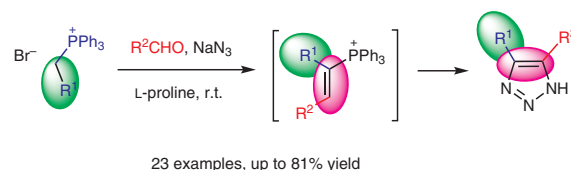


A Mild Multi-Component Reaction for the Synthesis of 4,5-Disubstituted 1*H*-1,2,3-Triazoles from Phosphonium Salts, Aldehydes, and Sodium Azide

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Received: 25.01.2018

Accepted after revision: 27.03.2018

Published online: 08.05.2018

DOI: 10.1055/s-0037-1609720; Art ID: ss-2018-h0049-op

Abstract A mild and metal-free multi-component reaction to synthesize 4,5-disubstituted 1*H*-1,2,3-triazoles from phosphonium salts, aldehydes, and sodium azide is described. The process undergoes an organocatalyzed coupling of formyl group with phosphonium to form a key intermediate, olefinic phosphonium salt, which is followed by the [3+2] cycloaddition of the azide to the activated alkene. A series of representative 4,5-disubstituted 1*H*-1,2,3-triazoles were prepared.

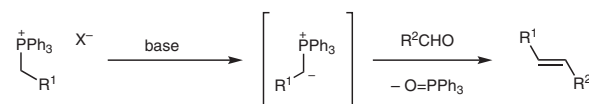
Key words phosphonium salt, triazole, organic catalyst, multicomponent reaction, cycloaddition

1,2,3-Triazoles are an important class of heterocyclic compounds, which have been widely used in organic synthesis,¹ medicinal chemistry,² and the development of new materials.³ Therefore, many methods have been developed to synthesize 1,2,3-triazoles till now.⁴ Among these developed approaches, most are for *N*-substituted 1,2,3-triazoles, and only a few are for *N*-unsubstituted 1,2,3-triazoles, which also have wide applications.⁵ Construction of 4,5-disubstituted 1*H*-1,2,3-triazoles can be achieved via a tandem three-component reaction, involving the coupling of Julia reagent,^{5h} nitroalkene,^{5e,j,k} or cyanocarbonyl compounds⁵ⁱ with aldehyde, followed by cycloaddition with sodium azide. In this paper, we report a mild method to synthesize 4,5-disubstituted 1*H*-1,2,3-triazoles by a multi-component reaction from commercially inexpensive phosphonium salts, aldehydes, and sodium azide.

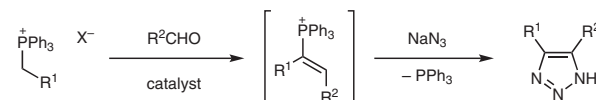
Phosphonium salts are usually deprotonated with a strong base to form phosphorus ylides, which have been studied intensively ever since the Wittig reaction became popular in the 1950s (Scheme 1)^{6a,b} including new methods for the generation of phosphorus ylides,^{6b,c,j} the synthesis of modified nucleosides,^{6d} vinyl isocyanides,^{6e} and macro-

cycles;^{6f} by-product separation,^{6g} and stereo- and regioselective olefination.^{6h,i} We envisioned that phosphonium salt could also couple with aldehyde to form olefinic phosphonium salt, which is followed by a [3+2] cycloaddition with azide to produce a triazole ring as do acrylonitriles^{5a} and α -haloacrylates (Scheme 1).^{5g}

Wittig reaction:



This work:



Scheme 1 Reactions of phosphonium salts

Olefinic sulfur salt intermediates are formed via the coupling of sulfur salts with aldehydes in the presence of *L*-proline.⁷ Thus, our initial experiment was performed with (ethoxycarbonylmethyl)triphenylphosphonium bromide (**1a**), benzaldehyde (**2a**), and NaN_3 catalyzed by *L*-proline. The mixture was stirred in DMSO solution at room temperature for 24 hours and the expected product, triazole **3a**, was obtained in a 75% isolated yield. The Wittig product **4a** was collected in an 11% yield (Table 1, entry 1). When the reaction was performed at 80 °C, the yield for the triazole product was reduced to 50%, and the yield of the by-product, olefin, increased to 25% (entry 2). Thus, high temperature does not favor triazole formation. When DMSO was replaced with EtOH, MeOH, or MeCN as the solvent, all the reactions were negative (entries 3–5). In DMF solution, the yield of the main product, triazole, was moderate (51%, en-

