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FULL PAPER

Facile One-Pot Synthesis of Methyl 1-Aryl-1*H*-1,2,4-triazole-3-carboxylates from Nitrilimines with Vilsmeier Reagent

Shuo-En Tsai,[a,b] Kun-Heng Chiang,[a] Ching-Chun Tseng,[a,b] Nai-Wei Chen,[c] Ching-Yuh Chern,*[d] and Fung Fuh Wong*[a]

Abstract: Two convenient and effective one-pot methods have been developed to synthesize methyl 1-aryl-1*H*-1,2,4-triazole1-3-carboxylates by using hydrazonoyl hydrochlorides (nitrilimines) with Vilsmeier reagent. The first, a direct one-pot method, involved the reaction between nitrilimines and Vilsmeier reagent at ~85°C for ~0.5 h. Another one-pot two-step cascade method proceeded via nucleophilic substitution with bis(trimethylsilyl)amine [$NH(SiMe_3)_2$] and subsequent intramolecular cycloaddition reaction with Vilsmeier reagent. Substrate scope, multicomponent examples, and mechanistic insights are discussed.

Introduction

1,2,4-Triazoles constitute an important class of heterocyclic compounds, having various biological activities,[1] such as antibacterial,[2] antifungal,[3] anti-inflammatory, [4] antituberculosis,[5] anticancer,[6] antioxidant[7] and InhA inhibitory activity.[8] Therefore, the development of simple and efficient synthetic methods of pharmaceutically active 1,2,4-triazoles is important to drug discovery.[9]

Syntheses of substituted 1,2,4-triazoles have been reported in the literature.[10] These included dehydrative cyclization of acylamidrazone intermediates[11] and formation of the 1,2,4-triazole motif from hydrazides and activated nitriles or amides including imidates and thioamides.[12] We have also successfully developed a number of syntheses to afford substituted 1,2,4-triazoles by reacting nitrilimines with aldehydes, nitriles, imidate hydrochlorides, oxime hydrochlorides, and carbodiimides via a 1,3-dipolar cycloaddition methodology.[13] Additional methodologies for the preparation of 1-aryl-1,2,4-triazoles have been developed. Examples included the direct condensation of hydrazine derivatives,[14,15] transition metal catalyzed C–N bond coupling,[16] and S_NAr-type chemistry of a halogenated arene with 1,2,4-triazole as a nucleophile.[17]

The Vilsmeier reagent is a versatile and widely-used synthetic agent. This reagent and its analogues have been used to achieve amindination,[18] formylation,[18,19] formyloxylation,[19] and heterocyclization[20] in organic and medicinal chemistry. In addition, Vilsmeier reagents provides some advantages such as high yield and purity of products, functional group tolerance, and simple manipulation.[20] Herein, we report two convenient and effective one-pot methods to synthesize methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2a**–**n** from nitrilimines using the Vilsmeier reagent ($HCONH_2/POCl_3$). The first is a direct method involving the reaction between 2-chloro-2-(2-phenylhydrazono)acetate nitrilimines **1a**–**n** and the Vilsmeier reagent. The other one is a two-step cascade method that gave methyl 2-amino-2-(2-phenylhydrazono)acetate **4** in the first step, via nucleophilic substitution reaction with bis(trimethylsilyl)amine [$NH(SiMe_3)_2$]. This was followed by an intramolecular cycloaddition reaction with the Vilsmeier reagent ($HCONH_2/POCl_3$) to form the corresponding 1,2,4-triazoles **2a**–**n** in good isolated yields (73–91%). Both approaches to the preparation of methyl 1-aryl-1*H*-1,2,4-triazole1-3-carboxylates are presented in Scheme 1.

Scheme 1

Results and Discussion

We reckoned that an intramolecular cyclization reaction between Vilsmeier reagents and hydrazonoyl hydrochlorides (nitrilimines) is highly feasible. To investigate the reactivity of such reactions, we prepared a series of methyl 2-chloro-2-(2-arylhydrazono)acetate **1a**–**n** as the starting material by literature methods.[13,21] To evaluate the reaction conditions, methyl 2-chloro-2-(2-phenylhydrazono)acetate **1a** was used as a model reactant with the Vilsmeier reagent ($HCONH_2$/3.0 equiv of $POCl_3$) under various reaction temperatures including ~25, 55, 75, 85, 125°C, and at reflux (see Scheme 1 and Table 1). We also studied the reaction time from 0.5 to 72 h and followed the reactions by TLC (see Table 1).

Table 1

Based on the results, we concluded that the intramolecular cyclization reaction required heating above 55°C even with reaction times as long as 72 h (see entry 1 and 2). Higher reaction temperatures (75–85°C) gave the desired product 1-aryl-1*H*-1,2,4-triazole **2a** and the minor decarboxylated product **3a** in 72%/90% and 14%/4%, respectively (see entry 3 and 4 of Table 1). When the reaction temperature increased to 125°C, formation of the decarboxylated product **3a** was promoted (see entry 5 of Table 1). Consequently, when we carried out the reaction under reflux (~175°C) for the same reaction time, **3a** predominated and was produced in 86% yield (see entry 6 of Table 1). Overall, the best reaction condition was 80-90°C and the reaction time was about 0.5 h (see Table 1 and Figure 1). To evaluate the generality of these conditions, we further prepared ethyl 2-chloro-2-(2-

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phenylhydrazono)acetate as the starting material. A similar reaction with the Vilsmeier reagent gave the corresponding 1-aryl-1*H*-1,2,4-triazole product **2b** in 74% yield. For economic and reaction efficiency reasons, methyl 2-chloro-2-(2-phenylhydrazono)acetates **1a-n** were chosen as the substrates in further studies.

Figure 1

Reliability of the optimized procedure was demonstrated with 2-chloro-2-(2-arylhydrazono)acetate **1b–n**. Despite various substituents including *o*-, *m*-, *p*-CF_3, *o*-, *m*-, *p*-F, *m*-, *p*-Cl, *m*-, *p*-Me, *p*-Br, *p*-OMe, and 3,4-di-Cl, the one-pot intramolecular heterocyclization reaction proceeded smoothly at ~85°C for ~0.5 h to give the corresponding methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2b–n** in good to excellent yields (82–95%, see Table 2). All 1-aryl-1*H*-1,2,4-triazoles **2a–n** were fully characterized by spectroscopic methods. For example, compound **2a** presented two singlet peaks at δ 8.61 ppm for the1,2,4-triazolic ring and δ 4.01 ppm for the –OMe group in the ^{1}H NMR. In the ^{13}C NMR spectrum, compound **2a** showed characteristic absorption at δ 160.1 ppm for the carboxylate carbon O=^{13}COMe. The structure of methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a** was further charactered by X-rays crystallographic analysis and a single-crystal X-ray diffraction study (ORTEP) was presented in Figure 2.

