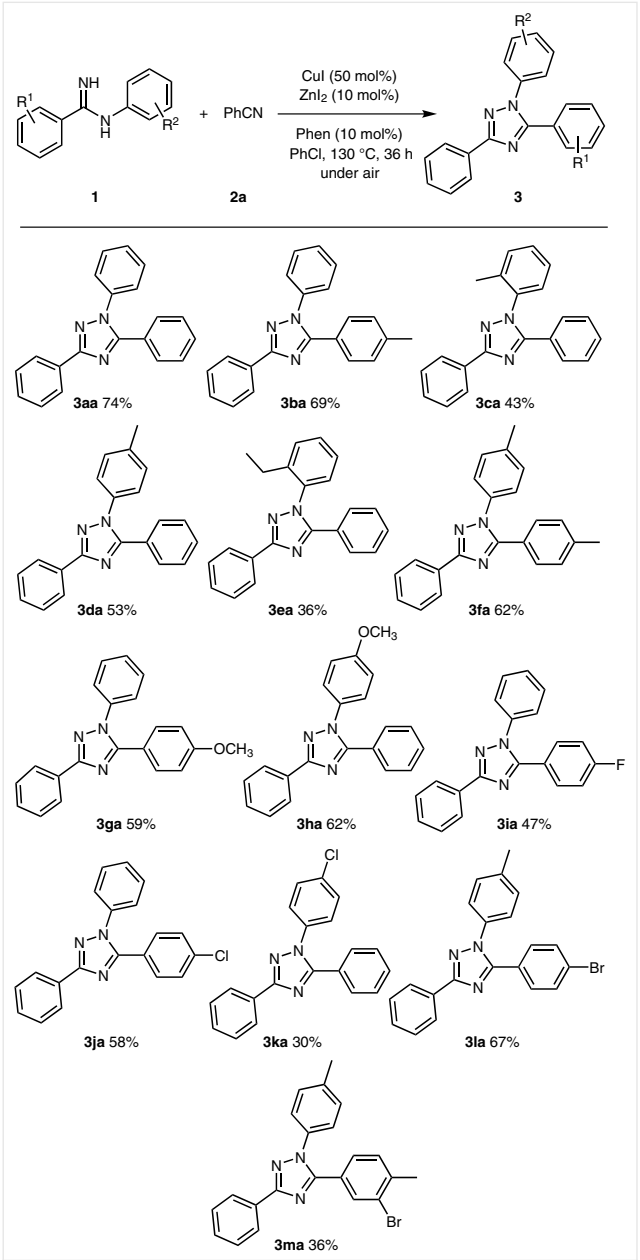
1a 2a 3aa

Entry	Catalyst (equiv)	Additive	Ligand	Solvent	Yield[b] (%)
1	CuI (0.1)	ZnI_2	Phen	ODCB	36
2	CuI (0.1)	ZnI_2	Bipy	ODCB	19
3	CuI (0.1)	ZnI_2	Phen	PhCl	37
4	CuI (0.1)	ZnI_2	Phen	DMSO	16
5	AgOAc (0.1)	ZnI_2	Phen	PhCl	0
6	I_2 (0.1)	TBHP	–	PhCl	0
7	CuI (0.5)	ZnI_2	Phen	PhCl	56
8	CuI (1.0)	ZnI_2	Phen	PhCl	41
9	$Cu(OAc)_2$ (0.5)	ZnI_2	Phen	PhCl	33
10	$Cu(OTf)_2$ (0.5)	ZnI_2	Phen	PhCl	19
11	CuBr (0.5)	ZnI_2	Phen	PhCl	33
12	CuCl (0.5)	ZnI_2	Phen	PhCl	54
13	CuI (0.5)	BF_3	Phen	PhCl	46
14	CuI (0.5)	$FeCl_3$	Phen	PhCl	26
15	CuI (0.5)	I_2	Phen	PhCl	28
16[c]	CuI (0.5)	ZnI_2	Phen	PhCl	55
17[d]	CuI (0.5)	ZnI_2	Phen	PhCl	74
18[e]	CuI (0.5)	ZnI_2	Phen	PhCl	64

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (2.0 equiv), additive (10 mol%), ligand (10 mol%), solvent (1 mL), 130 °C, 24 h; reactions performed under air.
[b] Isolated yield.
[c] 4 Å MS (100 mg) were added.
[d] 36 h.
[e] 140 °C, 36 h.

