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Iodine Catalyzed Oxidative Coupling of Diaminoazines and Amines for the Synthesis of 3,5-Disubstituted-1,2,4-Triazoles

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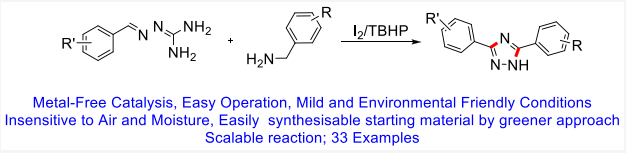
ABSTRACT: A simple, convenient, transition metal-free one pot synthesis of 3,5-disubstituted-1,2,4-triazoles has been established. The innovation in this reaction is the use of easily available 1,1-diaminoazines as substrates. This method provides the products with wider substrate scope, at an expedited rate, and with relatively better yields in comparison to the reported methods. The reaction mechanism involves an initial intermolecular nucleophilic addition (facilitated by I_2) followed by intramolecular nucleophilic cyclization.



INTRODUCTION

Azines are 2,3-diaza-1,3-butadienes,[1] which gained the attention of organic as well as material chemists because of their diverse structural,[2] chemical,[3] and biological properties.[4] 1,1-diaminoazines are a subclass of azines, which are proven to have interesting structural properties[5] and medicinal chemistry applications.[1a,5−7] The antihypertensive drug guanabenz is a representative example containing 1,1-diaminoazine moiety.[5c,6] Recently, our group has explored the ring−chain tautomerism[8a] and dimerization[8b] of 1,1-diaminoazines in the synthesis of heterocyclic species. In this work, we report the application of 1,1-diaminoazines in the generation of 3,5-disubstituted-1,2,4-triazoles.

1,2,4-Triazoles are important structural moieties, which attracted considerable attention of heterocyclic chemists owing to their importance in the fields of medicine,[9] pesticides, insecticides,[10] material chemistry,[11] as well as in organocatalysis.[12] 1,2,4-Triazoles are useful as bioisosteres of *cis*-amide bonds to mimic peptides and in drug design to improve the pharmacological properties of the corresponding lead molecules.[13] Such heterocycles have been studied extensively in metal-coordination chemistry also due to their ability to form stable complexes.[14] Among these, 3,5-disubstituted-1,2,4-triazoles found many therapeutic applications. Topiroxostat is a well-known antigout drug that belongs to this class of molecules.[15a] A few derivatives of 3,5-disubstituted-1,2,4-triazoles (Figure 1) are known for their neuroprotective, antimicrobial, antifertility, and antiviral activities.[15]

Owing to their broad spectrum of functions, several synthetic methods have been developed for the generation of 3,5-disubstituted 1*H*-1,2,4-triazoles.[16] Scheme 1A includes a few representative metal-free methods for the synthesis of 3,5-disubstituted-1,2,4-trizaoles (more examples are provided in Scheme S1, SI). The most commonly studied pathways involve cyclodehydration of *N*-acylamidrazone derivatives, which can be obtained from several precursors, such as amides, amidrazones, *N*-acetyl-*N*,*N*-dimethylhydrazonamides and *N*-acylhydrazides.[16r,s,u] Boyle et al. in 1967 reported the formation of 3,5-diphenyl-1,2,4-triazoles by the treatment of benzaldehyde azine with potassium t-butoxide (1−2 mol) in boiling toluene for 40 h.[16b] Scheiner and co-workers in 1970 reported the synthesis of 3,5-diphenyl-1,2,4-triazoles by tetrazole photolysis. In this method, nitrogen is expelled exclusively from positions 3 and 4 of the tetrazole ring resulting in the formation of 1,2-dihydro-3,6-diphenyl-1,2,4,5-tetrazine which subsequently produces 3,5-diphenyl-1,2,4-triazole.[16c] Francis et al. in 1987 reported the condensation of an acyl hydrazide and an amidine to afford an acylamidrazone which upon the thermal cyclization gives 3,5-disubstituted-1,2,4-triazoles.[16e] Kelarev et al. in 1993 reported the reaction of indole substituted methyl acetimidates with acid hydrazides giving *N*-acylamidrazones, which upon heating, were converted to 3,5-disubstituted 1*H*-1,2,4-triazoles.[16f] Rostamizadeh et al. in 2003 reported the synthesis of 1,2,4-triazoles by three component condensation reaction of acid hydrazide, *S*-methyl isothioamide hydroiodide, and ammonium acetate on the surface of silica gel under microwave irradiation.[16i] A one step base-catalyzed synthesis of 3,5-disubstituted 1,2,4-triazoles by the condensation of a nitrile and a hydrazide under microwave conditions (150 °C)

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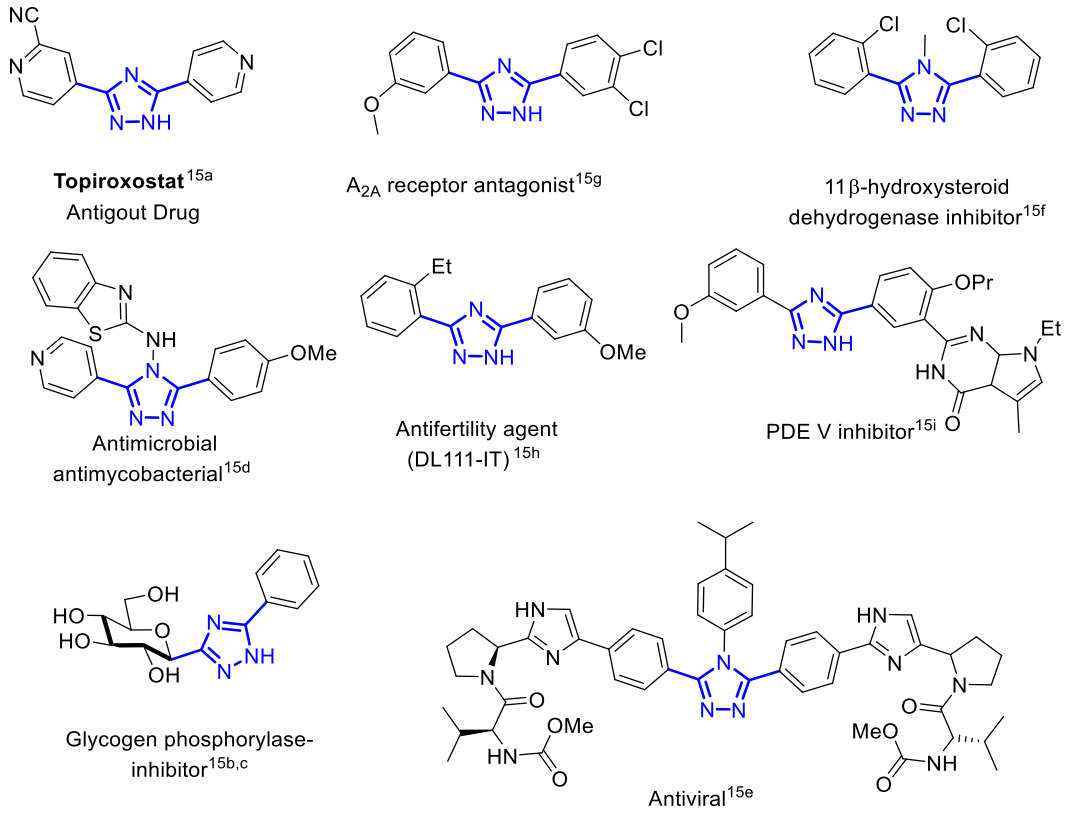

Figure 1. Drugs/leads containing 3,5-disubstituted-1,2,4-triazole moiety.

was reported by Yeung et al. in 2005.[16n] Al-Masoudi et al. in 2007 reported the synthesis of 1,2,4-triazole C-nucleosides from hydrazonyl chlorides and nitriles.[16o] Szöcs et al. in 2015 reported the synthesis of 5-aryl-3-C-glycosyl- and unsymmetrical 3,5-diaryl-1,2,4-triazoles from alkylidene-amidrazones due to intramolecular cyclization.[16aa] Inturi and co-workers in 2016 reported I_2 mediated one-pot synthesis of 1,2,4-triazoles from amidines and imidates through sequential C−N and N−N bond formation. This method was not suitable for the synthesis of unsymmetrical triazoles as the mixture of symmetrical and unsymmetrical products were obtained.[16ab] This method can produce the symmetrical products in good yields. Though this method involves the use of readily available and inexpensive reagents, however, when tried for the synthesis of unsymmetrical products, a mixture of symmetrical and unsymmetrical products was obtained.