Table 2

Figure 2

For further investigation into the reaction temperature effect, 2-chloro-2-(2-arylhydrazono)acetates substituted with *o*-, *m*-, *p*-CF_3, *o*-, *m*-, *p*-F, *m*-, *p*-Cl, or *m*-, *p*-Me **1a–k** were allowed to react with Vilsmeier reagent ($HCONH_2$/3.0 equiv of $POCl_3$) at reflux. The corresponding decarboxylated products **3a–k** predominated as a single product in 82–94% yields (see Table 3). The decarboxylated 1-aryl-1*H*-1,2,4-triazoles **3a–k** were identified by spectroscopic methods. Compound **3a** exhibited two singlet peaks at δ 7.99 and 8.47 ppm for the 1,2,4-triazole ring in the ^{1}H NMR spectrum. Furthermore, compound 1-(4-Fluorophenyl)-1*H*-1,2,4-triazole **3g** was further identified by X-ray crystallography as shown in Figure 3. Following the above results (Table 2 and Table 3), we assumed that 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2** were unstable and readily decarboxylated to give **3** under acidic condition and high temperature (> 125°C).

Table 3

Figure 3

To evaluate alternative ways for the synthesis of 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2**, we developed another one-pot strategy by treating 2-chloro-2-(2-arylhydrazono)acetates **1a**, **1d–g**, **1i** and **1k** with 3.0 equiv of bis(trimethylsilyl)amine [$NH(SiMe_3)_2$] in THF solution at 60°C (see Scheme 2). When the starting materials **1a**, **1d–g**, **1i** and **1k** were fully consumed as shown by TLC, the reaction mixtures were worked up with saturated aqueous $NaHCO_3$ solution to give the corresponding 2-(2-arylhydrazono)acetates **4a**, **4d–g**, **4i**, and **4k** in high crude yields (>95%, see Scheme 2).

Scheme 2

Our strategy intended to skip all the intermediate isolations. Compound **1** was treated with bis(trimethylsilyl)amine [$NH(SiMe_3)_2$] under the above reaction conditions. When the amination reaction was complete, fresh Vilsmeier reagent (2.0 mL of $HCONH_2$/3.0 equiv of $POCl_3$) [18–20] was added to the resulting solution and the mixture was heated to ~85°C for ~0.5 h. As expected, the corresponding 1-phenyl-1*H*-1,2,4-triazole-3-carboxylates **2a**, **2d–g**, **2i**, and **2k** were successfully afforded in 73–91% goods yields (see Scheme 2 and Table 4). Compared to the direct one-pot method, no decarboxylation was found with this two-step cascade strategy. However, this cascade procedure was more tedious and troublesome than the straightforward one-pot process.

Table 4

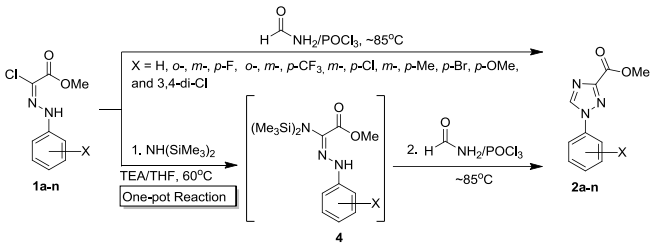
To interpret the reactivity difference between the direct method and the two-step cascade strategy in terms of formation of methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a**, we proposed a mechanism as shown in Scheme 3. Methyl 2-Chloro-2-(2-phenylhydrazono)acetate **1a** and Vilsmeier reagent belonged to the acidic species and they can be simultaneously reacted at ~85°C to give imine intermediate **5**. Subsequently, intramolecular cycloaddition reaction happened effectively under heating condition. The expected product **2a** was smoothly provided in good yields. For two-step cascade method, methyl 2-chloro-2-(2-phenylhydrazono)acetate **1a** in THF solution was reacted with bis(trimethylsilyl)amine [$NH(SiMe_3)_2$] in presence of excess amount of TEA. The amination reaction was carried out to give methyl 2-(2-phenylhydrazono)acetate **4a**. When fresh Vilsmeier reagent was added towards the resulting solution, compound **4a** was transferred into intermediate **6.** Because the protonated bis(trimethylsilyl)amino group was also a leaving group,[22] the intramolecular cyclization reaction could smoothly and gradually occur at ~85°C to obtain the desired methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate product **2a** without the detectable decarboxylated product **3a** (see Scheme 3). To prove the mechanism of two-step cascade one-pot reaction, we tried to isolate the intermediate methyl 2-(2-phenylhydrazono)acetate **4a.** Then crude intermediate **4a** was directly reacted towards Vilsmeier reagent at ~85°C. The expected result was obtained under the same reaction condition. Therefore, it provided the strong evidence for demonstrating our plausible mechanism.

Scheme 3

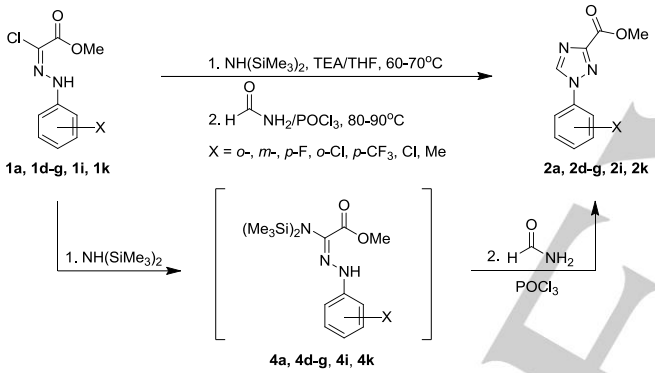
Conclusions

We have developed two simple one-pot methods for synthesis of methyl 3-carboxylate-1-aryl-1H-1,2,4-triazoles, which involved the direct one-pot reaction and two-step cascade synthetic

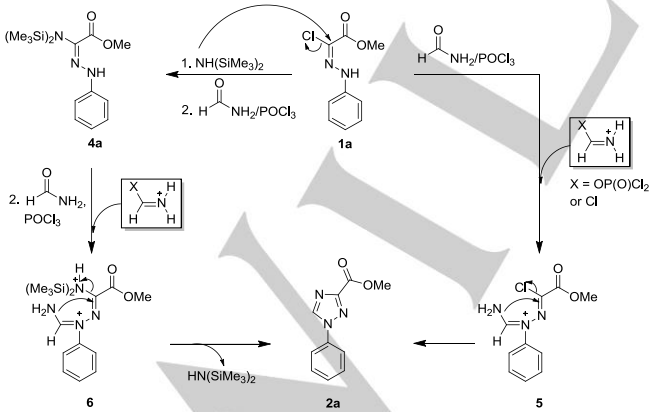
procedure. Under the normal heating condition, methyl 3-carboxylate-1-aryl-1H-1,2,4-triazoles **2** was able to be generated successfully in presence of Vilsmeier reagent and nitrilimines. Compare with these two methods, we conceived the straightforward one-pot method was more efficient and economic. On the other hand, we observed that methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2** were unstable under the high temperature (> 125°C) and gradually converted to the decarboxylated 1-aryl-1*H*-1,2,4-triazole products **3**.