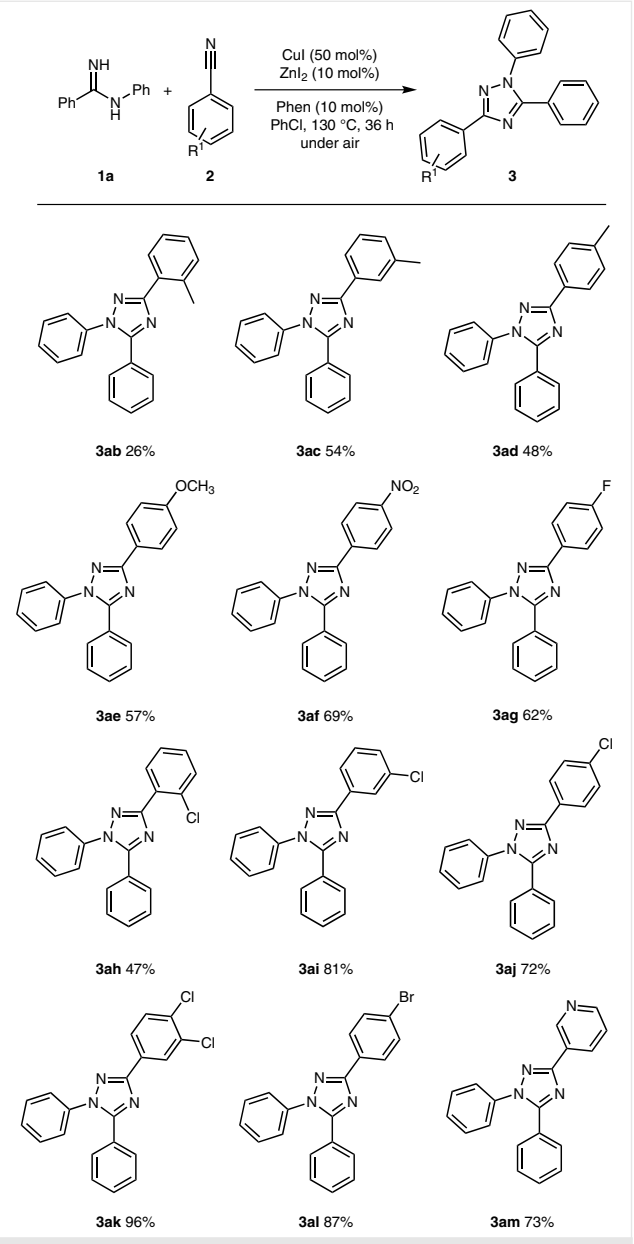
the reduced effort required for reaction workup, chlorobenzene is a more suitable solvent than ODCB. The use of AgOAc or I_2 without the presence of copper catalyst resulted in none of the desired product **3aa** (Table 1, entries 5, 6). When the amount of CuI was increased to 50 mol%, **3aa** was formed in 56% yield; however, higher equivalents of CuI proved to be detrimental (Table 1, entries 7, 8). Various copper catalysts were examined, including $Cu(OAc)_2$, $Cu(OTf)_2$, CuBr and CuCl (Table 1, entries 7, 9–12), with the result that CuI performed best among the copper compounds tested. Of the Lewis acid additives that were evaluated (ZnI_2, BF_3, $FeCl_3$), ZnI_2 provided the best outcome (Table 1, entries 7, 13, 14). Interestingly, a 28% yield of **3aa** was obtained when I_2 was employed as an additive (Table 1, entry 15). Addition of 4 Å molecular sieves had no significant effect on the yield (Table 1, entry 16). The yield of **3aa** was further improved to 74% with an increased reaction time of 36 hours, but was reduced to 64% yield with an amplified temperature of 140 °C (Table 1, entries 17, 18). The presence of side products was not observed.