Table 1 Optimization of the Reaction Conditions^a

Entry	Solvent	Catalyst (mol%)	Yield of 3a (%) ^b	Yield of 4a (%) ^b
1	DMSO	Proline (10)	75	11
2 ^c	DMSO	Proline (10)	50	25
3	MeOH	Proline (10)	trace	trace
4	EtOH	Proline (10)	trace	trace
5	MeCN	Proline (10)	trace	trace
6	DMF	Proline (10)	51	15
7	THF	Proline (10)	trace	61
8	1,4-Dioxane	Proline (10)	trace	52
9	H ₂ O	Proline (10)	trace	trace
10	DMSO/H ₂ O (9:1)	Proline (10)	32	40
11	DMSO	Morpholine (10)	71	16
12	DMSO	Piperidine (10)	68	18
13	DMSO	Glycine (10)	67	15
14	DMSO	Serine (10)	71	13
15	DMSO	K ₂ CO ₃ (100)	trace	81
16	DMSO	K ₂ CO ₃ (10)	trace	13
17	DMSO	TsOH (20)	NR	NR
18	DMSO	–	NR	NR

^a Reagents and conditions: **1a** (345 mg, 0.8 mmol), PhCHO (**2a**; 128 mg, 1.2 mmol), NaN₃ (79 mg, 1.2 mmol), catalyst, and solvent (5 mL), r.t., 24 h. NR: No reaction.

^b Isolated yields.

^c The reaction was performed at 80 °C for 24 h.

try 6). In a weak polar solvent, tetrahydrofuran or 1,4-dioxane, only the olefin product was produced in a yield of 61% or 52%, respectively, which is the Wittig reaction, and was probably attributable to the insolubility of NaN₃ (entries 7 and 8). Neither triazole **3a** nor olefin **4a** was observed in the water solution (entry 9). However, in a solution of DMSO/H₂O (9:1, v/v), triazole **3a** and olefin **4a** were obtained in isolated yields of 32% and 40%, respectively (entry 10).

The catalytic activities of both morpholine and piperidine were also examined and both proved to be effective in selectively producing the triazole product **3a** in yields of 71% and 68%, respectively (Table 1, entries 11 and 12). Other amino acids like glycine and serine were also examined and good yields were observed (entries 13 and 14). Notably, the amount of L-proline or amines used in this procedure was only 10 mol% of the phosphonium salt, rather than the stoichiometric amount of a base that is usually involved in the Wittig reaction.⁸ Additionally, Wittig product **3a** was

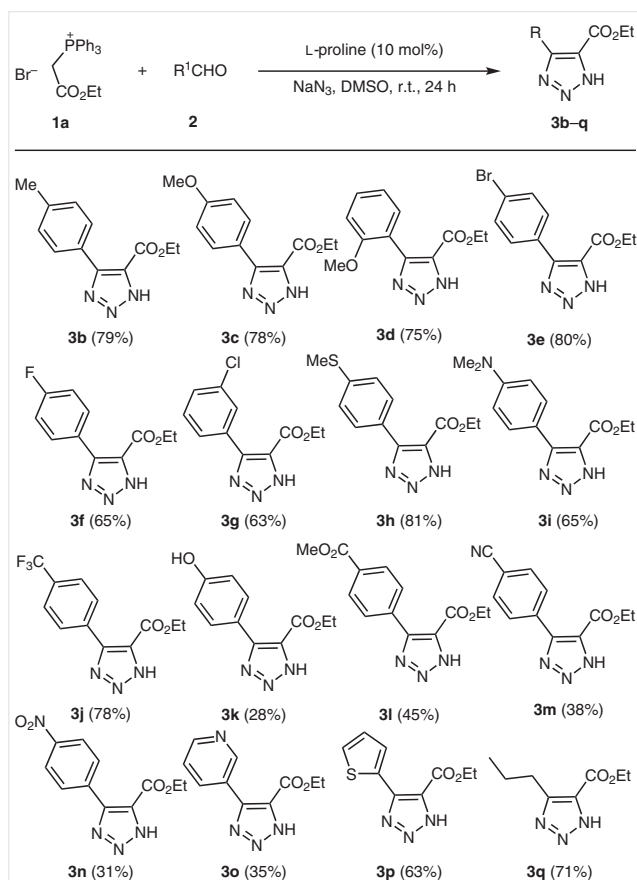
obtained in 81% and 13% yields and trace triazole product was observed when K₂CO₃ was used in 100 mol% and 10 mol%, respectively (entries 15 and 16), indicating that strong bases promote the formation of the Wittig product.⁹ *p*-Toluenesulfonic acid was unsuitable for the formation of triazole or olefins (entry 17). In the control experiment, no product was formed in the absence of L-proline or amines (entry 18).

