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Palladium-Catalyzed Ortho-Alkoxylation of 2-Aryl-1,2,3-Triazoles

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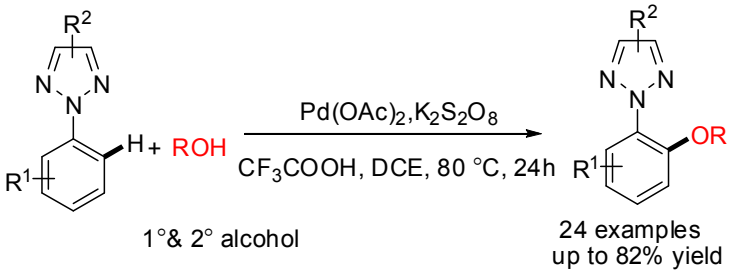


Palladium-catalyzed alkoxylation of 2-aryl-1,2,3-triazoles was described in the presence of various groups in the aromatic rings. In additiaon, some other directing groups of heterocycles containing nitrogen were explored.

INTRODUCTION

Transition-metal-catalyzed C–H functionalization has become a highly efficient and applicable method for the synthesis of natural and unnatural compounds.[1] However, the development of metal-catalyzed methods for direct conversion of C–H bond into C–O bond remains a tremendous challenge in elaborating complex organic structure,[2] because of the electronegativity of the oxygen element as well as the metal-ligand bond strength.[3] As important structural motifs, ethers are omnipresent in complex and biologically active compounds.[4] Traditionally, ethers are formed *via* acid-catalyzed condensation of alcohols, coupling of alkoxides and alkyl halides (Williamson synthesis), and alkoxymercuration/demercuration of alkenes. More recently, various strategies for the synthesis of aryl alkyl ethers have been reported.[5,6] All of these strategies are appealing, but each one has its

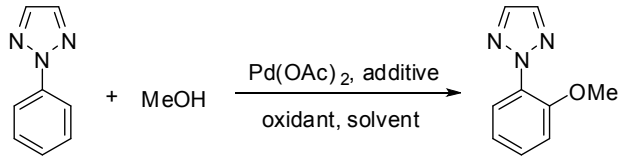
shortcomings, such as limited substrate range, multi-step reaction, significant formation of byproducts, and so on. Therefore, developing novel method for the preparation of ethers become an important and challenging task. Sanford[7] and Yu[8] have reported palladium-catalyzed directed *ortho*-alkoxylation of the C(sp^2)–H bonds, and these works addressed some of the challenges. Despite the achievement of C–H oxygenation,[9] C–H alkoxylation still reactions remain relatively scarce.

1,2,3-triazole, due to its special chemical and medicinal properties, has been widely applied in pharmaceutical , bulk, and fine chemical industries over the past decades.[10] Recently, we have reported the *ortho*-acylation and halogenation of 2-aryl-1,2,3-triazoles.[11] Motivated by our interest in the C–H bond activation, we explore C–H functionalization with the assistance of 1,2,3-triazole. Herein, we describe an efficient and selective method for the palladium-catalyzed alkoxylation of 2-aryl-1,2,3-triazole at the *ortho*-position of the N^2-arene using alcohols as alkoxylated reagents.

RESULTS AND DISCUSSION

Alcohols can be used as solvent in palladium-catalyzed C–H bond functionalization.[7a,7b,9c,12] Therefore, we performed the reaction of 2-phenyl-1,2,3-triazole **1a** with 10 mol% of $Pd(OAc)_2$ and 4 equiv of $K_2S_2O_8$ in methanol placed in a sealed tube, as shown in Table 1. To our delight, the desired compound **3a** was identified with a 45% yield after stirring for 24 h at 80 °C (Entry 1). The alkoxylation did not proceed at all in the absence of palladium catalyst. The reduction of palladium(II) by the alcohol solvent lead to the irreversible formation of palladium black.[7b,9c] To improve the yield, we reduced the amount of methanol to 25 equiv and added other solvents including dioxane, 1,2-dichloroethane (DCE), *N*,*N*-dimethylformamide (DMF), acetonitrile, dichloromethane (DCM) and *p*-xylene (Entry 2-7). DCE gave the best result among these common solvents to afford 55% yield (Entry 3). However, when 10 equiv methanol was used in DCE, the yield was reduced to 43% (Entry 8).