Scheme 1. Two convenient and effective one-pot methods for synthesis of methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2a–n** from nitrilimines **1a–n** or **4** with Vilsmeier reagent.



Scheme 2. The new developed one-pot two-step cascade method for synthesis of methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2**.



Scheme 3. The plausible mechanism of two new developed one-pot methods for synthesis of methyl 3-carboxylate-1-aryl-1*H*-1,2,4-triazole **2a**.

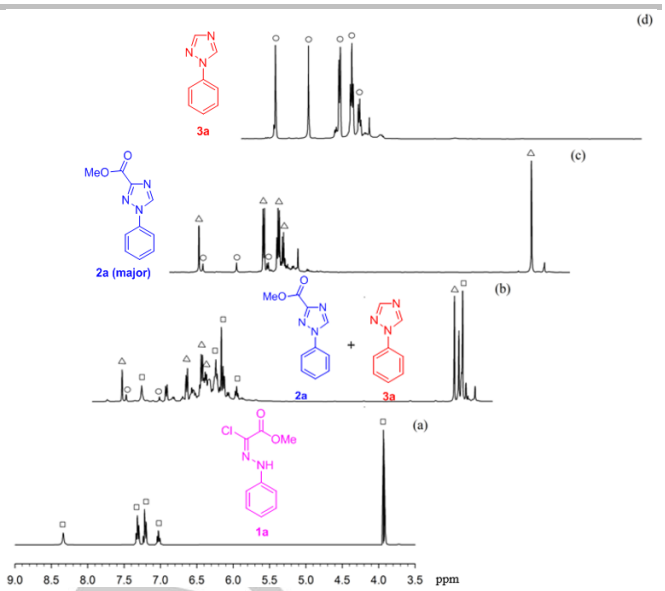


Figure 1. (a) The reaction condition started at ~25°C (□: ^{1}H NMR of the hydrazonoyl hydrochloride starting material **1a**), (b) The reaction condition was at ~55°C for 0.5 h, (c) The reaction condition was at ~85°C for 0.5 h (Δ:^{1}H NMR of 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a**), (d) The reaction condition was at ~175°C for 0.5 h (○: ^{1}H NMR of 1-phenyl-1*H*-1,2,4-triazole **3a**).

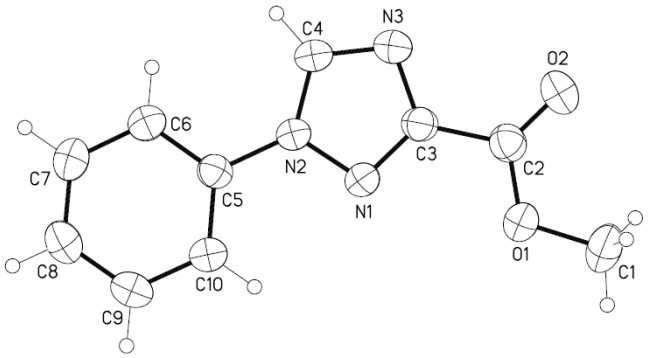


Figure 2. The ORTEP diagram of methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a** (CCDC 1865434).

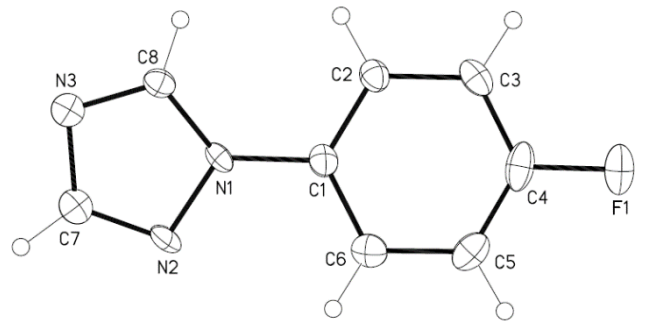
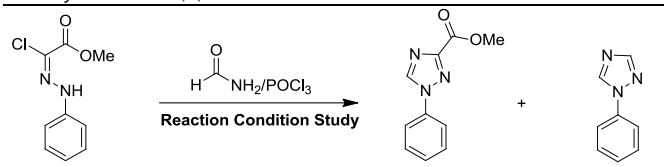


Figure 3. The ORTEP diagram of 1-(4-Fluorophenyl)-1*H*-1,2,4-triazole **3g** (CCDC 1865435).

Table 1. The reaction condition study for synthesis of 1,2,4-triazole-3-carboxylate **2a** and 1,2,4-triazole **3a**.

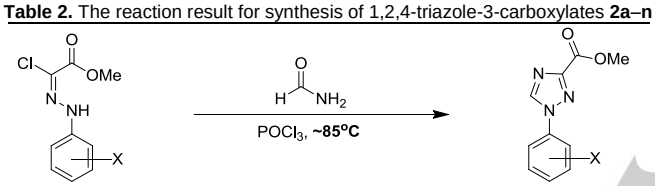


1a **2a** **3a**

Entry	Reaction temperature	Reaction Time	Yields (%)[a]	
			Compound **2a**	Compound **3a**
1	~ 25 °C	> 72 h	N/A[b]	N/A[b]
2	~ 55 °C	24 h	16	10
3	~ 75 °C	~0.5 h	72	14
4	~ 85 °C	~0.5 h	90	4
5	~ 125 °C	~0.5 h	66	33
6	~ 175 °C (at reflux)	~0.5 h	N/A	86

[a] The results were identified by the isolated yields.
[b] The starting material **1a** was recovered.