With the optimized conditions, the scope of aldehydes in this multistep reaction was screened (Scheme 2). The results indicated that electron-donating groups (Me, MeO, MeS, or NMe₂) or weakly electron-withdrawing groups (F, Cl, Br, or CF₃) on the aromatic aldehydes favored the generation of the corresponding triazoles in yields of 63–81% (compounds **3b–j**). However, strong electron-withdrawing groups (CN, NO₂, and CO₂Me) did not favor this tandem reaction (yields: 31–45%, **3l–n**). 4,5-Disubstituted 1*H*-1,2,3-triazole **3k** containing a phenol hydroxyl group was formed in a much lower yield (28%). Compared with thiophen-2-yl aldehyde, pyridine-3-yl aldehyde gave rise to a much lower yield (yield: 35% and 63% for compounds **3o** and **3p**, respectively). Furthermore, butyraldehyde produced the corresponding triazole **3q** in a 71% yield, similar to the results for aromatic aldehydes with an electron-donating group (compounds **3a–d**).

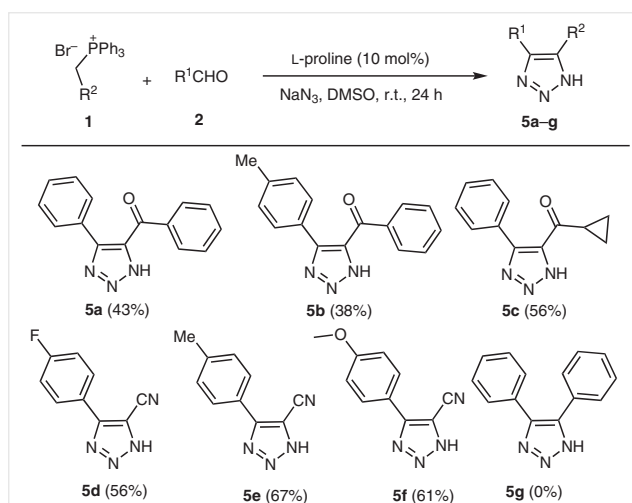
Besides the (ethoxycarbonylmethyl)triphenylphosphonium bromide (**1a**) described above, phosphonium salts prepared by the quaternization of triphenylphosphine with bromomethyl ketone compounds were also examined under mild conditions (Scheme 3). The results indicated that the electron-withdrawing phenyl ketone produced α -keto 1*H*-1,2,3-triazoles in lower yields (**5c** vs **5a** and **5b**) than the cyclopropyl bromomethyl ketone. Under similar conditions, (cyanomethyl)triphenylphosphonium bromide showed good reactivity in the formation of a few corresponding 1*H*-1,2,3-triazoles **5d–f**. (Benzyl)triphenylphosphonium bromide failed to be transformed to the corresponding triazole product **5g** possibly because of the failure in the coupling of benzaldehyde with the phosphonium salt under these mild conditions. However, acylmethyl and cyanomethylphosphonium salts can generate 4,5-disubstituted 1*H*-1,2,3-triazoles through their sequential coupling with aldehyde and NaN₃ under these mild metal-free conditions.

To clarify the mechanism, LC-MS was used to monitor the reaction of (ethoxycarbonylmethyl)triphenylphosphonium bromide (**1a**) with 4-methylthiobenzaldehyde, and NaN₃ for triazole **3h**. The mass spectrum (positive ESI) showed a peak at *m/z* = 263.1, exactly matching the calculated value for the molecular weight of protonated triphenylphosphine (C₁₈H₁₅P–H⁺, *m/z* = 263.9).¹⁰ Moreover, in the absence of NaN₃, a peak at *m/z* = 483.1 is observed, which exactly matches the calculated value for the molecular weight of the olefinic triphenylphosphonium ion **II** (C₃₀H₂₈O₂SP⁺, *m/z* = 483.1) (vide infra, Scheme 4).¹⁰ In the ³¹P NMR spectra for the by-product, a strong signal at –5.41

ppm should also be assigned to triphenylphosphine.¹⁰ Triphenylphosphine oxide, however, is a well-known by-product of the Wittig reaction.¹¹ In addition, the possibility