There are numerous available methods for the synthesis of 1,2,4-triazoles[16] (Schemes 1A, S1), but most of the methods require multistep synthetic procedures as well as the use of nonreadily available starting materials. The metal-catalyzed reactions (Scheme S1), although having wide applications, suffer some specific limitations, especially in the pharmaceutical industry, where removing traces of the metallic species from the active pharmaceutical ingredient (API) turns out to be a big challenge.[17] There is a need for improved methods, and this article reports an alternate transition metal-free method which utilizes iodine catalysis[18] (Scheme 1B) for the generation of the title compounds. The noted advantages are (i) mild reaction conditions (I_2 catalysis and lower temperature), (ii) low cost and easily available starting materials, and (iii) shorter reaction time.

RESULTS AND DISCUSSION

Reaction of **1a** with **2a** was chosen as a model reaction to start this study. 1,1-Diaminobenzalazines (**1a**) could be synthesized by the condensation of aromatic aldehydes and aminoguanidine hydrochloride using water as solvent.[5b] Initially, a trial reaction was performed (Table 1, Entry 1) in the presence of 20 mol % I_2 and 3 equiv TBHP in MeCN at 90 °C. Delightfully the desired product 3,5-diphenyl-4*H*-1,2,4-triazole (**3a**) was formed with yield of 38%. The structure was confirmed through spectrometric [NMR: ^{1}H, ^{13}C, and high resolution mass spectrometry (HRMS): *m*/*z* 222.1050 $(M + H)^+$] data. The formation of triazole can be clearly seen by analyzing ^{1}H NMR spectra. The ^{1}H NMR spectra showed the appearance of a new peak at 14 ppm which is due to the ring NH. The initial success prompted us to optimize the reaction conditions. Hence, screening was carried out for solvents, amounts of I_2, TBHP, benzylamine and reaction temperature (Table 1). Various solvents were evaluated, and DMF was found to be the best solvent, providing the highest yield (Table 1, Entry 4).

The finalized optimal conditions are 1.8 equiv of **2a**, 20 mol % of iodine, and 1.5 equiv of TBHP and 80 °C (Table 1, Entry 21). With the optimal conditions in hand, the substrate scope and limitations of the developed method were explored. A variety of benzalazines and benzylamines containing both electron donating and electron withdrawing groups were screened, and the products were obtained with moderate to good yields (Scheme 2). When nitro group is at meta position (**3j**, **3ac**, **3af**) the products were obtained with higher yield in comparison to **3a** (may be due to −I effect). But when the nitro group is present at the para position, no products were obtained; this may be due to the −M effect of nitro group at

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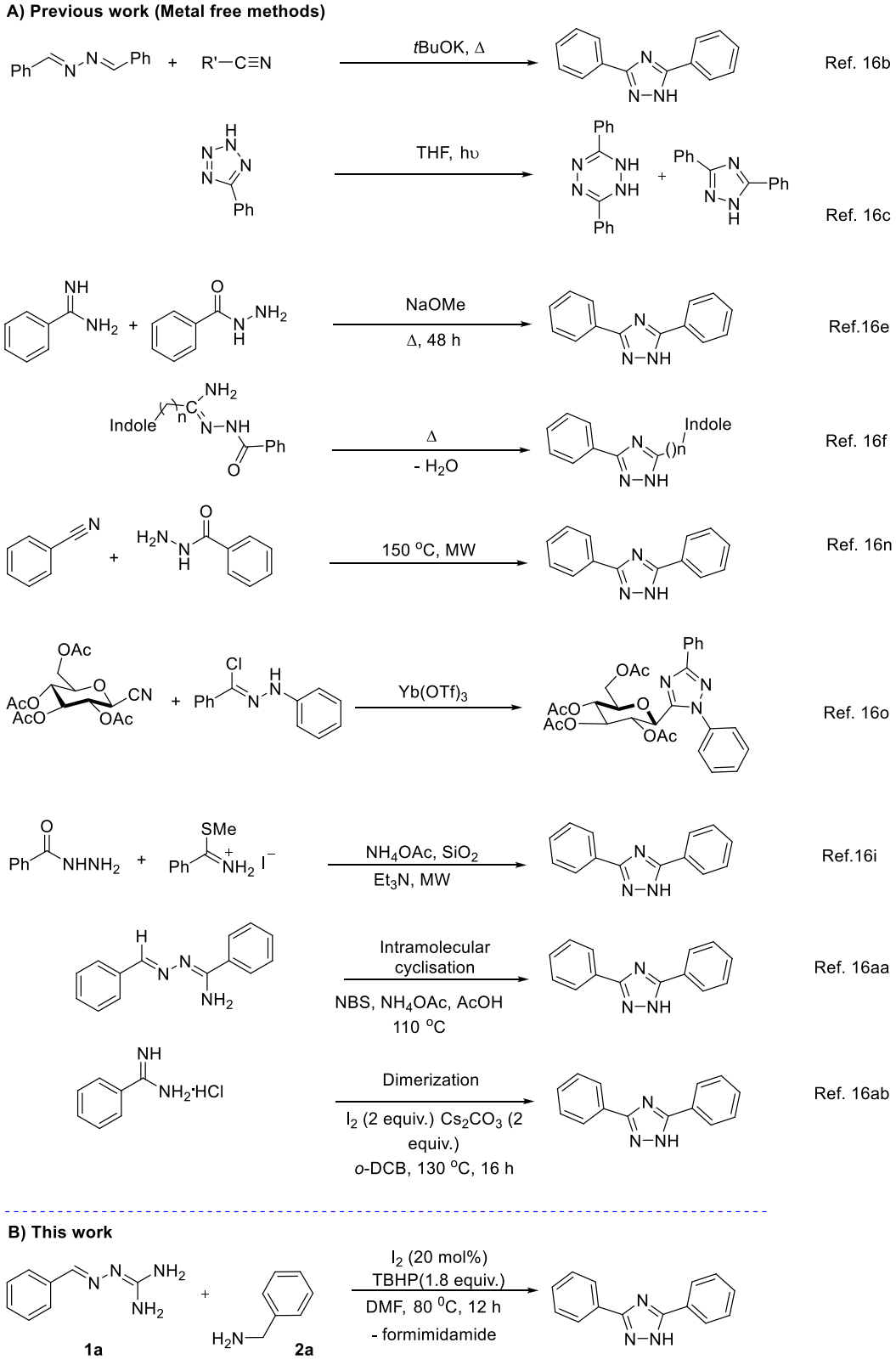
Scheme 1. Metal-Free Methods for the Synthesis of 3,5-Disubstituted-1,2,4-Triazoles



the para position. Slightly higher yield was also noticed in **3ad** which carries a methoxy group at the para position (may be due to +M effect). The very low yield of **3r** may be attributed to the +I effect from the alkyl group which decreases the electrophilicity of C5 position in intermediate **Int-2** (Scheme 3). The compounds containing heterocyclic substituents **3w**, **3x** could also be obtained using this method, however with low yields.