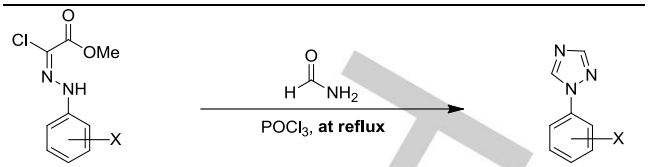
Table 2. The reaction result for synthesis of 1,2,4-triazole-3-carboxylates **2a–n**



1a-n **2a-n**

Entry	Nitrilimines		**2a–n**	Yields (%)
	1a–n	X		
1	**1a**	H	**2a**	90
2	**1b**	*o*-CF_3	**2b**	89
3	**1c**	*m*-CF_3	**2c**	91
4	**1d**	*p*-CF_3	**2d**	93
5	**1e**	*o*-F	**2e**	82
6	**1f**	*m*-F	**2f**	85
7	**1g**	*p*-F	**2g**	85
8	**1h**	*m*-Cl	**2h**	92
9	**1i**	*p*-Cl	**2i**	94
10	**1j**	*m*-Me	**2j**	95
11	**1k**	*p*-Me	**2k**	92
12	**1l**	*p*-Br	**2l**	87
13	**1m**	*p*-OMe	**2m**	95
14	**1n**	3,4-di-Cl	**2n**	88

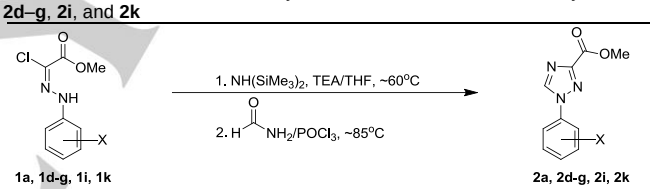
Table 3. The reaction result for synthesis of 1-aryl-1*H*-1,2,4-triazoles **3a–n**



1a-k **3a-k**

Entry	Nitrilimines		**3a–k**	Yields (%)
	1a–k	X		
1	**1a**	H	**3a**	86
2	**1b**	*o*-CF_3	**3b**	82
3	**1c**	*m*-CF_3	**3c**	87
4	**1d**	*p*-CF_3	**3d**	88
5	**1e**	*o*-F	**3e**	82
6	**1f**	*m*-F	**3f**	89
7	**1g**	*p*-F	**3g**	93
8	**1h**	*m*-Cl	**3h**	94
9	**1i**	*p*-Cl	**3i**	84
10	**1j**	*m*-Me	**3j**	83
11	**1k**	*p*-Me	**3k**	85

Table 4. The reaction result for synthesis of 1,2,4-triazole-3-carboxylates **2a**, **2d–g**, **2i**, and **2k**



1a, 1d-g, 1i, 1k **2a, 2d-g, 2i, 2k**

Entry	Nitrilimines		Compound**s 2**	Yields (%)
	1a, **1d–g**, **1i**, and **1k**	X		
1	**1a**	H	**2a**	73
2	**1d**	*o*-CF_3	**2d**	91
3	**1e**	*o*-F	**2e**	88
4	**1f**	*m*-F	**2f**	87
5	**1g**	*p*-F	**2g**	83
6	**1i**	*p*-Cl	**2i**	79
7	**1k**	*p*-Me	**2k**	86

Experimental Section

General

All chemicals were reagent grade and used as purchased except methyl 2-chloro-2-(2-arylhydrazono)acetate **1a–n** synthesized by the previously report methods.[13,21] All reactions were carried out under nitrogen atmosphere and monitored by TLC analysis. Flash column chromatography purification of compounds was carried out by gradient elution using hexanes in ethyl acetate (EA) unless otherwise stated. Commercially available reagents were used without further purification unless otherwise noted. ^{1}H NMR was recorded at 400 or 500 MHz and ^{13}C NMR recorded at 100 or 125 MHz, in $CDCl_3$. The standard abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively. Coupling constant (J), whenever discernible, have been reported in Hz. Infrared spectra (IR) were recorded as neat solutions or solids; and mass spectra were recorded using electron impact or electrospray ionization techniques. The wavenumbers reported are referenced to the polystyrene 1601 cm^{-1} absorption. High-resolution mass spectra were obtained by means of a JEOL JMS-HX110 mass spectrometer.

Method 1: Standard Procedure of the Directed One-Pot Method for Synthesis of Methyl 1-Aryl-1*H*-1,2,4-triazole-3-carboxylates 2a–n.

The reliable procedure involved the treatment of methyl 2-chloro-2-(2-phenylhydrazono)acetates (**1a–n**, 1.0 equiv), with $POCl_3$ (~3.0 equiv) in formamide solution (5 mL) at ~ 85 °C within 0.5 h. When the reaction was completed, the reaction mixture was added to water (15 mL) and extracted with dichloromethane (15 mL × 3). The combined organic layer was washed sodium bicarbonate (15 mL × 3), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue solution was purified by column chromatography on silica gel to give the corresponding methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2a–n** in 82–95% yields.

Methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate (2a). [23] The residue solution was purified by column chromatography on silica gel to give methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a** as brown solid (183 mg, 90%); mp 93–94 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.01 (s, 3H, OCH_3), 7.41–7.45 (m, 1H, ArH), 7.49–7.53 (m, 2H, ArH), 7.69–7.72 (m, 2H, ArH), 8.61 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.88, 120.51 (2 × C), 129.11, 129.86 (2 × C), 136.38, 142.20, 155.38, 160.03. IR (KBr): 2342, 1735, 1460, 1254, 1204, 1171, 758, 673 cm^{-1}. EIMS m/z: 203 (M$^+$, 91), 172 (100), 145 (52), 104 (20), 91 (58), 77 (23). HRMS calcd. for $C_{10}H_9N_3O_2$: 203.0695; found: 203.0690.

Methyl 1-[2-(trifluoromethyl)phenyl]-1H-1,2,4-triazole-3-carboxylate (2b). The residue solution was purified by column chromatography on silica gel to give methyl 1-[2-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate **2b** as brown liquid (241 mg, 89%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.98 (s, 3H, OCH_3), 7.53 (d, *J* = 7.6 Hz, 1H, ArH), 7.64–7.73 (m, 2H, ArH), 7.82 (d, *J* = 7.6 Hz, 1H, ArH), 8.37 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.86, 122.45 (q, *J* = 274.0 Hz), 126.39 (q, *J* = 32.0 Hz), 127.27 (q, *J* = 4.8 Hz), 129.23, 130.82, 133.15, 133.95, 146.16, 155.36, 159.76. IR (KBr): 3116, 2956, 1743, 1460, 1317, 1247, 1189, 1134, 1118, 815, 773, 675 cm^{-1}. EIMS m/z: 271 (M$^+$, 27), 240 (100), 213 (81), 207 (25), 172 (29), 159 (30), 145 (34). HRMS calcd. for $C_{11}H_8F_3N_3O_2$: 271.0569; found: 271.0574.