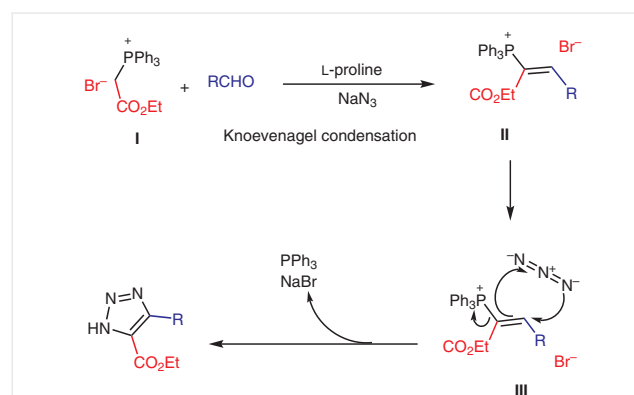


Scheme 2 Triazoles generated from various aldehydes

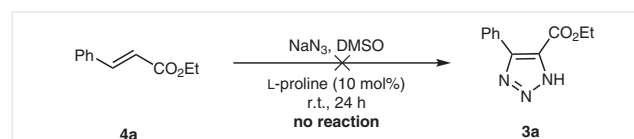


Scheme 3 Triazoles generated from various phosphonium salts and aldehydes

of the addition of azides to electron-deficient olefins like **4a** was examined by coupling ethyl cinnamate (**4a**) with sodium azide under similar conditions. A negative result was observed (Scheme 5), which indicates that **4a** is not an intermediate for triazole product but a by-product (Table 1). Accordingly, a plausible pathway for the formation of Ph_3P and the triazole product is described in Scheme 4. In the presence of L-proline and sodium azide, phosphonium salt **I** couples with protonated aldehyde to form the olefinic phosphorus salt **II**.^{12,13} A [3+2] cycloaddition between **II** and the azide anion generates the 4,5-disubstituted triazole product,¹⁴ and triphenylphosphine¹⁵ is released via the aromatization-promoted elimination.



Scheme 4 Proposed mechanism for sequentially coupling phosphonium salt with aldehyde and sodium azide



Scheme 5 No Reaction between **4a** and sodium azide

In conclusion, a multi-component reaction to construct 4,5-disubstituted 1H-1,2,3-triazoles by sequentially coupling phosphonium salts with aldehydes and azide has been developed. This method features mild and metal-free conditions. Starting from commercial and readily available reagents, it provides an easy access to diversely functionalized 4,5-disubstituted 1H-1,2,3-triazoles. Notably, the olefinic triphenylphosphonium salt was previously demonstrated to be generated via the coupling of phosphonium salts with aldehydes.

All reactions were performed under air. All reagents were used without further purification. Column chromatography was used for isolating the product and performed using 200–300 mesh silica gel with the proper solvent system according to TLC analysis using KMnO_4 stain and UV light to visualize the reaction components. NMR spectra

were recorded in CDCl₃, CD₃OD or DMSO-*d*₆, with proton and carbon resonances at 300 or 400 and 75 MHz, respectively, and are referenced to the residual solvent signal at δ = 7.28 (CDCl₃), 4.89 (CD₃OD), 2.50 ppm (DMSO-*d*₆) for ¹H and δ = 77.27 (CDCl₃), 47.82 (CD₃OD), 40.17 ppm (DMSO-*d*₆) for ¹³C. Data for ¹H are reported as follows: chemical shift (δ ppm), multiplicity (standard abbreviations), coupling constant, and integration. Data for ¹³C NMR are reported in terms of chemical shift. MS and HRMS were measured in ESI mode, and the mass analysis mode of the HRMS was TOF.

4,5-Disubstituted 1,2,3-Triazoles; Ethyl 4-Phenyl-1*H*-1,2,3-triazole-5-carboxylate (**3a**);¹⁶

Typical Procedure

To a reaction flask equipped with a magnetic stir bar was added (ethoxycarbonylmethyl)triphenylphosphonium bromide (**1a**; 345 mg, 0.8 mmol), benzaldehyde (**2a**; 128 mg, 1.2 mmol), NaN₃ (79 mg, 1.2 mmol), and L-proline (9 mg, 0.08 mmol). The mixture was dissolved in DMSO (5 mL) and stirred at r.t. for 24 h. After completion of the reaction, the mixture was poured into ice-water and extracted with EtOAc (4 × 20 mL). The combined organic layers were dried (Na₂SO₄), and the solvent was concentrated in vacuo. The residue was isolated by chromatography on silica gel with EtOAc/PE (1:2) as eluent to afford the product **3a**; yield: 131 mg (75%); white solid; mp 92–94 °C; *R*_f = 0.55 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 7.87–7.85 (m, 2 H_{arom}), 7.48–7.47 (m, 3 H_{arom}), 4.45 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 1.38 (t, 3 H, *J* = 7.1 Hz, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 161.1, 146.2, 134.1, 129.7, 129.3, 128.3, 127.7, 61.7, 14.1.

HRMS (ESI): *m/z* calcd for C₁₁H₁₂N₃O₂ [M + H]⁺: 218.0924; found: 218.0916.