With the optimized reaction conditions in hand, the substrate scope with respect to different kinds of *N*-phenylbenzamidines with various substituents on one or both phenyl rings was examined (Scheme 1). This reaction could tolerate *N*-phenylbenzamidines with electron-donating or electron-withdrawing moieties. Presumably as a result of steric hindrance, reagent **1** with alkyl substituent(s) at the *para* position(s) provided the desired products in moderate



Scheme 1 Substrate scope of *N*-phenylbenzamidines

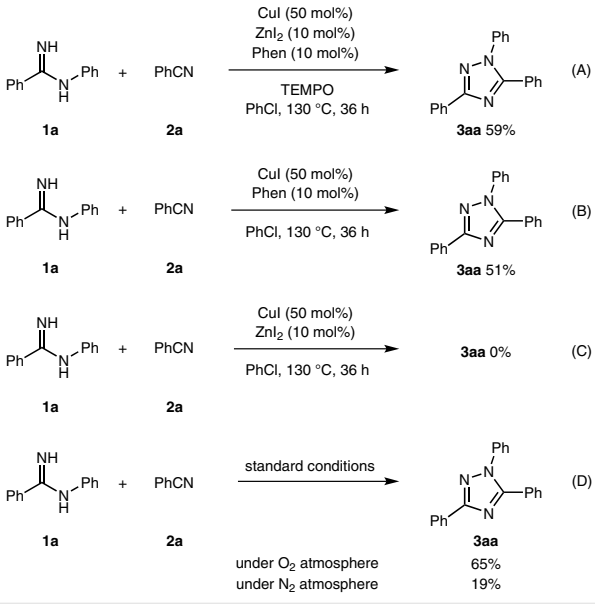
to high yields, higher than with 2-alkyl-substituted reactants (products **3ba** to **3fa**). Reactants **1** with a 4-methoxy group were also tested, yielding **3ga** and **3ha** in 59% and 62%, respectively. Halogen-containing *N*-phenylbenzamidines were also tolerated in the reaction. Fluoro-substituted **3ia** was obtained in 47% yield. Chlorinated product **3ja** was obtained in a yield similar to the corresponding methoxy-substituted **3ga**, while **3ka** was produced in a much lower yield than **3ha**. Reactants **1** with multiple methyl and bromo substituents gave **3la** and **3ma** with significantly different yields, with **3ma** lower than **3la**.



Scheme 2 Substrate scope of aryl nitriles

We then explored the feasibility of the reaction with respect to the aryl nitrile component. Under the standard conditions, substrates **2** containing various substituents also performed well (Scheme 2). Nitriles bearing an alkyl or methoxy group gave a lower yield of product than nitriles with nitro or halogen substituents. The sterically hindered *ortho*-substituted benzonitriles furnished triazoles **3ab** and **3ah** in lower yield than the *para*-substituted products; however, triazoles **3ac** and **3ai** with the corresponding substitution at the *meta* position were attained in the highest yields. To our delight, 3,4-dichlorobenzonitrile gave a superb 96% yield of **3ak**. Additionally, we tested the accessibility of nicotinonitrile in the reaction which resulted in a 73% yield of **3am**, similar to the original **3aa**. Following the successful trials with aryl nitriles, we undertook further experiments involving reactants with saturated hydrocarbon moieties, such as acetonitrile and cyclopropylnitrile. Unfortunately, those attempts did not provide the desired products.

To elucidate the mechanism of this reaction, some control experiments were carried out (Scheme 3). When the radical marker TEMPO (2.0 equiv) was added to **1a** and **2a** under the otherwise standard conditions, a major reduction in yield was not detected; hence, a radical process is unlikely to be implicated (equation A). No product **3aa** was formed in the absence of the ligand phenanthroline, whereas a 51% yield was obtained without ZnI_2, thus proving the importance of the presence of a ligand (equations B and C). There was no significant decrease in the yield of **3aa** when the reaction was tested under O_2 atmosphere whilst it dropped to 19% under inert N_2, thereby indicating probable stoichiometric oxidative procedures (equation D).