Compound **3j** was recrystallized from methanol using slow evaporation method, and the single needle shaped yellow crystals thus obtained were subjected to single crystal XRD study, which supported the expectations (Figure 2). In the

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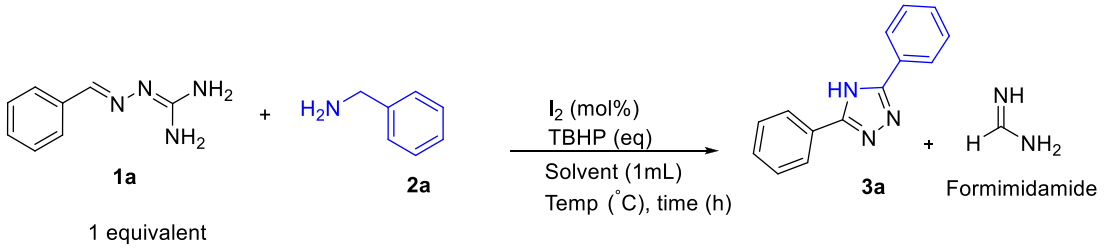
Table 1. Optimization of the Model Reaction



entry	iodine (mol %)	oxidant (equiv)	**2a** (equiv)	solvent	time (h)	temp (°C)	yield (**3a**) (%)
1	I_2 (20)	TBHP (3.0)	3.0	MeCN	4	90	38
2	I_2 (20)	TBHP (2.0)	3.0	DCE	12	80	21
3	I_2 (20)	TBHP (2.0)	3.0	Toluene	12	80	37
4	I_2 (20)	TBHP (2.0)	3.0	DMF	12	80	60
5	I_2 (20)	TBHP (2.0)	3.0	DMSO	12	80	26
6	I_2 (20)	TBHP (2.0)	3.0	MeCN	12	80	54
7	I_2 (20)	TBHP (2.0)	3.0	THF	12	80	traces
8	I_2 (20)	TBHP (2.0)	3.0	*t*-BuOH	12	80	18
9	I_2 (20)	TBHP (2.0)	3.0	NMP	12	80	39
10	I_2 (20)	TBHP (2.0)	3.0	1,4-dioxane	12	80	36
11	I_2 (20)	TBHP (2.0)	2.5	DMF	12	80	48
12	I_2 (20)	TBHP (2.0)	2.0	DMF	12	80	63
13	I_2 (20)	TBHP (2.0)	1.8	DMF	12	80	67
14	I_2 (20)	TBHP (2.0)	1.5	DMF	12	80	60
15	I_2 (20)	TBHP (0.5)	1.8	DMF	12	80	33
16	I_2 (20)	TBHP (1.0)	1.8	DMF	12	80	41
17	I_2 (20)	TBHP (1.5)	1.8	DMF	12	50	61
18	I_2 (20)	TBHP (2.0)	1.8	DMF	12	80	67
19	I_2 (10)	TBHP (1.5)	1.8	DMF	12	80	66
20	I_2 (20)	TBHP (1.5)	1.8	DMF	12	rt	53
21	**I_2 (20)**	**TBHP (1.5)**	**1.8**	**DMF**	**12**	**80**	**70**
22	I_2 (20)	TBHP (1.5)	1.8	DMF	12	90	65
23	I_2 (20)	TBHP (1.5)	1.8	DMF	12	100	65
24	I_2 (20)	TBHP (1.5)	1.8	DMF	12	120	52
25	I_2 (30)	TBHP (1.5)	1.8	DMF	12	80	70
26	I_2 (50)	TBHP (1.5)	1.8	DMF	12	80	55

solid state, the 1-*H* tautomer was found to be present. This tautomer is involved in intermolecular hydrogen bond between the two monomeric units in the unit cell (Figure 2).

Further, intermolecular C−H···O interaction also stabilizes the crystals. It can be attributed to the strong negative charge on oxygen atom of the nitro group. The π-stacking due to antiparallel arrangement of dimers stabilize the crystals (see SI, Figure S2). Quantum chemical studies confirmed the preference of this particular tautomeric state of the molecule—the 1-*H* tautomer is more stable than the 4-*H* tautomer by 4.83 kcal/mol according to B3LYP/6-31+G(d) level of quantum chemical analysis. The NH···N hydrogen bond and the CH···O(N) hydrogen bonds stabilize the dimer by >10 kcal/mol.

Finally, a DFT (density functional theory) study was carried out to explore the mechanism of formation of **3a** (Scheme 3). Molecular iodine being a Lewis acid forms a complex with **1a** initially to form **1a**-I_2; this process has been found to be endergonic by 9.94 kcal/mol. The coordinated molecular iodine activates the C4═N bond (iminic center) by making C4 center electron-deficient. The NBO (natural bond orbital) charge analysis as well as the local electrophilicity values indicated that the electrophilicity at C4 center is increased significantly after coordination with iodine. Thus, though the iodine coordination is an endergonic process, the change in the electrostatic characteristics facilitates the progress of the reaction. The next step involves the nucleophilic addition of N5 group of benzylamine **2a** at the iminic carbon C4 of **1a** to form the first C−N bond. This process leading to **Int-1** is exergonic by 2.11 kcal/mol, and involves an activation energy of 34.73 kcal/mol (a transient intermediate was also noticed along the reaction coordinate). **Int-1** undergoes oxidation in the presence of TBHP to form N5−C6 double bond which gives rise to a 2,3,5-triaza-1,3,5-triene intermediate (**Int-2**), it is an exergonic reaction (by 62.67 kcal/mol). The 3D geometry of **Int-2** suggests that the empty p-orbital of iminic carbon C6 and the lone pair of N2 of guanidine unit face each other and are ready to overlap with each other. Hence, the second C−N bond formation takes place easily by cyclization to form zwitterionic intermediate which undergoes proton exchange to produce **Int-3**.

The potential energy diagram (Figure 3) depicts that (i) the rate-determining step is the first C−N bond formation, (ii) formation of **Int-1** is not thermodynamically favorable (endergonic by 7.83 kcal/mol); however, the following step that is oxidation by TBHP is a highly favorable process (by 62.67 kcal/mol). Thus, the oxidation from **Int-1** to **Int-2** is the driving force facilitating the formation of product. **Int-2** to