Ethyl 4-(*p*-Tolyl)-1*H*-1,2,3-triazole-5-carboxylate (**3b**)^{5d}

Eluent: EtOAc/PE (1:2); yield: 185 mg (79%); white solid; mp 129–130 °C; *R*_f = 0.55 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 7.73 (d, *J* = 8.1 Hz, 2 H_{arom}), 7.16 (d, *J* = 8.1 Hz, 2 H_{arom}), 4.40 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 2.40 (s, 3 H, ArCH₃), 1.33 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 161.3, 146.2, 140.1, 134.1, 129.3, 129.3, 124.8, 61.9, 21.6, 14.3.

HRMS (ESI): *m/z* calcd for C₁₂H₁₄N₃O₂ [M + H]⁺: 232.1081; found: 232.1074.

Ethyl 4-(4-Methoxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (**3c**)¹⁷

Eluent: EtOAc/PE (1:2); yield: 133 mg (78%); white solid; mp 122–125 °C; *R*_f = 0.54 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 7.77 (d, *J* = 8.8 Hz, 2 H_{arom}), 6.92 (d, *J* = 8.9 Hz, 2 H_{arom}), 4.36 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 3.82 (s, 3 H, OCH₃), 1.30 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 161.6, 160.88, 145.3, 133.7, 130.9, 119.7, 113.9, 61.7, 55.5, 14.3.

HRMS (ESI): *m/z* calcd for C₁₂H₁₄N₃O₃ [M + H]⁺: 248.1030; found: 248.1027.

Ethyl 4-(2-Methoxyphenyl)-1*H*-1,2,3-triazole-5-carboxylate (**3d**)¹⁷

Eluent: EtOAc/PE (1:2); yield: 129 mg (75%); white solid; mp 123–125 °C; *R*_f = 0.53 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CD₃OD): δ = 7.62–7.28 (m, 2 H_{arom}), 7.28–6.82 (m, 2 H_{arom}), 4.23 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 3.77 (s, 3 H, OCH₃), 1.18 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 161.6, 157.3, 139.9, 135.7, 131.4, 131.0, 120.2, 116.3, 110.9, 60.9, 54.9, 13.2.

HRMS (ESI): *m/z* calcd for C₁₂H₁₄N₃O₃ [M + H]⁺: 248.1030; found: 248.1026.

Ethyl 4-(4-Bromophenyl)-1*H*-1,2,3-triazole-5-carboxylate (**3e**)^{5d}

Eluent: EtOAc/PE (1:2); yield: 169 mg (80%); white solid; mp 169–171 °C; *R*_f = 0.56 (PE/EtOAc 1:1).

¹H NMR (300 MHz, DMSO-*d*₆): δ = 7.74 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.68 (d, *J* = 8.6 Hz, 2 H_{arom}), 4.28 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 1.25 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, DMSO-*d*₆): δ = 161.4, 145.1, 131.9, 131.8, 131.5, 128.4, 123.4, 61.5, 14.6.

HRMS (ESI): *m/z* calcd for C₁₁H₁₁BrN₃O₂ [M + H]⁺: 296.0029, 298.0009; found: 296.0029, 298.0006.

Ethyl 4-(4-Fluorophenyl)-1*H*-1,2,3-triazole-5-carboxylate (**3f**)^{5e}

Eluent: EtOAc/PE (1:2); yield: 126 mg (65%); colorless oil; *R*_f = 0.55 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 7.91 (dd, *J*₁ = 5.6 Hz, *J*₂ = 8.4 Hz, 2 H_{arom}), 7.15–7.2 (m, 2 H_{arom}), 4.45 (q, *J* = 7.2 Hz, 2 H, OCH₂CH₃), 1.40 (t, *J* = 7.2 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 165.4 (d, *J* = 248 Hz), 161.2, 146.8, 134.2, 131.6 (d, *J* = 7.4 Hz), 124.5, 115.8 (d, *J* = 22.6 Hz), 62.2, 14.4.

HRMS (ESI): *m/z* calcd for C₁₁H₁₁FN₃O₂ [M + H]⁺: 236.0830; found: 236.0826.

Ethyl 4-(3-Chlorophenyl)-1*H*-1,2,3-triazole-5-carboxylate (**3g**)^{5e}

Eluent: EtOAc/PE (1:2); yield: 153 mg (63%); white solid; mp 101–103 °C; *R*_f = 0.56 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 7.90 (s, 1 H_{arom}), 7.81–7.70 (m, 1 H_{arom}), 7.54–7.42 (m, 2 H_{arom}), 4.39 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 1.36 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 160.8, 144.7, 133.9, 130.6, 129.7, 129.2, 129.1, 127.6, 127.5, 61.3, 13.2.