Scheme 3 Control experiments

A reaction mechanism is proposed on the basis of the experimental studies and related work in the literature (Scheme 4).[14] Taking the production of **3aa** as a model, the process begins with Cu(I)-promoted activation of *N*-phenylbenzamidine (**1a**) to form intermediate **1I**. Then, via tautomerization, **1II** is delivered after release of the proton adjacent to the phenyl-substituted nitrogen. Simultaneously, benzonitrile (**2a**) coordinates with Cu(I) to provide **2I** and subsequently **2II**. Then, **2II** combines with **1II** to give intermediate **III**. Nucleophilic attack of the nitrile by the amidine results in the formation of intermediate **IV**, then affords adduct **V**. Reductive elimination of **V** delivers the final cyclic product **3aa**. Detached Cu(0) is oxidized to Cu(I) to complete the catalytic cycle; it would further be oxidized to Cu(II), also catalytically active.[8,15] The ligand phenanthroline likely provides a linkage between Cu(I) catalysts, as is shown in Scheme 4. ZnI_2, usually employed as a facile Lewis acid,[16] may assist the initial coordination with nitrile.

By way of conclusion, we have developed an efficient and regioselective access to 1,3,5-trisubstituted 1*H*-1,2,4-triazoles from *N*-phenylbenzamidines and nitriles. This new route via copper-catalyzed tandem addition/oxidative cyclization employs easily available substances and tolerates a broad range of functional groups.

All reactions were carried out in oven-dried flasks. Commercially available reagents were used without further purification. Flash chromatography was carried out with Merck silica gel 60 (63–200 mesh). Analytical TLC was performed with Merck silica gel 60 F254 plates, and the products were visualized by UV detection. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ on an Agilent Mercury plus 300 BB spectrometer. Chemical shifts (δ) are reported in ppm using TMS as internal standard. Melting points were determined on an LJ-XLC microscopic apparatus. HRMS data were recorded on a ThermoFisher LTQ Orbitrap XL ETD.

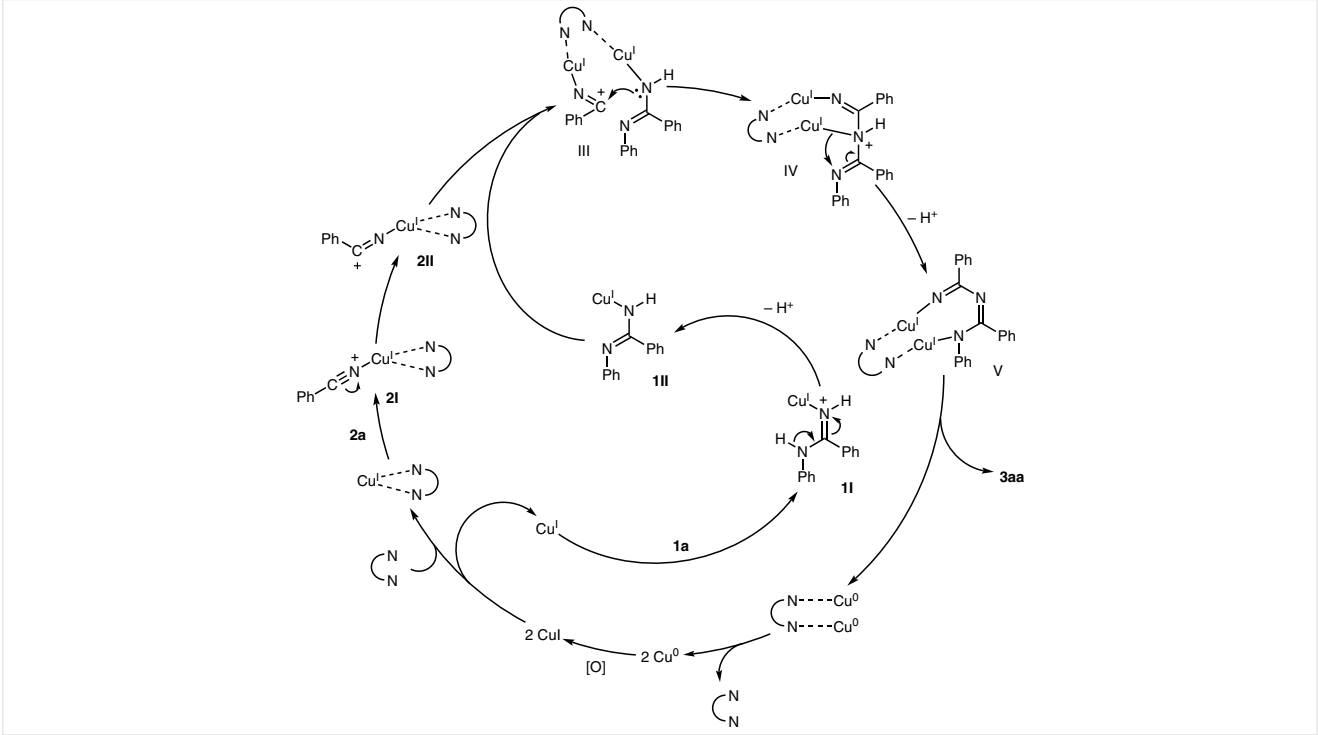
Several compounds are known: **3aa**,[2e] **3ab**,[18] **3ad**,[18] **3ae**,[18] **3ah**,[18] **3aj**,[18] **3am**,[18] **3ga**,[2e] **3ja**.[17]