Table 1. Optimization of Alkoxylation Reaction Conditions[a]



1a 2a 3a

entry	solvent	oxidant (equiv)	additive (equiv)	alcohol (equiv)	yield (%)
1	methanol	$K_2S_2O_8$ (4.0)	0		45
2	dioxane	$K_2S_2O_8$ (4.0)	0	25	40
3	DCE	$K_2S_2O_8$ (4.0)	0	25	55
4	DMF	$K_2S_2O_8$ (4.0)	0	25	trace
5	CH_3CN	$K_2S_2O_8$ (4.0)	0	25	trace
6	DCM	$K_2S_2O_8$ (4.0)	0	25	42
7	p-xylene	$K_2S_2O_8$ (4.0)	0	25	34
8	DCE	$K_2S_2O_8$ (4.0)	0	10	43
9	DCE	$PhI(OAc)_2$ (4.0)	0	25	35
10	DCE	TBHP (4.0)	0	25	10
11	DCE	O_2(1 atm)	0	25	trace
12	DCE	$Cu(OAc)_2$ (4.0)	0	25	trace
13	**DCE**	**$K_2S_2O_8$ (4.0)**	**CF_3COOH(0.5)**	**25**	**67**
14	DCE	$K_2S_2O_8$ (4.0)	CF_3SO_3H(0.5)	25	45
15	DCE	$K_2S_2O_8$ (4.0)	CH_3SO_3H(0.5)	25	38
16[c]	DCE	$K_2S_2O_8$ (4.0)	CF_3COOH(0.5)	25	23
17[d]	DCE	$K_2S_2O_8$ (4.0)	CF_3COOH(0.5)	25	52
18	DCE	$K_2S_2O_8$ (4.0)	CF_3COOH(1.0)	25	54
19	DCE	$K_2S_2O_8$ (4.0)	CF_3COOH(0.2)	25	62

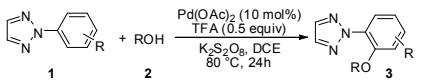
[a] Reaction conditions: 1a (0.3 mmol), $Pd(OAc)_2$ (10 mol%), oxidant (1.2 mmol) and solvent(2.0 mL) at 80 ° C for 24 h. [b] Yield of isolated product. [c] The reactions were carried out at 100 °C for 24 h. [d] The reactions were carried out at 60 °C for 24h.

Changing the oxidant to $PhI(OAc)_2$, *tert*-butyl hydroperoxide (TBHP), O_2 (1 atm) and $Cu(OAc)_2$, we found these oxidants were substantially less effective (Entry 9-12). In the previous studies, some additives brought important effects on C-H bond activation reaction. When 0.5 equiv of CF_3COOH was added, the yield was improved to 67% (Entry 13). Nevertheless, the stronger organic acids CH_3SO_3H and CF_3SO_3H, which have significant effects on palladium-catalyzed C–H bond activation reaction,[13]

failed to improve the yield under our catalytic conditions (Entries 14 and 15). However, the yield was not improved, even we adjusted the temperature (Entries 16 and 17). Similarly, the yield was still not improved when 1.0 equiv or 0.2 equiv of CF_3COOH were added, respectively (Entry 18 and 19).