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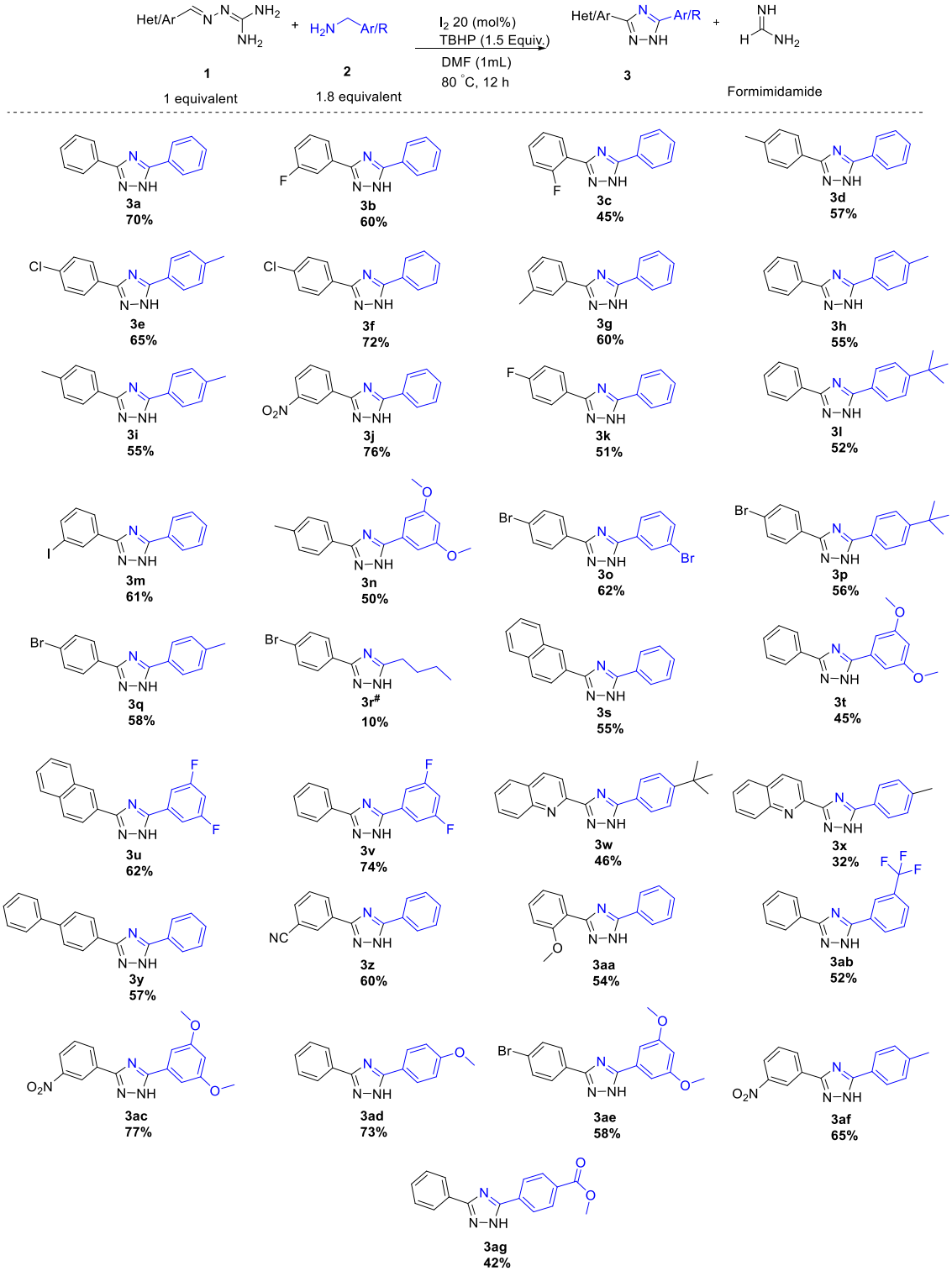
Scheme 2. Substrate Scope for the Synthesis of 3,5-Disubtituted-1,2,4-Triazoles Using Optimized Conditions[a]



[a](#) **3r** was the only isolable product with aliphatic amine where R is pentylamine. Several other aliphatic amines were tried using the developed protocol; however, the products were only detectable but not isolable. The data for **3a**, **3i**, and **3r** were compared with the literature,[16y] but the solvents utilized for obtaining the data are different.

Int-3 conversion is marginally endergonic by 1.35 kcal/mol, involving a reasonable activation energy (E_a = 15.70 kcal/mol). **Int-3** spontaneously releases formimidamide to yield the final product **3a**. The energy released during this aromatization followed by tautomerism is 23.23 kcal/mol (Figure 3).

To further support the proposed mechanism, cross control experiments were conducted. The oxidation of **Int-1** to **Int-2** mediated by TBHP[20] (which releases ~62 kcal/mol) must be following a radical pathway. This was confirmed by carrying out reaction using TEMPO (a radical scavenger) with the

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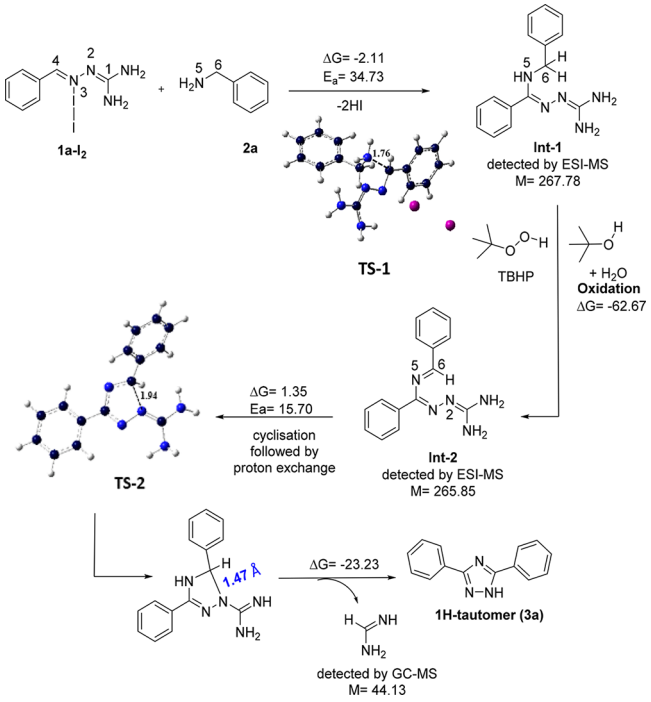
J. Org. Chem. 2021, 86, 7659−7671

Scheme 3. Plausible Mechanism of Triazole Formation with Energy Details[a]



[a]Gibbs free energies (ΔG) and activation energies (E_a) are in kcal/mol.

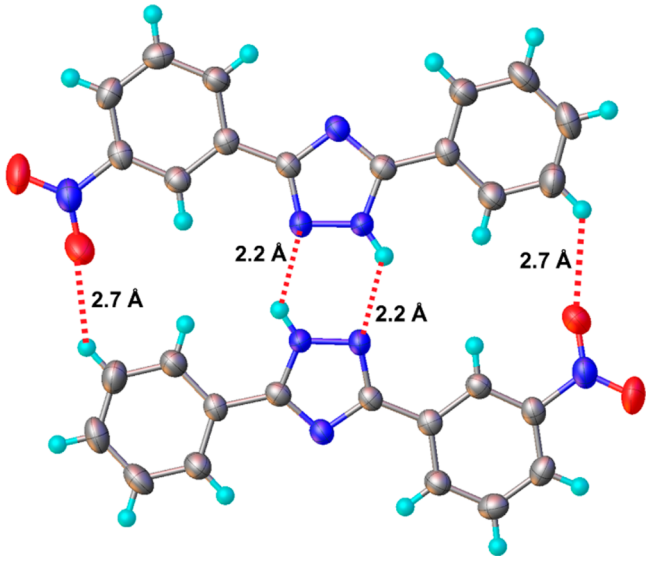


Figure 2. ORTEP diagram of dimer of **3j** showing intermolecular NH···N and CH···O hydrogen bonding between two monomer units (shown with red dotted lines). The ORTEP diagram of **3j** with 50% thermal probability ellipsoid plot is given as Figure S1. CCDC (2003067).[19]

optimized conditions, in which case, only trace amounts (10%) of the product were noticed (Scheme 4).