N-Phenylbenzamidines 1; General Procedure

A 100-mL round-bottomed two-neck flask was charged with an aniline (12.0 mmol), a nitrile (10.0 mmol) and NaH (11.0 mmol). The flask was then evacuated and flushed with N_2. DMSO (10 mL) was injected into the mixture at 0 °C. If reactants are liquids, they may be added subsequently. The mixture was stirred at 0 °C for 45 min, then at room temperature for 60 min, and was monitored by TLC until reaction completion. Then, the reaction was quenched with ice–water. Crystals separated and were collected using a sintered glass funnel. The crystals were washed multiple times in the funnel with petroleum ether, then were ground into a powder and oven-dried. The powder was further purified by washing with petroleum ether.

1,3,5-Triphenyl-1*H*-1,2,4-triazole (3aa); Typical Procedure

A sealed tube equipped with a stirrer bar was charged with *N*-phenylbenzamidine (**1a**; 0.0393 g, 0.2 mmol), benzonitrile (**2a**; 41 μL, 0.40 mmol), CuI (0.0190 g, 0.10 mmol), ZnI_2 (0.0063 g, 0.02 mmol), phenanthroline (0.0040 g, 0.02 mmol) and chlorobenzene (1 mL). The



Scheme 4 Possible reaction mechanism

resulting mixture was stirred at 130 °C for 36 h. After reaction completion, the residue was directly purified by flash column chromatography (EtOAc–petroleum ether) to afford pure product **3aa**.

White solid; yield: 44 mg (74%); mp 100–105 °C.

IR: 3430.2, 1592.1, 1517.8, 1496.1, 1476.3, 1441.6, 1397.9, 1350.4, 1271.9, 1138.5, 1070.7, 1025.8, 990.4, 923.3, 848.4, 771.7, 728.5, 695.3 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (dd, *J* = 7.9, 1.5 Hz, 2 H), 7.56 (dd, *J* = 8.0, 1.4 Hz, 2 H), 7.52–7.32 (m, 11 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.12, 154.93, 138.47, 130.91, 130.18, 129.58, 129.17, 129.00, 128.76, 128.20, 126.78, 125.61.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{16}N_3^+$: 298.1344; found: 298.1344.

1,3-Diphenyl-5-*p*-tolyl-1*H*-1,2,4-triazole (3ba)

White solid; yield: 43 mg (69%); mp 92–97 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (dd, *J* = 8.0, 1.6 Hz, 2 H), 7.49–7.39 (m, 10 H), 7.15 (d, *J* = 8.1 Hz, 2 H), 2.36 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.03, 155.07, 140.38, 138.61, 131.00, 129.55, 129.45, 129.05, 128.92, 128.73, 126.77, 125.65, 125.29, 21.62.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1500.

3,5-Diphenyl-1-*o*-tolyl-1*H*-1,2,4-triazole (3ca)

White solid; yield: 27 mg (43%); mp 73–75 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 6.6 Hz, 2 H), 7.55 (d, *J* = 6.9 Hz, 2 H), 7.50–7.28 (m, 10 H), 2.06 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.14, 155.53, 137.92, 135.56, 131.67, 131.06, 130.15, 129.55, 128.77, 128.34, 127.96, 127.90, 127.37, 126.77, 17.78.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1501.