With the optimal conditions in hand (Table 1, entry 13), we then explored other 2-aryl-1,2,3-triazole **1** and alcohol **2** to examine the scope of the current reaction, as shown in Table 2. A variety of 2-aryl-1,2,3-triazoles could be coupled with primary and secondary alcohols, and for most cases, the alkoxylated products were obtained in moderate yields. The results generally showed that substrates with electron-donating groups gave higher yield than those with electron-withdrawing groups (Entries 2-7). Furthermore, functional groups such as aryl halide, ester, ether and ketone were tolerated under the oxidizing reaction conditions. Subsrates with a *meta*-substituent on the phenyl ring was more efficient than those with a *para*-substituent (Entry 8 vs 4). Other primary alcohols, including EtOH, *n*-BuOH and $HO(CH_2)_2OH$, were applied to afford the correspondly alkoxylated products with 39% to 67% yields (Entries 10-13). The results indicated that alcohols with linear chains gave high yields (Entry 1 vs 10, 12). It was worth noting that for the 2-(naphthalen-1-yl)-1,2,3-triazole, methoxylation occurred on 8-position instead of the 2-position (Entry 9). The reason may be that a cyclopalladated intermediate formed with the carbon atom on 8-position is more stable than on 2-position. *Ortho*-substitution on phenyl rings is known to hinder the *ortho*-C–H bond insertions in Palladium-catalyzed C–H activation.[14] However, the subsrate with *ortho*-Me substituent did not display the "*ortho*-substituent" effect, and in contrast, gave a high yield (Entries 2, 11, 15). This phenomenon also occured in other C–H funtionalization,[9a] and the exact reason is still unclear. Moreover, the secondary alcohol *i*-PrOH could aslo react with a variety of 2-aryl-1,2,3-triazoles in yield of 52%-82% (Entries 14-17).

Table 2. Direct Alkoxylation of 1,2,3-Triazole[a]

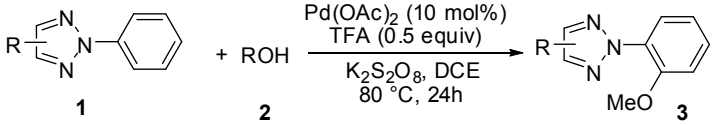


Entry	1	ROH (2)	Product (3)	Yield of 3 (%)[b]
1	1a	MeOH 2a	3a	65
2	1b	MeOH 2a	3b	77
3	1c	MeOH 2a	3c	62
4	1d	MeOH 2a	3d	57
5	1e	MeOH 2a	3e	54
6	1f	MeOH 2a	3f	45
7	1g	MeOH 2a	3g	58
8	1h	MeOH 2a	3h	68
9	1i	MeOH 2a	3i	75
10	1a	EtOH 2b	3j	61
11	1b	EtOH 2b	3k	67
12	1a	*n*-BuOH 2c	3l	39
13	1a	$HO(CH_2)_2OH$ 2d	3m	44
14	1a	*i*-PrOH 2e	3n	64
15	1b	*i*-PrOH 2e	3o	82
16	1c	*i*-PrOH 2e	3p	60
17	1e	*i*-PrOH 2e	3q	52
18	1j	*c*-PenOH[c] 2f	3r	71
19	1b	*c*-HexOH[c] 2g	3s	74
20	1a	Benzyl alcohol[d] 2h	3t	35

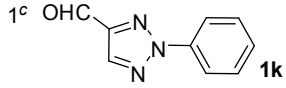
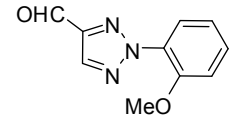
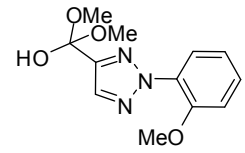
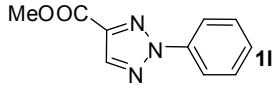
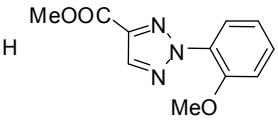
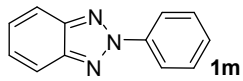
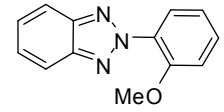
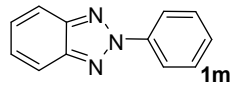
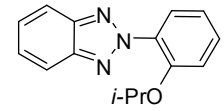
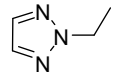
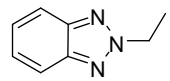
[a] Reaction conditions: 1a (0.5 mmol), alcohol (12.5 mmol), $Pd(OAc)_2$ (10 mol%), $K_2S_2O_8$ (2 mmol), CF_3COOH(0.5 equiv) in DCE (3.0 mL) at 80 °C for 24h. [b] Yield of isolated product. [c] 10 equiv of alcohol was used. [d] 5 equiv of alcohol was used.