HRMS (ESI): *m/z* calcd for C₁₁H₁₁ClN₃O₂ [M + H]⁺: 252.0534; found: 252.0524.

Ethyl 4-[4-(Methylthio)phenyl]-1*H*-1,2,3-triazole-5-carboxylate (**3h**)

Eluent: EtOAc/PE (1:2); yield: 152 mg (81%); white solid; mp 118–120 °C; *R*_f = 0.51 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 7.78 (d, *J* = 8.4 Hz, 2 H_{arom}), 7.29 (d, *J* = 8.4 Hz, 2 H_{arom}), 4.40 (q, *J* = 7.1 Hz, 2 H, OCH₂CH₃), 2.51 (s, 3 H, SCH₃), 1.33 (t, *J* = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 161.3, 141.3, 129.7, 129.7, 125.8, 124.3, 124.1, 62.0, 15.5, 14.3.

HRMS (ESI): *m/z* calcd for C₁₂H₁₄N₃O₂S [M + H]⁺: 264.0801; found: 264.0793.

Ethyl 4-[4-(Dimethylamino)phenyl]-1H-1,2,3-triazole-5-carboxylate (3i)¹⁸

Eluent: EtOAc/PE (2:3); yield: 183 mg (65%); white solid; mp 124–126 °C; R_f = 0.43 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 7.68 (d, J = 8.9 Hz, 2 H_{arom}), 6.83 (d, J = 8.9 Hz, 2 H_{arom}), 4.38 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 3.04 [s, 6 H, N(CH₃)₂], 1.37 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 161.6, 151.8, 143.8, 130.0, 128.7, 113.7, 111.5, 60.9, 39.2, 13.3.

HRMS (ESI): m/z calcd for C₁₃H₁₆N₄O₂ [M + H]⁺: 261.1346; found: 261.1344.

Ethyl 4-[4-(Trifluoromethyl)phenyl]-1H-1,2,3-triazole-5-carboxylate (3j)¹⁷

Eluent: EtOAc/PE (1:2); yield: 147 mg (78%); white solid; mp 151–152 °C; R_f = 0.51 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 8.04 (d, J = 8.2 Hz, 2 H_{arom}), 7.79 (d, J = 8.2 Hz, 2 H_{arom}), 4.39 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.35 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 160.8, 145.1, 132.9, 130.7, 129.8, 126.1, 124.9 (q, J = 204 Hz), 122.5, 61.4, 13.2.

HRMS (ESI): m/z calcd for C₁₂H₁₁F₃N₃O₂ [M + H]⁺: 286.0798; found: 286.0788.

Ethyl 4-(4-Hydroxyphenyl)-1H-1,2,3-triazole-5-carboxylate (3k)¹⁷

Eluent: EtOAc/PE (1:1); yield: 106 mg (28%); white solid; mp 164–166 °C; R_f = 0.40 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 7.64 (d, J = 8.7 Hz, 2 H_{arom}), 6.90 (d, J = 8.7 Hz, 2 H_{arom}), 4.36 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.35 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 161.4, 159.1, 144.0, 130.7, 125.5, 118.0, 115.0, 61.0, 13.3.

HRMS (ESI): m/z calcd for C₁₁H₁₂N₃O₃ [M + H]⁺: 234.0873; found: 234.0867.

Ethyl 4-[4-(Methoxycarbonyl)phenyl]-1H-1,2,3-triazole-5-carboxylate (3l)¹⁷

Eluent: EtOAc/PE (1:2); yield: 107 mg (45%); white solid; mp 108–110 °C; R_f = 0.50 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 8.12 (d, J = 8.5 Hz, 2 H_{arom}), 7.95 (d, J = 8.5 Hz, 2 H_{arom}), 4.39 (d, J = 7.1 Hz, 2 H, OCH₂CH₃), 3.96 (s, 3 H, OCH₃), 1.35 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 166.7, 160.9, 145.1, 133.3, 130.6, 129.2, 129.1, 126.4, 61.4, 51.6, 13.3.

HRMS (ESI): m/z calcd for C₁₃H₁₄N₃O₄ [M + H]⁺: 276.0979; found: 276.0969.

Ethyl 4-(4-Cyanophenyl)-1H-1,2,3-triazole-5-carboxylate (3m)¹⁷

Eluent: EtOAc/PE (1:1); yield: 135 mg (38%); white solid; mp 119–122 °C; R_f = 0.47 (PE/EtOAc 1:1).

¹H NMR (301 MHz, CD₃OD): δ = 8.01 (d, J = 8.4 Hz, 2 H_{arom}), 7.79 (d, J = 8.4 Hz, 2 H_{arom}), 4.34 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.31 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 160.6, 145.2, 133.8, 132.2, 131.9, 130.0, 118.2, 112.6, 61.5, 13.2.