3,5-Diphenyl-1-*p*-tolyl-1*H*-1,2,4-triazole (3da)

White solid; yield: 33 mg (53%); mp 106–110 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 6.5 Hz, 2 H), 7.56 (d, *J* = 8.2 Hz, 2 H), 7.49–7.27 (m, 8 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 2.40 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.97, 154.83, 139.12, 136.02, 131.00, 130.14, 130.08, 129.51, 129.14, 128.72, 128.28, 126.76, 125.45, 21.41.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1503.

1-(2-Ethylphenyl)-3,5-diphenyl-1*H*-1,2,4-triazole (3ea)

White solid; yield: 23 mg (36%); mp 61–65 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 6.0 Hz, 2 H), 7.55 (d, *J* = 6.5 Hz, 2 H), 7.50–7.27 (m, 10 H), 2.42 (q, *J* = 7.6 Hz, 2 H), 1.05 (t, *J* = 7.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.95, 155.59, 141.26, 137.40, 131.08, 130.40, 130.12, 130.01, 129.54, 128.77, 128.74, 128.47, 128.06, 127.90, 127.25, 126.77, 24.21, 14.22.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{20}N_3^+$: 326.1657; found: 326.1659.

3-Phenyl-1,5-di-*p*-tolyl-1*H*-1,2,4-triazole (3fa)

White solid; yield: 40 mg (62%); mp 133–136 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.23 (d, *J* = 6.4 Hz, 2 H), 7.49–7.39 (m, 5 H), 7.30 (d, *J* = 8.3 Hz, 2 H), 7.22 (d, *J* = 8.3 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 2.40 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.86, 154.96, 140.25, 139.02, 136.15, 131.08, 130.11, 129.40, 129.01, 128.70, 126.75, 125.49, 125.37, 21.60, 21.39.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{20}N_3^+$: 326.1657; found: 326.1656.

5-(4-Methoxyphenyl)-1,3-diphenyl-1*H*-1,2,4-triazole (3ga)

Yellow solid; yield: 39 mg (59%); mp 97–98 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 6.5 Hz, 2 H), 7.52–7.36 (m, 10 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 3.77 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.86, 160.96, 154.76, 138.60, 130.98, 130.58, 129.51, 129.43, 128.85, 128.67, 126.68, 125.61, 120.42, 114.10, 55.40.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O^+$: 328.1450; found: 328.1449.

1-(4-Methoxyphenyl)-3,5-diphenyl-1*H*-1,2,4-triazole (3ha)

Yellow solid; yield: 41 mg (62%); mp 128–130 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 6.6 Hz, 2 H), 7.56 (d, *J* = 6.2 Hz, 2 H), 7.49–7.29 (m, 8 H), 6.91 (d, *J* = 8.9 Hz, 2 H), 3.80 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.07, 160.17, 155.06, 131.70, 131.24, 129.50, 129.19, 128.95, 128.73, 128.43, 127.47, 126.95, 115.06, 56.09.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O^+$: 328.1450; found: 328.1445.

5-(4-Fluorophenyl)-1,3-diphenyl-1*H*-1,2,4-triazole (3ia)

White solid; yield: 30 mg (47%); mp 98–101 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (dd, *J* = 7.9, 1.7 Hz, 2 H), 7.59–7.51 (m, 2 H), 7.50–7.39 (m, 8 H), 7.05 (t, *J* = 8.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.49, 162.14, 154.05, 138.35, 131.33, 131.21, 130.81, 129.71, 129.67, 129.20, 128.80, 126.76, 125.66, 124.41, 116.15, 115.86.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}FN_3^+$: 316.1250; found: 316.1252.

5-(4-Chlorophenyl)-1,3-diphenyl-1*H*-1,2,4-triazole (3ja)

White solid; yield: 39 mg (58%); mp 122–125 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 7.0 Hz, 2 H), 7.53–7.37 (m, 10 H), 7.33 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.24, 153.90, 138.29, 136.44, 130.75, 130.45, 129.76, 129.71, 129.29, 129.10, 128.81, 126.77, 126.64, 125.67.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3^+$: 332.0955; found: 332.0954.