Methyl 1-[3-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate (2c). The residue solution was purified by column chromatography on silica gel to give methyl 1-[3-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate **2c** as yellow solid (247 mg, 91%); mp 146–147 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.02 (s, 3H, OCH_3), 7.65–7.72 (m, 2H, ArH), 7.94 (d, *J* = 7.6 Hz, 1H, ArH), 8.03 (s, 1H, ArH), 8.70 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.04, 117.53, 123.25 (q, *J* = 513.0 Hz), 123.45, 125.79, 130.70, 132.70 (q, *J* = 33.3 Hz), 136.78, 142.36, 155.79, 159.79. IR (KBr): 2359, 1726, 1458, 1329, 1317, 1159, 1115, 1069 cm^{-1}. EIMS m/z: 271 (M$^+$, 47), 240 (100), 213 (61), 207 (50), 172 (31), 159 (38), 145 (39). HRMS calcd. for $C_{11}H_8F_3N_3O_2$: 271.0569; found: 271.0561.

Methyl 1-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate (2d). The residue solution was purified by column chromatography on silica gel to give methyl 1-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate **2d** as light yellow solid (252 mg, 93%); mp 171–172 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.04 (s, 3H, OCH_3), 7.80 (d, *J* = 8.8 Hz, 2H, ArH), 7.90 (d, *J* = 8.4 Hz, 2H, ArH), 8.69 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.05, 120.42 (2 × C), 123.36 (q, *J* = 272.5 Hz), 123.37, 127.25 (q, *J* = 3.4 Hz) , 131.13 (q, *J* = 32.7 Hz), 138.81, 142.35, 155.85, 159.77. IR (KBr): 3105, 2359, 1721, 1341, 1155, 1112 cm^{-1}. EIMS m/z: 271 (M$^+$, 48), 240 (100), 213 (54), 172 (26), 159 (28), 145 (31). HRMS calcd. for $C_{11}H_8F_3N_3O_2$: 271.0569; found: 271.0568.

Methyl 1-(2-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2e).[24] The residue solution was purified by column chromatography on silica gel to give methyl 1-(2-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2e** as yellow solid (181 mg, 82%); mp 81–82 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.01 (s, 3H, OCH_3), 7.26–7.32 (m, 2H, ArH), 7.38–7.42 (m, 1H, ArH), 7.92 (dd, *J* = 8.0, 16.0 Hz, 1H, ArH), 8.68 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.92, 117.00 (d, *J* = 20.0 Hz), 124.66 (2 × C), 125.41 (d, *J* = 3.2 Hz), 130.26 (d, *J* = 7.9 Hz), 145.22 (d, *J* = 12.55 Hz), 153.74 (d, *J* = 250.6 Hz), 154.85, 159.89. IR (KBr): 1744, 1514, 1462, 1252, 1202, 1171, 751 cm^{-1}. EIMS m/z: 221 (M$^+$, 66), 190 (100), 163 (87), 122 (32), 109 (84), 95 (24), 83 (21). HRMS calcd. for $C_{10}H_8FN_3O_2$: 221.0601; found: 221.0608.

Methyl 1-(3-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2f). The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2f** as brown solid (188 mg, 85%); mp 144–145 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.01 (s, 3H, OCH_3), 7.11–7.16 (m, 1H, ArH), 7.45–7.53 (m, 3H, ArH), 8.63 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.97, 108.40 (d, *J* = 26.0 Hz), 115.67, 116.10 (d, *J* = 21.0 Hz), 131.36 (d, *J* = 9.0 Hz), 137.54 (d, *J* = 10.0 Hz), 142.27, 155.56, 159.84, 163.13 (d, *J* = 284.0 Hz). IR(KBr): 3132, 1727, 1606, 1471, 1274, 1218, 867, 774, 672 cm^{-1}. EIMS m/z: 221 (M$^+$, 67), 190 (100), 163 (68), 122 (29), 109 (66), 95 (41), 83 (17), 81 (17), 75 (15). HRMS calcd. for $C_{10}H_8FN_3O_2$: 221.0601; found: 221.0597.

Methyl 1-(4-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2g). The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2g** as white solid (187 mg, 85%); mp 152–153 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.02 (s, 3H, OCH_3), 7.21 (dd, *J* = 8.0, 20.0 Hz, 2H, ArH), 7.70 (dd, *J* = 4.4, 12.0 Hz, 2H, ArH), 8.56 (s, 1H, triazole-H). ^{13}C NMR (100MHz, $CDCl_3$): δ 52.94, 116.91 (d, *J* = 23.4 Hz, 2 × C), 122.63 (d, *J* = 8.7 Hz, 2 × C), 132.62, 142.28, 155.49, 159.93, 162.58 (d, *J* = 250.0 Hz). IR (KBr): 2922, 1728, 1514, 1470, 1258, 1209, 1177, 839 cm^{-1}. EIMS m/z: 221 (M$^+$, 100), 190 (100), 163 (39), 149 (39), 135 (14), 122 (32), 109 (65), 95 (34), 83 (18), 75 (13), 57 (16). HRMS calcd. for $C_{10}H_8FN_3O_2$: 221.0601; found: 221.0593.

Methyl 1-(3-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2h).[25] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2h** as yellow solid (218 mg, 92%); mp 136–137 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.01 (s, 3H, OCH_3), 7.39–7.46 (m, 2H, ArH), 7.61 (dt, *J* = 1.6, 7.5 Hz, 1H, ArH), 7.79 (t, *J* = 1.9 Hz, 1H, ArH), 8.63 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.00, 118.27, 120.79, 129.21, 130.92, 135.84, 137.19, 142.26, 155.56, 159.82. IR (KBr): 3132, 2358, 1726, 1267,

669 cm^{-1}. EIMS m/z: 239 (M^+ + 2, 24), 237 (M^+, 75), 208 (44), 207 (68), 206 (100), 182 (29), 179 (82), 151 (12), 138 (31), 133 (12), 127 (20), 125 (61), 111 (31), 105 (13), 90 (27), 75 (21), 69 (14), 63 (16). HRMS calcd. for $C_{10}H_8ClN_3O_2$: 237.0305; found: 237.0312.

Methyl 1-(4-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2i).[26] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2i** as light yellow solid (222 mg, 94%); mp 182–183 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.99 (s, 3H, OCH_3), 7.46 (dt, *J* = 2.0, 8.5, Hz, 2H, ArH), 7.67 (dt, *J* = 1.9, 8.9 Hz, 2H, ArH), 8.61 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.90, 121.63 (2 × C), 130.02 (2 × C), 134.84, 134.91, 142.19, 155.49, 159.84. IR (KBr): 2359, 1722, 1456, 1348, 1261, 1074, 887, 667 cm^{-1}. EIMS m/z: 239 (M^+ + 2, 26), 237 (M^+, 75), 208 (21), 206 (61), 195 (21), 181 (17), 179 (52), 151 (11), 138 (24), 127 (38), 125 (100), 111 (27), 99 (15), 90 (30), 75 (22), 63 (18). HRMS calcd. for $C_{10}H_8ClN_3O_2$: 237.0305; found: 237.0304.