HRMS (ESI): m/z calcd for C₁₂H₁₁N₄O₂ [M + H]⁺: 243.0877; found: 243.0866.

Ethyl 4-(4-Nitrophenyl)-1H-1,2,3-triazole-5-carboxylate (3n)¹⁸

Eluent: EtOAc/PE (1:1); yield: 157 mg (31%); white solid; mp 178–180 °C; R_f = 0.45 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CD₃OD): δ = 8.29 (d, J = 9.0 Hz, 2 H_{arom}), 8.10 (d, J = 9.0 Hz, 2 H_{arom}), 4.37 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.34 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 160.6, 148.3, 145.1, 145.1, 135.6, 130.2, 123.1, 61.6, 13.2.

HRMS (ESI): m/z calcd for C₁₁H₁₁N₄O₄ [M + H]⁺: 263.0775; found: 263.0768.

Ethyl 4-(Pyridin-3-yl)-1H-1,2,3-triazole-5-carboxylate (3o)¹⁹

Eluent: EtOAc/PE (1:1); yield: 171 mg (35%); white solid; mp 158–160 °C; R_f = 0.48 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CD₃OD): δ = 9.61 (s, 1 H_{pyridyl}), 9.33 (d, J = 4.8 Hz, 1 H_{pyridyl}), 8.86 (d, J = 7.8 Hz, 1 H_{pyridyl}), 8.22–8.18 (m, 1 H_{pyridyl}), 4.97 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.92 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 161.2, 151.0, 150.7, 150.1, 137.3, 137.0, 125.6, 123.9, 61.6, 14.6.

HRMS (ESI): m/z calcd for C₁₀H₁₁N₄O₂ [M + H]⁺: 219.0877; found: 219.0870.

Ethyl 4-(Thiophen-2-yl)-1H-1,2,3-triazole-5-carboxylate (3p)^{5h}

Eluent: EtOAc/PE (1:2); yield: 118 mg (63%); white solid; mp 144–146 °C; R_f = 0.50 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD₃OD): δ = 7.97 (d, J = 3.8 Hz, 1 H_{thiophenyl}), 7.56 (d, J = 4.9 Hz, 1 H_{thiophenyl}), 7.14 (dd, J = 4.9, 3.8 Hz, 1 H_{thiophenyl}), 4.42 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 1.40 (t, J = 7.1 Hz, 3 H, OCH₂CH₃).

¹³C NMR (75 MHz, CD₃OD): δ = 160.8, 138.6, 136.3, 130.5, 129.5, 127.9, 127.3, 61.4, 13.3.

HRMS (ESI): m/z calcd for C₉H₁₀N₃O₂S [M + H]⁺: 224.0488; found: 224.0482.

Ethyl 4-Propyl-1H-1,2,3-triazole-5-carboxylate (3q)²⁰

Eluent: EtOAc/PE (1:1); yield: 104 mg (71%); white solid; mp 93–95 °C; R_f = 0.46 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 4.41 (q, J = 7.1 Hz, 2 H, OCH₂CH₃), 3.04 (t, J = 7.5 Hz, 2 H, CH₂CH₂CH₃), 1.79–1.67 (m, 2 H, CH₂CH₂CH₃), 1.35 (t, J = 7.1 Hz, 3 H, OCH₂CH₃), 0.94 (t, J = 7.4 Hz, 3 H, CH₂CH₂CH₃).

¹³C NMR (75 MHz, CDCl₃): δ = 161.9, 146.3, 135.2, 61.4, 26.2, 22.4, 14.4, 13.9.

HRMS (ESI): m/z calcd for C₈H₁₄N₃O₂ [M + H]⁺: 184.1081; found: 184.1077.

Phenyl(4-phenyl-1H-1,2,3-triazol-5-yl)methanone (5a)²¹

Eluent: EtOAc/PE (1:3); yield: 162 mg (43%); white solid; mp 117–120 °C; R_f = 0.62 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl₃): δ = 8.34–7.97 (m, 2 H_{arom}), 7.97–6.94 (m, 8 H_{arom}).

¹³C NMR (75 MHz, CDCl₃): δ = 188.4, 171.6, 146.2, 133.8, 130.8, 130.4, 130.0, 129.1, 128.8, 128.7, 128.6.

HRMS (ESI): m/z calcd for C₁₅H₁₂N₃O [M + H]⁺: 250.0975; found: 250.0963.