1-(4-Chlorophenyl)-3,5-diphenyl-1*H*-1,2,4-triazole (3ka)

White solid; yield: 20 mg (30%); mp 105–110 °C.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 8.2 Hz, 2 H), 7.55 (d, *J* = 6.5 Hz, 2 H), 7.51–7.34 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.35, 155.03, 136.96, 134.78, 130.72, 130.44, 129.78, 129.19, 128.95, 128.82, 127.99, 126.80, 126.72.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3^+$: 332.0955; found: 332.0953.

5-(4-Bromophenyl)-3-phenyl-1-*p*-tolyl-1*H*-1,2,4-triazole (3la)

White solid; yield: 52 mg (67%); mp 150–155 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 6.4 Hz, 2 H), 7.59–7.36 (m, 7 H), 7.32–7.25 (m, 4 H), 2.42 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.13, 153.87, 139.52, 135.82, 132.02, 131.12, 130.83, 130.63, 130.34, 129.64, 129.04, 128.79, 127.18, 126.76, 125.52, 124.70, 21.45.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{17}BrN_3^+$: 390.0606; found: 390.0609.

5-(3-Bromo-4-methylphenyl)-3-phenyl-1-*p*-tolyl-1*H*-1,2,4-triazole (3ma)

White solid; yield: 29 mg (36%); mp 127–130 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 6.2 Hz, 2 H), 7.54–7.35 (m, 4 H), 7.34–7.24 (m, 5 H), 7.16 (d, *J* = 8.0 Hz, 1 H), 2.42 (s, 3 H), 2.40 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.03, 153.40, 140.16, 139.43, 135.82, 132.90, 130.84, 130.26, 129.60, 128.78, 127.67, 126.77, 125.52, 23.13, 21.46.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}BrN_3^+$: 404.0762; found: 404.0766.

1,5-Diphenyl-3-*o*-tolyl-1*H*-1,2,4-triazole (3ab)

White solid; yield: 16 mg (26%); mp 73–78 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (dd, *J* = 5.3, 2.1 Hz, 1 H), 7.57 (d, *J* = 7.5 Hz, 2 H), 7.47–7.27 (m, 11 H), 2.73 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.98, 138.58, 137.52, 131.35, 130.13, 129.82, 129.52, 129.24, 129.14, 128.85, 128.76, 125.95, 125.50, 22.09.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1500.

1,5-Diphenyl-3-*m*-tolyl-1*H*-1,2,4-triazole (3ac)

White solid; yield: 34 mg (54%); mp 100–103 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 0.6 Hz, 1 H), 8.04 (d, *J* = 8.1 Hz, 1 H), 7.57 (t, *J* = 1.4 Hz, 1 H), 7.54 (d, *J* = 1.7 Hz, 1 H), 7.43–7.32 (m, 10 H), 2.43 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.24, 154.89, 138.43, 130.74, 130.39, 130.16, 129.58, 129.17, 128.99, 128.75, 128.69, 128.21, 127.35, 125.62, 123.92, 21.59.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1505.

1,5-Diphenyl-3-*p*-tolyl-1*H*-1,2,4-triazole (3ad)

White solid; yield: 30 mg (48%); mp 138–142 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.1 Hz, 2 H), 7.55 (dd, *J* = 7.8, 1.3 Hz, 2 H), 7.43–7.26 (m, 10 H), 2.40 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.20, 154.81, 139.54, 138.50, 130.13, 129.56, 129.48, 129.30, 129.18, 128.93, 128.74, 128.26, 128.11, 126.70, 125.61, 21.66.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3^+$: 312.1501; found: 312.1499.

3-(4-Methoxyphenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3ae)

Yellow solid; yield: 37 mg (57%); mp 109–114 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.4 Hz, 2 H), 7.55 (d, *J* = 7.5 Hz, 2 H), 7.47–7.31 (m, 8 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 3.86 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.99, 160.83, 154.77, 138.51, 130.11, 129.55, 129.16, 128.89, 128.74, 128.28, 128.22, 125.59, 123.64, 114.13, 55.49.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O^+$: 328.1450; found: 328.1452.

3-(4-Nitrophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3af)

White solid; yield: 47 mg (69%); mp 169–174 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.45–8.36 (m, 2 H), 8.35–8.26 (m, 2 H), 7.59–7.53 (m, 2 H), 7.42 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.13, 155.57, 148.47, 138.16, 137.03, 130.55, 129.72, 129.42, 129.12, 128.88, 127.65, 127.40, 125.53, 124.13.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}N_4O_2^+$: 343.1195; found: 343.1195.