Methyl 1-(3-methylphenyl)-1*H*-1,2,4-triazole-3-carboxylate (2j). The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-methyl phenyl)-1*H*-1,2,4-triazole-3-carboxylate **2j** as yellow solid (222 mg, 95%); mp 119–120 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.40 (s, 3H, CH_3), 4.00 (s, 3H, OCH_3), 7.22 (d, *J* = 7.6 Hz, 1H, ArH), 7.36 (t, *J* = 7.8 Hz, 1H, ArH), 7.47 (d, *J* = 8.1 Hz, 1H, ArH), 7.55 (s, 1H, ArH), 8.58 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.27, 52.83, 117.38, 121.13, 129.57, 129.81, 136.29, 140.23, 142.17, 155.25, 160.04. IR (KBr): 3121, 1724, 1464, 1267, 1207, 1173, 775, 671 cm^{-1}. EIMS m/z: 217 (M^+, 100), 186 (90), 159 (37), 118 (25), 105 (52), 104 (24), 91 (23). HRMS calcd. for $C_{11}H_{11}N_3O_2$: 217.0851; found: 217.0842.

Methyl 1-(4-methylphenyl)-1*H*-1,2,4-triazole-3-carboxylate (2k).[26] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-methyl phenyl)-1*H*-1,2,4-triazole-3-carboxylate **2k** as brown solid (222 mg, 95%); mp 151–152 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H, CH_3), 4.00 (s, 3H, OCH_3), 7.28 (d, *J* = 8.2 Hz, 2H, ArH), 7.57 (d, *J* = 8.4 Hz, 2H, ArH), 8.55 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.03, 52.80, 120.40 (2 × C), 130.32 (2 × C), 134.09, 139.31, 142.08, 155.20, 160.07. IR (KBr): 3111, 2358, 1740, 1468, 1258, 1207, 1175 cm^{-1}. EIMS m/z: 217 (M^+, 100), 186 (62), 159 (39), 118 (26) , 105 (81), 104 (20), 91 (26), 77 (22). HRMS calcd. for $C_{11}H_{11}N_3O_2$: 217.0851; found: 217.0844.

Methyl 1-(4-bromophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2l). The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-bromo phenyl)-1*H*-1,2,4-triazole-3-carboxylate **2l** as white solid (245 mg, 87%); mp 188–189 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.00 (s, 3H, OCH_3), 7.59–7.65 (m, 4H, ArH), 8.61 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.94, 121.85 (2 × C), 122.81, 133.02 (2 × C), 135.34, 142.14, 155.54, 159.85. IR (KBr): 3111, 2359, 1724, 1459, 1348, 1260 cm^{-1}. EIMS m/z: 283 (M^+ + 2, 99), 282 (12), 281 (M^+, 100), 252 (64), 250 (65), 225 (60), 223 (223), 184 (24), 182 (25), 171 (69), 169 (68), 157 (24), 155 (24), 143 (34), 116 (18), 90 (64), 76 (25), 75 (24), 63 (35). HRMS calcd. for $C_{10}H_8BrN_3O_2$: 280.9800; found: 280.9796.

Methyl 1-(4-methoxyphenyl)-1*H*-1,2,4-triazole-3-carboxylate (2m).[26] The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-methoxylphenyl)-1*H*-1,2,4-triazole-3-carboxylate **2m** as light yellow solid (221 mg, 95%); mp 134–135 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.83 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 6.99 (td, *J* = 2.2, 9.4 Hz, 2H, ArH), 7.60 (dt, *J* = 2.2, 9.1 Hz, 2H, ArH), 8.50 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.87, 55.65, 114.90 (2 × C), 122.28 (2 × C), 129.75, 142.15, 155.16, 160.10, 160.15. IR (KBr): 3121, 2922, 1738, 1520, 1482, 1252, 1204, 1171 cm^{-1}. EIMS m/z: 233 (M^+, 100), 202 (20), 121 (50). HRMS calcd. for $C_{11}H_{11}N_3O_3$: 233.0800; found: 233.0797.

Methyl 1-(3,4-dichlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2n). The residue solution was purified by column chromatography on silica gel to give methyl 1-(3,4-dichloro phenyl)-1*H*-1,2,4-triazole-3-carboxylate **2n** as light yellow solid (240 mg, 88%); mp 169–170 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.03 (s, 3H, OCH_3), 7.60 (s, 2H, ArH), 7.92 (s, 1H, ArH), 8.62 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.07, 119.24, 122.35, 131.60, 133.42, 134.35, 135.39, 142.21, 155.76, 159.72. IR (KBr): 3108, 1720, 1458, 1347, 999, 666, 437 cm^{-1}. EIMS m/z: 273 (M^+ + 2, 64), 271 (100), 244 (23), 242 (61), 240 (95), 215 (57), 213 (90), 185 (13), 174 (25), 172 (38), 161 (50), 159 (71), 149 (16), 147 (17), 145 (26), 133 (15), 126 (19), 124 (56), 109 (20), 97 (13), 59 (17). HRMS calcd. for $C_{10}H_7Cl_2N_3O_2$: 270.9915; found: 270.9922.

Method 2: Standard Procedure of the One-Pot Two-Step Cascade Method for Synthesis of Methyl 1-Aryl-1*H*-1,2,4-triazole-3-carboxylates 2a, 2d–g, 2i, and 2k.

The reliable procedure involved the treatment of 2-chloro-2-(2-phenylhydrazono)acetate (**1a**, **1d–g**, **1i**, and **1k**, 1.0 equiv) and 3.0 equivalent of triethylamine was stirred in THF solution (5 mL) at room temperature for 0.5–1 h. Consequently, aminating agent bis(trimethylsilyl)amine ($NH(SiMe_3)_2$, 3.0 equiv) was added into the resulting mixture and heated at 60 °C for 3–5 h. When the starting material **1a**, **1d–g**, **1i**, or **1k** was fully completed (monitored by TLC), the resulting mixture was added to water (15 mL) and extracted with dichloromethane (15 mL × 3). The organic extracts were washed with saturate sodium bicarbonate (15 mL × 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue solution was treated with $POCl_3$ (~3.0 equiv) in formamide solution (5 mL) at ~ 85 °C within 0.5 h. When the reaction was completed, the reaction mixture was added to water (15 mL) and extracted with dichloromethane (15 mL × 3). The combined organic layer was washed sodium bicarbonate (15 mL × 3), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue solution was purified by column chromatography on silica gel to give the corresponding methyl 1-aryl-1*H*-1,2,4-triazole-3-carboxylates **2a**, **2d–j**, **2i**, and **2k** in 73–91% yields.

Methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate (2a).[23] The residue solution was purified by column chromatography on silica gel to give methyl 1-phenyl-1*H*-1,2,4-triazole-3-carboxylate **2a** as brown solid (148 mg, 73%).

Methyl 1-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate (2d) The residue solution was purified by column chromatography on silica gel to give methyl 1-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole-3-carboxylate **2d** as light yellow solid (246 mg, 91%).

Methyl 1-(2-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2e). [24] The residue solution was purified by column chromatography on silica gel to give methyl 1-(2-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2e** as yellow solid (194 mg, 88%).

Methyl 1-(3-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2f). The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2f** as brown solid (192 mg, 87%).

Methyl 1-(4-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2g). The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-fluorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2g** as white solid (183 mg, 83%).

Methyl 1-(4-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (2i).[26] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate **2i** as light yellow solid (187 mg, 79%).

Methyl 1-(4-methylphenyl)-1*H*-1,2,4-triazole-3-carboxylate (2k).[26] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-methyl phenyl)-1*H*-1,2,4-triazole-3-carboxylate **2k** as brown solid (200 mg, 86%).

Standard Procedure of the Directed One-Pot Method for Synthesis of 1-Aryl-1*H*-1,2,4-triazoles 3a–n.

The reliable procedure involved the treatment of 2-chloro-2-(2-phenylhydrazono)acetate (**1a–n**, 1.0 mmol), with $POCl_3$ (3.0 mmol) in formamide solution (5 mL) at reflux within 0.5 h. When the reaction was completed, the reaction mixture was added to water (15 mL) and extracted with dichloromethane (15 mL × 3). The combined organic layer was washed sodium bicarbonate (15 mL × 3), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue solution was purified by column chromatography on silica gel to give the corresponding 1-aryl-1*H*-1,2,4-triazoles **3a–n** in 82–94% yields.

1-Phenyl-1*H*-1,2,4-triazole (3a). [26] The residue solution was purified by column chromatography on silica gel to give methyl 1-phenyl-1*H*-1,2,4-triazole **3a** as brown liquid (125 mg, 86%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.23–7.27 (m, 1H, ArH), 7.36 (dd, *J* = 7.6, 15.2 Hz, 2H, ArH), 7.56 (d, *J* = 8.0 Hz, 2H, ArH), 7.99 (s, 1H, triazole-H), 8.48 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.65 (2 × C), 127.81, 129.40 (2 × C), 136.67, 140.60, 152.22. IR (KBr): 3420, 3117, 1569, 1512, 1279, 1217, 1146, 758, 673 cm^{-1}. EIMS m/z: 145 (M^+, 96), 118 (21), 91 (100), 64 (19). HRMS calcd. for $C_8H_7N_3$: 145.0640; found: 145.0642.

1-[2-(Trifluoromethyl)phenyl]-1*H*-1,2,4-triazole (3b).[28] The residue solution was purified by column chromatography on silica gel to give methyl 1-[2-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole **3b** as yellow liquid (175 mg, 82%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47 (d, *J* = 8.00 Hz, 1H, ArH), 7.58–7.69 (m, 2H, ArH), 7.79 (d, *J* = 7.6 Hz, 1H, ArH), 8.07 (s, 1H, triazole-H), 8.28 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.57 (q, *J* = 273.5 Hz), 126.22 (q, *J* = 31.7 Hz), 127.22 (d, *J* = 4.9 Hz), 128.95, 130.08, 132.99, 134.69, 144.66, 152.32. IR (KBr): 1514, 1318, 1277, 1180, 1134, 1117, 1076, 1040, 772 cm^{-1}. EIMS m/z: 213 (M^+, 95), 186 (31), 159 (100), 132 (17), 109 (37). HRMS calcd. for $C_9H_6F_3N_3$: 213.0514; found: 213.0505.

1-[3-(Trifluoromethyl)phenyl]-1*H*-1,2,4-triazole (3c).[28] The residue solution was purified by column chromatography on silica gel to give methyl 1-[3-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole **3c** as brown solid (185 mg, 87%); mp 50–51 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.62–7.66 (m, 2H, ArH), 7.86–7.89 (m, 1H, ArH), 7.97 (s, 1H, ArH), 8.12 (s, 1H, triazole-H), 8.61 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.01 (q, *J* = 3.7 Hz), , 122.90, 123.31 (q, *J* = 271.1 Hz) 124.81 (q, *J* = 3.3 Hz), 130.54, 132.49 (q, *J* = 33.2 Hz), 137.34, 140.95, 152.99. IR (KBr): 1514, 1325, 1279, 1173, 1128 cm^{-1}. EIMS m/z: 213 (M^+, 100), 186 (16), 159 (84), 109 (17), 105 (60). HRMS calcd. for $C_9H_6F_3N_3$: 213.0514; found: 213.0511.

1-[4-(Trifluoromethyl)phenyl]-1*H*-1,2,4-triazole (3d).[28] The residue solution was purified by column chromatography on silica gel to give methyl 1-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole **3d** as brown solid (187 mg, 88%); mp 96–97 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.78 (dd, *J* = 32.0, 8.7 Hz, 4H, ArH), 8.1 1 (s, 1H, triazole-H), 8.62 (s, 1H, triazole-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 119.82, 123.52 (q, *J* = 338.1 Hz), 127.08, 127.12, 130.14 (q, *J* = 270.6 Hz), 139.40, 140.97, 153.03. IR (KBr): 2359, 1130, 845, 669 cm^{-1}. EIMS m/z: 213 (M^+, 88), 186 (19), 159 (100), 139 (22). HRMS calcd. for $C_8H_6FN_3$: 271.0569; found: 213.0506.

1-(2-Fluorophenyl)-1*H*-1,2,4-triazole (3e). The residue solution was purified by column chromatography on silica gel to give methyl 1-(2-fluoromethylphenyl)-1*H*-1,2,4-triazole **3e** as yellow liquid (134 mg, 82%); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.20–7.25 (m, 3H, ArH), 7.28–7.33 (m, 1H, ArH), 7.80–7.84 (m, 1H, ArH), 8.06 (s, 1H, triazole-H), 8.61 (d, 1H, *J* = 2.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 116.85, 116.69, 124.02 , 125.13 (d, *J* = 3.5 Hz), 129.06 (d, *J* = 7.9 Hz), 143.77 (d, *J* = 12.7 Hz), 151.78, 153.41 (d, *J* = 249.7 Hz). IR (KBr): 3120, 1517, 1281, 1227, 1145, 759 cm^{-1}. EIMS m/z: 163 (M^+, 88), 136 (21), 109 (100), 82 (16). HRMS calcd. for $C_8H_6FN_3$: 163.0546; found: 163.0542.