Phenyl[4-(*p*-tolyl)-1*H*-1,2,3-triazol-5-yl]methanone (5b)²²

Eluent: EtOAc/PE (1:3); yield: 149 mg (38%); white solid; mp 138–140 °C; R_f = 0.62 (PE/EtOAc 1:1).

¹H NMR (300 MHz, DMSO-*d*₆): δ = 8.11 (d, J = 7.6 Hz, 2 H_{arom}), 7.67–7.59 (m, 3 H_{arom}), 7.48 (t, J = 7.6 Hz, 2 H_{arom}), 7.22 (d, J = 7.9 Hz, 2 H_{arom}), 2.39 (s, 3 H, ArCH_3).

¹³C NMR (75 MHz, DMSO-*d*₆): δ = 188.5, 145.1, 141.3, 139.7, 137.9, 133.9, 130.8, 129.7, 129.1, 125.9.

HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{14}\text{N}_3\text{O}$ [$M + H$]⁺: 264.1131; found: 264.1130.

Cyclopropyl(4-phenyl-1*H*-1,2,3-triazol-5-yl)methanone (5c)

Eluent: EtOAc/PE (1:2). Yield: 120 mg (56%); white solid; mp 113–116 °C; R_f = 0.59 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CDCl_3): δ = 7.82–7.54 (m, 2 H_{arom}), 7.54–7.19 (m, 3 H_{arom}), 3.08–3.01 (m, 1 H, CH), 1.24–1.23 (m, 2 H, CH_2), 1.05–1.01 (m, 2 H, CH_2).

¹³C NMR (75 MHz, CDCl_3): δ = 195.9, 144.1, 141.8, 133.9, 130.4, 130.1, 129.4, 128.6, 127.5, 29.9, 19.5, 12.9.

HRMS (ESI): m/z calcd for $\text{C}_{12}\text{H}_{12}\text{N}_3\text{O}$ [$M + H$]⁺: 214.0975; found: 214.0968.

4-(4-Fluorophenyl)-1*H*-1,2,3-triazole-5-carbonitrile (5d)²³

Eluent: EtOAc/PE (1:1); yield: 163 mg (56%); white solid; mp 190–192 °C; R_f = 0.37 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CD_3OD): δ = 7.97 (dd, J_1 = 6.8 Hz, J_2 = 11.6 Hz, 2 H_{arom}), 7.41–7.15 (m, 2 H_{arom}).

¹³C NMR (75 MHz, CD_3OD): δ = 165.7 (d, J = 247.6 Hz), 147.1, 129.1 (d, J = 8.6 Hz), 123.4, 116.9, 116.3 (d, J = 22.2 Hz), 112.7.

HRMS (ESI): m/z calcd for $\text{C}_9\text{H}_6\text{FN}_4$ [$M + H$]⁺: 189.0571; found: 189.0565.

Spectral data match with those previously reported in the literature.¹⁴

4-(*p*-Tolyl)-1*H*-1,2,3-triazole-5-carbonitrile (5e)²³

Eluent: EtOAc/PE (1:1); yield: 133 mg (67%); white solid; mp 173–175 °C; R_f = 0.38 (PE/EtOAc 1:1).

¹H NMR (400 MHz, CD_3OD): δ = 7.81 (d, J = 8.2 Hz, 2 H_{arom}), 7.38 (d, J = 8.0 Hz, 2 H_{arom}), 2.43 (s, 3 H, ArCH_3).

¹³C NMR (75 MHz, CD_3OD): δ = 147.0, 141.0, 130.0, 126.5, 123.3, 116.5, 112.9, 20.2.

HRMS (ESI): m/z calcd for $\text{C}_{10}\text{H}_9\text{N}_4$ [$M + H$]⁺: 185.0822; found: 185.0813.

4-(4-Methoxyphenyl)-1*H*-1,2,3-triazole-5-carbonitrile (5f)²³

Eluent: EtOAc/PE (1:1); yield: 166 mg (61%); white solid; mp 197–200 °C; R_f = 0.33 (PE/EtOAc 1:1).

¹H NMR (300 MHz, CD_3OD): δ = 7.85 (d, J = 8.8 Hz, 2 H_{arom}), 7.09 (d, J = 8.9 Hz, 2 H_{arom}), 3.86 (s, 3 H, OCH_3).

¹³C NMR (75 MHz, CD_3OD): δ = 161.8, 128.2, 118.3, 116.1, 114.6, 113.0, 89.8, 54.8.

HRMS (ESI): m/z calcd for $\text{C}_{10}\text{H}_9\text{N}_4\text{O}$ [$M + H$]⁺: 201.0771; found: 201.0775.

Funding Information

This work was financially supported by the National Science Foundation of China (Grant No. 21172019).

Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0037-1609720>.

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