To trace the intermediate, the aliquots of reaction mixtures were collected at different time intervals of 5, 20, and 25 min of onset of reaction and analyzed after 24 h. The intermediates **Int-1** and **Int-2** could be traced in the mass spectrum (LC-MS), though these species could not be isolated. To establish the formation of formimidamide as

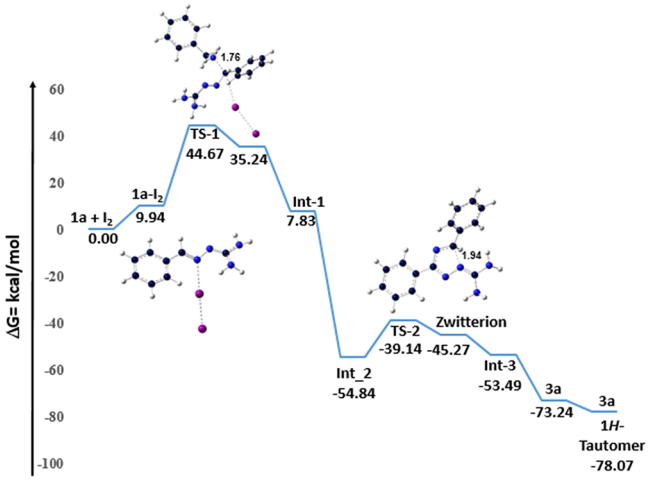


Figure 3. Potential energy surface (PES) diagram depicting the energetic pathway for the formation of **3a**.

side product, GC-MS analysis (see SI) has been carried out which showed a mass peak at 44.13 (m/z) with 6.60 retention time confirming the hypothesis [GC conditions: (1) 50 °C/min, 2 min hold time; (2) 8 °C/min −280 °C/min, 5 min hold time; (3) He flow rate 1 mL/min; (4) 1 μL split injection, 50:50; (5) column: DB-5MS, 5% phenyl and 95% polysiloxane; (6) Range 50−650 MS (m/z)]. To further confirm the formation of formimidamide in the reaction mixture, benzaldehyde (Scheme 5, R1) and acetophenone (Scheme 5, R2) were separately added to the reaction mixture. The formation of benzylideneformamide and benzylideneacetamide, respectively, confirms the release of side product in the title reaction.

These control experiments demonstrated the catalytic role of iodine,[21] revealed that the co-oxidant TBHP is required for the progress of the reaction and that the reaction follows a radical pathway. Apart from playing the role as co-oxidant, TBHP may also be playing a role in the regeneration of the molecular iodine from HI[22] (see SI), evidenced by changes in color.

CONCLUSIONS

In conclusion, an efficient method for the generation of 3,5-disubstituted-1,2,4-triazoles using diaminoazines and benzylamines as substrates has been developed. This reaction provides triazoles containing symmetrical as well as unsymmetrical substituents under mild reaction conditions. The mechanism of the reaction has been established with the help of cross control experiments and by exploring each step using quantum chemical methods. This method offers an efficient (alternative) procedure for the generation of 3,5-disubstituted-1,2,4-triazoles using low cost and easily available starting materials.

EXPERIMENTAL SECTION

Computational Methods. The quantum chemical calculations were carried out using the Gaussian 09 suite of programs.[23] Geometry optimization of compounds was performed by DFT using B3LYP method.[24] The basis set used was 6-31+G(d) for C, H, N, O and LANL2DZ for I_2. The frequency calculations were carried out on all the structures to verify character of stationary points (minima v/s saddle point). The NBO[25] charges were estimated to explore nucleophilicity and electrophilicity of the reacting centers.

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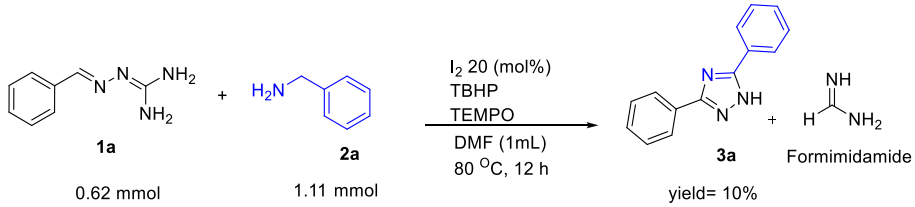
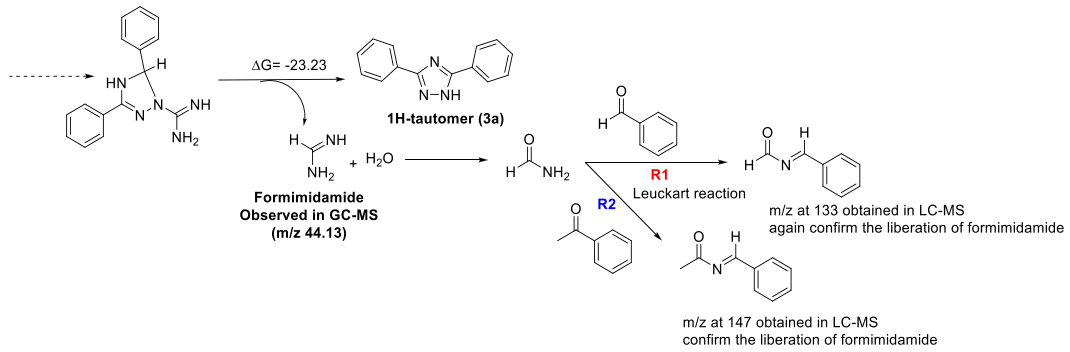
Scheme 4. Determining the Nature of the Reaction Mechanism



Scheme 5. Chemical Evidence for the Formation of Formimidamide



Electrophilicity (ω) values have been estimated using density functional methods.[26]

Chemistry. The reagents and chemicals required for the study were procured and all the reagents were used as such without further purification unless otherwise mentioned. The progress of the reaction was monitored by thin layer chromatography (TLC) performed on silica gel aluminum plates and visualization was done by UV light. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively, with TMS as an internal standard. The ^{1}H NMR and ^{13}C NMR spectra were recorded for MeOH-d_6 and for a few compounds DMSO-d_6 at 2.50 and 39.51 ppm respectively. Chemical shifts (δ) are reported in parts per million (ppm). Coupling constants (J) were reported in hertz (Hz). The abbreviations used to characterize the signals are as follows: s = singlet, m = multiplet, d = doublet, br. s. = broad singlet, dd = doublet of doublet, t = triplet. High resolution mass spectra were recorded using ESI-TOF method.

General Procedure for the Preparation of 3a. To the neat and dried round-bottom flask with 25 mL capacity, azine **1a** (100 mg, 0.61 mmol), benzylamine **2a** (122 mg, 1.11 mmol) and molecular iodine (31 mg, 20 mol %) were charged followed by addition of 1 mL DMF. The reaction mass was stirred, and to the reaction mass TBHP (84 mg, 0.93 mmol) was added. The reaction mass was heated to 80 °C for 12 h using oil bath. The progress of the reaction was monitored by TLC. After the completion of reaction, the reaction mass was quenched with saturated aqueous solution of sodium thiosulfate (5 mL). The reaction mass was extracted with ethyl acetate/water (3 × 50 mL). The organic layers were combined and subjected to drying by rotary evaporator to get crude **3a** which were purified by using column chromatography (hexane−EtOAc). The product was obtained in 70% yield (95 mg). The representative procedure was employed for the synthesis of **3b**−**3ag**.

The Scale-up Reaction (3a). To the neat and dried round-bottom flask with 25 mL capacity, azine **1a** (1 g, 6.17 mmol), benzylamine **2a** (1.22 g, 11.11 mmol) and molecular iodine (0.310 g, 20 mol %) were charged followed by addition of 1 mL DMF. The reaction mass was stirred and to the reaction mass TBHP (0.832 g, 9.25 mmol) was added. The reaction mass was heated to 80 °C for 12 h using oil bath. The progress of the reaction was monitored by TLC. After the completion of reaction, the reaction mass was quenched with saturated aqueous solution of sodium thiosulfate (20 mL). The reaction mass was extracted with EtOAc/water (3 × 50 mL). The organic layers were combined and subjected to drying by rotary evaporator to get crude **3a**. The crude **3a** was purified by column chromatography using 30:70 EtOAC/Hexane as eluent to get pure **3a** with 72% yield (0.995 g).

3,5-Diphenyl-1*H*-1,2,4-triazole (3a).[16y] The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 70% (95.20 mg), white solid, mp 190−191 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.09 (s, 4 H), 7.54−7.52 (m, 6 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 159.3, 138.8, 130.1, 129.8, 127.5; IR (KBr, cm^{-1})3435 (−N-H), 1657 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{12}N_3$ 222.1026, found 222.1050.