1-(3-Fluorophenyl)-1*H*-1,2,4-triazole (3f).[29] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-fluoromethylphenyl)-1*H*-1,2,4-triazole **3f** as brown solid (145 mg, 89%); mp 69–70 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.04–7.09 (m, 1H, ArH), 7.43–7.44 (m, 3H, ArH), 8.07 (s, 1H, triazole-H), 8.54 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.79 (d, *J* = 26.0 Hz), 114.91, 115.11, 131.15 (d, *J* = 8.9 Hz), 138.15 (d, *J* = 10.0 Hz), 140.88, 152.70, 163.12 (d, *J* = 246.9 Hz). IR (KBr): 3107, 1607, 1518, 866, 669 cm^{-1}. EIMS m/z: 163 (M^+, 79), 109 (100), 105 (13), 82 (16), 77 (15). HRMS calcd. for $C_8H_6FN_3$: 163.0546; found: 163.0538.

1-(4-Fluorophenyl)-1*H*-1,2,4-triazole (3g).[29] The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-fluoromethylphenyl)-1*H*-1,2,4-triazole **3g** as brown solid (151 mg, 93%); mp 73–74 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.14–7.20 (m, 2H, ArH), 7.60–7.64 (m, 2H, ArH), 8.06 (s, 1H, triazole-H), 8.47 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.56, 116.79, 121.99, 122.07, 133.24, 140.86, 152.63, 162.00 (d, *J* = 248.18 Hz). IR (KBr): 1524, 1275, 1275, 1234, 831, 675, 514 cm^{-1}. EIMS m/z: 163 (M^+, 85), 136 (16), 109 (100), 82 (16). HRMS calcd. for $C_8H_6FN_3$: 163.0546; found: 163.0541.

1-(3-Chlorophenyl)-1*H*-1,2,4-triazole (3h).[30] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-chloromethylphenyl)-1*H*-1,2,4-triazole **3h** as brown solid (168 mg, 94%); mp 82–83 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35 (d, *J* = 8.0 Hz, 1H, ArH), 7.41 (t, *J* = 8.0 Hz , 1H, ArH), 7.55 (d, *J* = 8.0 Hz, 1H, ArH), 7.71 (s, 1H, ArH), 8.08 (s, 1H, triazole-H), 8.54 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.83, 120.33, 128.23, 130.80, 135.62, 137.83, 140.88, 152.77. IR (KBr): 3094, 1599, 1514, 1493, 880, 775, 669 cm^{-1}. EIMS m/z: 181 (M^+ + 2, 26), 179 (M^+, 93), 154 (13), 152 (44), 127 (31), 125 (100), 90 (36), 75 (13), 69 (17), 63 (21). HRMS calcd. for $C_8H_6ClN_3$: 179.0250; found: 179.0257.

1-(4-Chlorophenyl)-1*H*-1,2,4-triazole (3i).[30] **T**he residue solution was purified by column chromatography on silica gel to give methyl 1-(4-chlorophenyl)-1*H*-1,2,4-triazole **3i** as brown solid (150 mg, 84%); mp 108–109 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.42–7.46 (m, 2H, ArH), 7.58–7.61 (m, 2H, ArH), 8.06 (s, 1H, triazole-H), 8.51 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.15 (2 × C), 129.87 (2 × C), 133.83, 135.44, 140.75, 152.70. IR (KBr): 2359, 1514, 1275, 824, 675 cm^{-1}. EIMS m/z: 181 (M^+ + 2, 33), 179 (M^+, 96), 152 (27), 127 (33), 125 (100), 90 (24), 75 (15), 63 (24). HRMS calcd. for $C_8H_6ClN_3$: 179.0250; found: 179.0255.

1-(3-Methylphenyl)-1*H*-1,2,4-triazole (3j).[30] The residue solution was purified by column chromatography on silica gel to give methyl 1-(3-methylphenyl)-1*H*-1,2,4-triazole **3j** as brown liquid(132 mg, 83%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.15 (d, *J* = 7.6 Hz, 1H, ArH), 7.32 (t, *J* = 7.8, 1H, ArH), 7.40 (d, *J* = 8.0 Hz, 1H, ArH), 7.45 (s, 1H, ArH), 8.04 (s, 1H, triazole-H), 8.50 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.27, 116.97, 120.63, 128.86, 129.42, 136.81, 139.91, 140.77, 152.33. IR (KBr): 3117, 1690, 1593, 1506, 1279, 1215, 1146, 783, 675 cm^{-1}. EIMS m/z: 159 (M^+, 100), 132 (17), 106 (12), 105 (80), 104 (37), 78 (17), 77 (17), 65 (11). HRMS calcd. for $C_9H_9N_3$: 159.0796; found: 159.0802.

1-(4-Methylphenyl)-1*H*-1,2,4-triazole (3k).[31] The residue solution was purified by column chromatography on silica gel to give methyl 1-(4-methylphenyl)-1*H*-1,2,4-triazole **3k** as brown solid (135 mg, 85%); mp 57–58 °C (hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.21 (d, *J* = 8.0 Hz, 2H, ArH), 7.47 (d, *J* = 8.6 Hz, 2H, ArH), 8.01 (s, 1H, triazole-H), 8.45 (s, 1H, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.81, 119.78 (2 × C), 130.03 (2 × C), 134.48, 138.03, 140.58, 152.17. IR (KBr): 3445, 1526, 1277, 812, 673 cm^{-1}. EIMS m/z: 159 (M^+, 100), 91 (59), 77 (31), 57 (39). HRMS calcd. for $C_9H_9N_3$: 159.0796; found: 159.0792.

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Keywords: 1,2,4-Triazole •Nitrilimines • Vilsmeier reagent • Amination • Heterocycles

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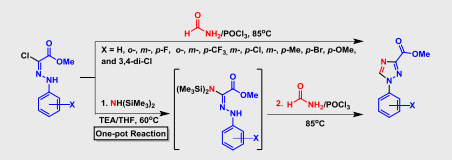
FULL PAPER

The selectively convenient one-pot methods have been developed for synthesis of 1,2,4-triazoles and methyl 1*H*-1,2,4-triazole-3-carboxylates by using hydrazonoyl hydrochlorides (nitrilimines) with Vilsmeier reagent. 2-Amino-2-(2-arylhydrazono)acetates were prepared from 2-chloro-2-(2-arylhydrazono)acetates with bis(trimethylsilyl)amine [$NH(SiMe_3)_2$] as the isolated intermediates for the further mechanistic study.



Heterocylclization*

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Facile One-Pot Synthesis of Methyl 1-Aryl-1*H*-1,2,4-triazole-3-carboxylates from Nitrilimines with Vilsmeier Reagent