3-(4-Fluorophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3ag)

White solid; yield: 39 mg (62%); mp 114–119 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.22 (dd, *J* = 8.7, 5.5 Hz, 2 H), 7.55 (dd, *J* = 7.9, 1.2 Hz, 2 H), 7.46–7.32 (m, 8 H), 7.14 (t, *J* = 8.7 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.48, 162.20, 161.34, 155.00, 138.40, 130.25, 129.61, 129.14, 129.07, 128.79, 128.75, 128.63, 128.09, 127.17, 125.58, 115.90, 115.62.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}FN_3^+$: 316.1250; found: 316.1250.

3-(2-Chlorophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3ah)

White solid; yield: 31 mg (47%); mp 94–99 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (dd, *J* = 6.0, 3.5 Hz, 1 H), 7.57 (d, *J* = 6.7 Hz, 2 H), 7.52 (dd, *J* = 5.9, 3.4 Hz, 1 H), 7.47–7.33 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.68, 154.32, 138.34, 133.18, 131.85, 131.68, 130.52, 130.10, 129.80, 129.36, 129.01, 128.00, 127.07, 126.62, 125.81, 125.37.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3^+$: 332.0955; found: 332.0956.

3-(3-Chlorophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3ai)

White solid; yield: 53 mg (81%); mp 138–141 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28–8.24 (m, 1 H), 8.14–8.10 (m, 1 H), 7.56–7.54 (m, 1 H), 7.53 (dd, *J* = 1.7, 0.5 Hz, 1 H), 7.43–7.34 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.91, 155.08, 138.30, 134.81, 132.70, 130.30, 130.06, 129.61, 129.11, 128.79, 127.93, 126.82, 125.54, 125.35, 124.80.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3^+$: 332.0955; found: 332.0954.

3-(4-Chlorophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3aj)

White solid; yield: 48 mg (72%); mp 126–130 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21–8.18 (m, 1 H), 8.17–8.15 (m, 1 H), 7.55 (t, *J* = 1.4 Hz, 1 H), 7.53 (t, *J* = 2.0 Hz, 1 H), 7.45–7.32 (m, 10 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.19, 155.05, 138.34, 135.47, 130.53, 130.30, 130.06, 129.83, 129.59, 129.47, 129.32, 129.12, 129.01, 128.90, 128.78, 128.06, 128.00, 125.78.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3^+$: 332.0955; found: 332.0957.

3-(3,4-Dichlorophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3ak)

White solid; yield: 70 mg (96%); mp 65–70 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 1.5 Hz, 1 H), 8.06 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.57–7.50 (m, 3 H), 7.46–7.33 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.18, 155.24, 138.25, 133.52, 133.09, 131.00, 130.81, 130.42, 129.67, 129.26, 129.11, 128.84, 128.60, 127.82, 125.90, 125.55.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{14}Cl_2N_3^+$: 366.0565; found: 366.0561.

3-(4-Bromophenyl)-1,5-diphenyl-1*H*-1,2,4-triazole (3al)

White solid; yield: 65 mg (87%); mp 147–151 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.5 Hz, 2 H), 7.58 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 6.7 Hz, 2 H), 7.44–7.32 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.21, 155.05, 138.32, 137.88, 131.92, 130.28, 129.91, 129.60, 129.11, 128.78, 128.44, 128.32, 127.97, 125.54, 123.80.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{15}BrN_3^+$: 376.0449; found: 376.0448.

3-(1,5-Diphenyl-1*H*-1,2,4-triazol-3-yl)pyridine (3am)

White solid; yield: 44 mg (73%); mp 107–111 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.47 (s, 1 H), 8.66 (d, *J* = 4.8 Hz, 1 H), 8.49 (d, *J* = 7.9 Hz, 1 H), 7.58–7.53 (m, 2 H), 7.45–7.36 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.79, 155.21, 150.44, 148.21, 138.23, 133.97, 130.38, 129.64, 129.22, 129.10, 128.81, 127.81, 126.96, 125.54, 123.60.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{15}N_4^+$: 299.1297; found: 299.1299.

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Supporting Information

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