3-(3-Fluorophenyl)-5-phenyl-1*H*-1,2,4-triazole (3b). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 60% (79.20 mg), white solid, mp 196−197 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.29 (s, 1 H), 8.10−8.07 (m, 3 H), 7.65 (d, J = 7.5 Hz, 1 H), 7.56−7.54 (m, 3 H), 7.45 (t, J = 7.9 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 164.6 (d, $^1J_{C-F}$ = 234 Hz), 151.7, 148.1, 137.5, 133.0 (d, $^2J_{C-F}$ = 55 Hz), 129.8, 129.8, 127.6, 116.9, 116.7, 111.2; IR (KBr, cm^{-1}) 3337(N−H), 1631(C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{11}FN_3$ 240.0932, found 240.0951.

3-(2-Fluorophenyl)-5-phenyl-1*H*-1,2,4-triazole (3c). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 45% (59.71 mg), white solid, mp 186−188 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.04−7.96 (m, 3 H), 7.47−7.34 (m, 4 H), 7.29−7.18 (m, 2 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 159.9 (d, $^1J_{C-F}$ = 250 Hz), 151.6, 145.2, 133.7, 129.8, 129.5, 128.4, 126.2, 124.5, 116.0, 115.8; IR (KBr, cm^{-1}) 3337 (N−H), 1640 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{11}FN_3$ 240.0932, found 240.0950.

3-Phenyl-5-(*p*-tolyl)-1*H*-1,2,4-triazole (3d). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 57% (76.10 mg), white solid, mp 244−246 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 14.43 (s, 1H), 8.10 (d, J = 8.0 Hz, 2 H), 8.08 (d, J = 7.9 Hz, 2 H), 7.51 (bs, 3H), 7.35 (m, 2H), 7.33 (d, J = 7.5 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 157.1, 141.9, 138.9, 131.3, 129.2, 128.1, 127.0, 126.9, 126.7, 126.1, 20.0.IR (KBr, cm^{-1}) 3337 (N−H), 1631 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{14}N_3$ 236.1183, found 236.1189.

3-(4-Chlorophenyl)-5-(*p*-tolyl)-1*H*-1,2,4-triazole (3e). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 65% (89.20 mg), white solid, mp 292−294 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, J = 8.5 Hz, 2 H), 7.94 (d, J

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J. Org. Chem. 2021, 86, 7659−7671

= 8.0 Hz, 2 H), 7.53 (d, J = 8.5 Hz, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 2.44 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 157.7, 133.0, 129.3, 128.7, 128.6, 128.3, 127.6, 127.2, 126.2, 20.02; IR (KBr, cm^{-1}) 3361 (N−H),1628 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{13}ClN_3$ 270.0793, found 270.0807.

3-(4-Chlorophenyl)-5-phenyl-1*H*-1,2,4-triazole (3f). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 72% (93.67 mg), white solid, mp 187−189 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.11 (t, J = 8.0 Hz, 4H), 7.61 (d, J = 8.0 Hz, 2 H), 7.5 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 159.4, 138.6, 137.4, 132.9, 128.5, 128.3, 128.0, 127.2, 126.7, 126.1; IR (KBr, cm^{-1}) 3681 (N−H), 1633 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}ClN_3$ 256.0637, found 256.0652.

5-Phenyl-3-(*m*-tolyl)-1*H*-1,2,4-triazole (3g). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 60% (80.11 mg), white solid, mp 239−240 °C; ^1H NMR (400 MHz,CD_3OD) δ 8.09 (dd, J = 1.5, 7.8 Hz, 2 H), 7.92 (s, 1 H), 7.87 (d, J = 7.8 Hz, 1 H), 7.56−7.49 (m, 3 H), 7.42 (t, J = 7.7 Hz, 1 H), 7.33 (d, J = 7.5 Hz, 1 H), 2.46 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 159.7, 142.7, 140.4, 140.0, 131.9, 131.1, 130.0, 129.9, 128.2, 127.6, 124.8, 21.5; IR (KBr, cm^{-1}) 3356 (N−H), 1636 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{14}N_3$ 236.1183, found 236.1189.

3-Phenyl-5-(*p*-tolyl)-1*H*-1,2,4-triazole (3h). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 55% (79.70 mg), white solid, mp 245−247 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.08 (d, J = 6.5 Hz, 2 H), 7.96 (d, J = 7.8 Hz, 2 H), 7.56−7.49 (m, 3 H), 7.36 (d, J = 7.8 Hz, 2 H), 2.44 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 159.4, 140.3, 137.5, 129.6, 129.2, 128.5, 126.1, 20.0; IR (KBr, cm^{-1}) 3393 (N−H), 1637 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{14}N_3$ 236.1183, found 236.1189.

3,5-Di-*p*-tolyl-1*H*-1,2,4-triazole (3i).[16y] The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 55% (73.45 mg), white solid, mp 249−251 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.96 (d, J = 4 Hz, 4 H), 7.36 (d, J = 8.0 Hz, 4 H), 2.43 (s, 6 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 157.9, 129.6, 129.2, 127.1, 126.9, 20.0; IR (KBr, cm^{-1}) 3457 (N−H), 1630 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{16}N_3$ 250.1339, found 250.1367.

3-(3-Nitrophenyl)-5-phenyl-1*H*-1,2,4-triazole (3j). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 76% (97.66 mg), white solid, mp 250.0−252.0 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.98 (s, 1 H), 8.53 (d, J = 8.0 Hz, 1 H), 8.35 (d, J = 8.0 Hz, 1 H), 8.10 (dd, J = 8.0 Hz, 2 H), 7.80 (t, J = 7.7 Hz, 1 H) 7.60−7.53 (m, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 159.2, 148.6, 131.7, 130.1, 129.8, 128.7, 128.1, 127.5, 126.2, 123.5, 120.6; IR (KBr, cm^{-1}) 3411 (N−H), 1637(C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_4O_2$ 267.0877, found 267.0892.

3-(4-Fluorophenyl)-5-phenyl-1*H*-1,2,4-triazole (3k). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 51% (67.71 mg), white solid, mp 188−189 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.06−8.12 (m, 4H), 7.40−7.56 (m, 3H), 7.26−7.36 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 164.9 (d, $^1J_{C-F}$ = 234 Hz), 159.0, 145.2, 131.2, 130.0,129.8, 129.7, 127.1, 126.1, 116.8 (d, $^2J_{C-F}$ = 22 Hz);IR (KBr, cm^{-1}) 3436 (N−H), 1635 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}FN_3$ 240.0932, found 240.0950.

5-(4-(*tert*-Butyl)phenyl)-3-phenyl-1*H*-1,2,4-triazole (3l). The title compound was isolated by column chromatography (hexane−EtOAc 3:1) Yield: 52% (88.90 mg), white solid, mp 234−236 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.10 (d, J = 8.0 Hz, 2 H), 8.02 (d, J = 8.0 Hz, 2 H), 7.60 (d, J = 8.0 Hz, 2 H), 7.55−7.50 (m, 3 H), 1.40 (s, 9 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 153.3, 129.6, 128.5, 128.1, 126.9, 126.2, 126.0, 125.5, 125.0, 30.3, 30.2; IR (KBr, cm^{-1}) 3436 (N−H), 1642 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{20}N_3$ 278.1652, found 278.1664.

3-(3-Iodophenyl)-5-phenyl-1*H*-1,2,4-triazole (3m). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 61% (73.49 mg), white solid, m.p.177−178 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.49 (s, 1 H), 8.15−8.02 (m, 3 H), 7.85 (d, J = 6.8 Hz, 1 H), 7.55 (d, J = 6.8 Hz, 3 H), 7.30 (t, J = 7.8 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 160.8, 149.0, 143.0, 138.6, 138.4, 135.0, 130.3, 129.9, 128.6, 126.2, 125.3; IR (KBr, cm^{-1}) 3290 (N−H),1640 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{11}IN_3$ 347.9993, found 347.9997.

5-(3,5-Dimethoxyphenyl)-3-(*p*-tolyl)-1*H*-1,2,4-triazole (3n). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 50% (83.80 mg), white solid, mp 196−197 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.95 (brs, 2 H) 7.36−7.28 (m, 4H), 6.61 (s, 1 H), 3.88 (s, 6 H), 2.43 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 161.3, 155.8, 143.0, 132.5, 129.3, 128.7, 128.0, 126.9, 126.1, 104.0, 101.5, 54.5, 20.0; IR (KBr, cm^{-1}) 3390 (N−H), 1639 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{17}H_{18}N_3O_2$ 296.1394, found 296.1405.

5-(3-Bromophenyl)-3-(4-bromophenyl)-1*H*-1,2,4-triazole (3o). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 62% (97.50 mg), white solid, mp 292−294 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.28 (s, 1 H), 8.07 (d, J = 8.0 Hz, 1 H), 8.01 (d, J = 8.5 Hz, 2 H), 7.71 (d, J = 8.5 Hz, 2 H), 7.66 (d, J = 7.8 Hz, 1 H), 7.46 (t, J = 7.9 Hz, 1 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 158.0, 132.4, 131.8, 131.4, 131.2, 130.3, 130.2, 129.8, 129.0, 128.8, 127.8, 125.9, 124.7, 123.8, 122.4; IR (KBr, cm^{-1}) 3681 (N−H), 1657 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{10}Br_2N_3$ 379.9216, found 379.9225.

3-(4-Bromophenyl)-5-(4-(*tert*-butyl)phenyl)-1*H*-1,2,4-triazole (3p). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 56% (82.71), white solid, mp 286−287 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.03−7.98 (m, 4 H), 7.69 (d, J = 8.0 Hz, 2 H), 7.61 (d, J = 8.0 Hz, 2 H), 1.39 (s, 9 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 153.5, 140.2, 138.7, 131.7, 131.6, 127.8, 126.0, 125.6, 123.4, 30.2, 29.3; IR (KBr, cm^{-1}) 3412 (N−H), 1631 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{19}BrN_3$ 356.0757, found 356.0755.

3-(4-Bromophenyl)-5-(*p*-tolyl)-4*H*-1,2,4-triazole (3q). The title compound was isolated by column chromatography (hexane−EtOAc 3:1), Yield: 58% (72.96 mg), white solid, mp 262−263 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.02 (d, J = 8.3 Hz, 2 H), 7.94 (d, J = 8.0 Hz, 2 H), 7.68 (d, J = 8.0 Hz, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 2.44 (s, 3 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 157.6, 138.2, 137.3, 135.2, 133.4, 133.3, 131.6, 127.9, 126.2, 20.0; IR (KBr, cm^{-1}) 3342 (N−H), 1620 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{13}BrN_3$ 314.0288, found 314.0299.

3-(4-Bromophenyl)-5-butyl-1*H*-1,2,4-triazole (3r).[16y] The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 10% (11.60 mg), white solid, mp 123−124 °C; ^1H NMR (400 MHz, CD_3OD) δ 7.80 (d, J = 7.8 Hz, 2 H), 7.53 (d, J = 7.3 Hz, 2 H), 2.73 (t, J = 6.9 Hz, 2 H), 1.67 (t, 2 H), 1.37−1.19 (m, 2 H), 0.88 (t, J = 7.0 Hz, 3 H); ESI-MS $[M + H]^+$ m/z 188.1.

3-(Naphthalen-2-yl)-5-(phenyl)-1*H*-1,2,4-triazole (3s). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 55% (70.30 mg), white solid, mp 223−224 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.62 (s, 1 H), 8.19 (d, J = 8.8 Hz, 1 H), 8.13 (d, J = 6.5 Hz, 2 H), 8.02 (d, J = 8.5 Hz, 2 H), 7.98−7.91 (m, 1 H), 7.62−7.51 (m, 5 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 162.6, 134.1, 133.3, 129.8, 128.6, 128.4, 128.2, 127.5, 126.7, 126.4, 126.2, 125.8, 123.3; IR (KBr, cm^{-1}) 3373 (N−H), 1637 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{14}N_3$ 272.1183, found 272.1194.

5-(3,5-Dimethoxyphenyl)-3-phenyl-1*H*-1,2,4-triazole (3t). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 45% (78.05 mg), white solid, mp 175−177 °C; ^1H NMR (400 MHz, CD_3OD) δ 8.15−8.01 (m, 2H), 7.61−7.45 (m, 4 H), 7.28 (br. s., 2 H), 6.62 (br. s., 1 H), 3.89 (s, 6 H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3OD) δ 161.4, 147.8, 146.5, 138.2, 137.4,129.6, 128.5, 128.2, 126.9, 126.2, 104.0, 54.6; IR (KBr, cm^{-1}) 3452 (N−H), 1602 (C═N). HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{16}N_3O_2$ 282.1238, found 282.1248.

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J. Org. Chem. 2021, 86, 7659−7671

5-(3,5-Difluorophenyl)-3-(naphthalen-2-yl)-1*H*-1,2,4-triazole (3u). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 62% (89.78 mg), white solid, mp 215−216 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.58 (s, 1 H), 8.14 (dd, J = 1.8, 8.5 Hz, 1 H), 8.06−7.99 (m, 2 H), 7.95 (dd, J = 3.3, 6.0 Hz, 1 H), 7.74 (dd, J = 2.3, 8.5 Hz, 2 H), 7.62−7.56 (m, 2 H), 7.08 (tt, J = 2.3, 9.0 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 163.5 (d, $^1J_{C-F}$ = 258 Hz), 163.3 (d, $^1J_{C-F}$ = 233 Hz), 134.2, 133.2, 128.5, 128.2, 127.5, 127.0, 126.6, 126.0, 123.1, 109.1, 109.0, 108.8 (d, $^3J_{C-F}$ = 12 Hz), 104.1, 103.8; IR (KBr, cm^{-1}) 3461(N−H), 1636 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{12}F_2N_3$ 308.0994, found 308.1000.

5-(3,5-Difluorophenyl)-3-phenyl-1*H*-1,2,4-triazole (3v). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 74% (117.39 mg), white solid, mp 193−194 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.11−8.00 (m, 2 H), 7.72 (d, J = 5.5 Hz, 2 H), 7.55 (br. s., 3 H), 7.13−7.00 (m, 1 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 163.4(d, $^1J_{C-F}$ = 258 Hz), 163.3(d, $^1J_{C-F}$ = 247 Hz), 155.5, 140.1, 137.9, 130.1, 128.7, 126.2, 109.0, 108.8 (d, $^3J_{C-F}$ = 12 Hz), 104.0; IR (KBr, cm^{-1}) 3318 (N−H),1631 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{14}H_{10}F_2N_3$ 258.0838, found 258.0841.

2-(5-(4-(*tert*-Butyl)phenyl)-1*H*-1,2,4-triazol-3-yl)quinoline (3w). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 46% (70.83 mg), white solid, mp 230−232 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.50 (d, J = 8.0 Hz, 1 H), 8.35 (d, J = 8.0 Hz, 1 H), 8.24 (d, J = 8.5 Hz, 1 H), 8.09 (d, J = 8.0 Hz, 2 H), 8.01 (d, J = 8.0 Hz, 1 H), 7.86 (t, J = 7.8 Hz 1 H), 7.60 (t, J = 7.6 Hz, 1 H), 7.62−7.60 (m, 2 H), 1.4 (s, 9 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 165.0, 161.1, 155.7, 147.7, 136.4, 138.0, 136.5, 130.8, 129.3, 129.2, 128.6, 127.7, 126.1, 119.8, 35.0, 31.5; IR (KBr, cm^{-1}) 3448 (N−H), 1637 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{21}H_{21}N_4$ 329.1761, found 329.1774.

2-(5-(*p*-Tolyl)-1*H*-1,2,4-triazol-3-yl)quinoline (3x). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 32% (42.96 mg), white solid, mp 240−241 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (d, J = 8.0 Hz, 1 H), 8.35 (d, J = 8 Hz, 1 H), 8.22 (d, J = 8 Hz, 1 H), 8.05−7.99 (m, 3 H), 7.83 (d, J = 4 Hz 1 H), 7.6 (t, J = 7.66 Hz 1 H), 7.38 (d, 2 H), 2.45 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 160.3, 159.1, 147.7, 142.5, 139.5, 138.1, 130.9, 129.9, 129.4, 128.6, 128.4, 127.8, 126.4, 119.8, 21.4; IR (KBr, cm^{-1}) 3317 (N−H), 1681 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{15}N_4$ 287.1292, found 287.1299.

3-([1,1′-Biphenyl]-4-yl)-5-phenyl-1*H*-1,2,4-triazole (3y). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 57% (71.12 mg), white solid, 222−223 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.16−8.09 (m, 4 H), 7.85−7.77 (m, 2 H), 7.76−7.67 (m, 2 H), 7.59−7.45 (m, 5 H), 7.41 (d, J = 8.0 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 160.4, 142.6, 140.9, 135.2, 129.7, 128.6, 128.1, 127.5, 127.4, 127.0, 126.7, 126.6, 126.2; IR (KBr, cm^{-1}) 3435 (N−H), 1638 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{16}N_3$ 298.1339, found: 298.1339.

3-(5-Phenyl-1*H*-1,2,4-triazol-3-yl)benzonitrile (3z). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 60% (78.93 mg), white solid, 202−203 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.45 (s, 1 H), 8.41 (d, J = 8.0 Hz, 1 H), 8.07 (d, J = 6.5 Hz, 2 H), 7.82 (d, J = 7.5 Hz, 1 H), 7.70 (t, J = 7.8 Hz, 1 H), 7.55 (d, J = 5.3 Hz, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 158.4, 133.3, 130.8, 130.7, 130.5, 129.6, 129.5, 128.7, 127.8, 126.6, 118.8, 112.5; IR (KBr, cm^{-1}) 3435 (N−H),1659 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{11}N_4$ 247.0978, found 247.0976.

3-(2-Methoxyphenyl)-5-phenyl-1*H*-1,2,4-triazole (3aa). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 54% (70.58 mg), white solid, mp 183−184 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (d, J = 8.0 Hz, 2 H), 7.54−7.47 (m, 5 H), 7.26 (d, J = 8.0 Hz, 1 H), 7.17 (t, J = 7.15 Hz, 1 H), 3.95 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 157.1, 155.6, 131.6, 130.6, 129.3, 128.9, 128.2, 126.9, 126.1, 120.7, 111.1, 54.8; IR (KBr, cm^{-1}) 3245 (N−H), 1606 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{14}N_3O$ 252.1137, found 252.1148.

3-Phenyl-5-(3-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole (3ab). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 52% (76.71 mg), white solid, mp 185−186 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.44 (s, 1 H), 8.39 (d, J = 8.0 Hz, 1 H), 8.09 (d, J = 8.0 Hz, 2 H), 7.89−7.64 (m, 2 H), 7.55−7.48 (m, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 167.8 (d, $^1J_{C-F}$ = 263 Hz), 131.0 (d, $^2J_{C-F}$ = 71 Hz), 130.0, 129.5, 129.4, 128.7, 128.2, 126.9, 126.2, 125.7, 122.7(d, $^3J_{C-F}$ = 12 Hz), 122.7; IR (KBr, cm^{-1}) 3356 (N−H), 1658 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{11}F_3N_3$ 290.0900, found 290.0916.

5-(3,5-Dimethoxyphenyl)-3-(3-nitrophenyl)-1*H*-1,2,4-triazole (3ac). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 77% (121.25 mg), white solid, mp 193−195 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.93 (s, 1 H), 8.49 (d, J = 8.0 Hz, 1 H), 8.32 (d, J = 8.0 Hz, 1 H), 7.77 (t, J = 7.75, 1H), 7.23 (s, 2 H), 6.62 (s, 1 H), 3.88 (s, 6 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 161.4, 160.6, 148.6, 146.9, 138.6, 131.7, 129.8, 123.5, 120.6, 118.0, 104.0, 109.0, 102.2, 54.6; IR (KBr, cm$^-$): 3316 (N−H),1615 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{15}N_4O_4$ 327.1088, found 327.1094.

5-(4-Methoxyphenyl)-3-phenyl-1*H*-1,2,4-triazole (3ad). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 73% (112.36 mg), white solid, mp 188−190 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, J = 4.0 Hz, 2 H), 8.01 (d, J = 4 Hz, 2 H), 7.51 (br. s., 3 H), 7.09 (br. s., 2 H), 3.88 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 161.3, 158.7, 148.6, 136.7, 129.5, 128.5, 127.7, 126.1, 113.9, 54.4; IR (KBr, cm^{-1}) 3351(N−H), 1615 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{14}N_3O$ 252.1132, found 252.1146.

3-(4-Bromophenyl)-5-(3,5-dimethoxyphenyl)-1*H*-1,2,4-triazole (3ae). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 58% (86.63 mg), white solid, mp 180−181 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.79 (d, J = 8.0 Hz, 2 H), 7.67 (d, J = 8 Hz, 2 H), 6.53 (br. s., 2 H), 6.40 (t, J = 6.4 Hz, 1 H), 3.77 (s, 6 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 161.4, 158.4, 140.3, 138.8, 131.6, 129.7, 127.8, 123.5, 113.6, 104.0, 102.0, 54.0. IR (KBr, cm^{-1}) 3337 (N−H), 1640 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{15}BrN_3O_2$ 360.0343, found 360.0347.

3-(3-Nitrophenyl)-5-(*p*-tolyl)-1*H*-1,2,4-triazole (3af). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 65% (87.91 mg), white solid, mp 252−253 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.98 (s, 1 H), 8.53 (d, J = 8.0 Hz, 1 H), 8.35 (d, J = 8.0 Hz, 1 H), 7.98 (d, J = 8.0 Hz, 2 H), 7.80 (d, J = 7.78 Hz, 1 H), 7.41 (d, J = 8.0 Hz, 2 H), 2.45 (s, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 165.3, 161.0, 148.7, 142.0, 140.7, 131.7, 129.8, 129.4, 126.1, 123.5, 120.7, 19.9; IR (KBr, cm^{-1}) 3329 (N−H), 1610 (C═N). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{13}N_4O_2$ 281.1034, found 281.1040.

Methyl 4-(5-phenyl-1*H*-pyrrol-2-yl)benzoate (3ag). The title compound was isolated by column chromatography (hexane−EtOAc 3:2), Yield: 42% (90.30 mg), white solid, mp 240−242 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28 (d, J = 8 Hz, 2 H), 8.07(t, J = 8.06 Hz, 4 H), 7.52 (m, 3 H); ^{13}C{^{1}H} NMR (100 MHz, CD_3OD) δ 166.39, 158.83, 144.83, 130.34, 129.72, 129.57, 129.07, 128.87, 127.48, 126.84, 52.66; IR (KBr, cm^{-1}) 3350 (N−H), 1640 (C═N), 1740 (C═O). HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{14}N_3O_2$ 280.1081, found 280.1083.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00704.

Scanned spectra (^{1}H NMR, ^{13}C NMR, and HRMS) for all the new compounds, computational data, and mechanistic studies (PDF)

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CCDC 2003067 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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