When other secondary alcohols such as cyclopentanol and cyclohexanol were used, the alkoxylation could also proceed smoothly with 71% and 74% yield, respectively (Entries 18 and 19). Benzyl alcohol can be employed to gave corresponding product with a low yield of 38% with the generation of benzaldehyde (Entry 20). However, the reaction did not take place when *t*-BuOH and phenol were used. It was noted that none or trace dialkoxylated product was observed under the reaction conditions. The reason for the low yields of some products was that the starting material could not be consumed completely even after longer reaction time.

Table 3. Direct Alkoxylation of Further SubstitutedTriazole Units [a]



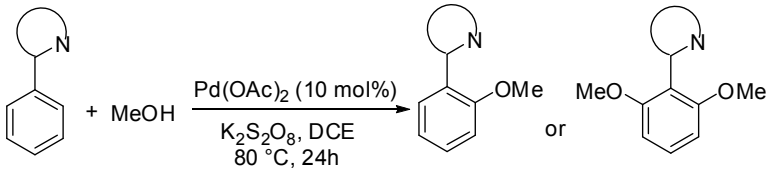
1 2 3

Entry	1	ROH (2)	Product (3)	Yield of 3 (%)[b]
1[c]	 1k	MeOH 2a	 3ua	38
			 3ub	40
2	 1l	MeOH 2a	 3v	60
3	 1m	MeOH 2a	 3w	62
4	 1m	*i*-PrOH 2e	 3x	58
5		MeOH 2a	no	
6		MeOH 2a	no	

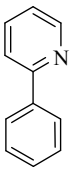
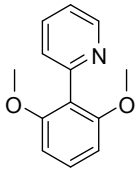
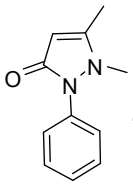
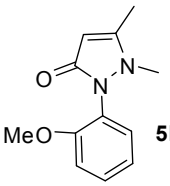
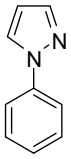
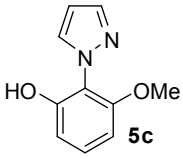
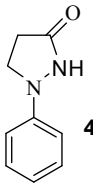
[a] Reaction conditions: 1a (0.5 mmol), alcohol (12.5 mmol), $Pd(OAc)_2$ (10 mol%), $K_2S_2O_8$(2 mmol),TFA(0.5 equiv) in DCE (3.0 mL) at 80 °C for 24h. [b] Yield of isolated product. [c] No TFA was used.

Inspired by the promising results above, we then focused on the directing effect of further substituted triazole units. We performed the reactions of 2-phenyl-1,2,3-triazoles bearing substitution on the heteroarene, i.e., -CHO (**1k**), –COOMe (**1l**) and phenyl (**1m**) with MeOH and *i*-PrOH in Table 3. The results generally showed that the electronic property of the substituents on the heteroarene of 2-ary-1,2,3-triazoles had no obvious effect on the reaction efficiency (Entries 2 and 3). Substrate **1k** gave the alkoxylated product accompanied by the generation of **3ub** due to the chemical activity of aldehyde (Entry 1). However, when 2-ethyl-1,2,3-triazole and 2-ethyl-1,2,3-benzotriazole were used, no alkoxylated products were observed (Entries 5 and 6).

Table 4. Different Directing Groups[a]



4 **2a** **5**

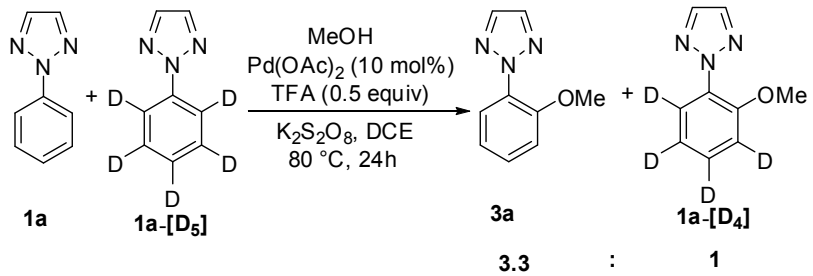
Entry	**4**	MeOH (**2**)	Product (**5**)	Yield of **5** (%)[b]
1	 **4a**	MeOH **2a**	 **5a**	88%
2	 **4b**	MeOH **2a**	 **5b**	45%
3	 **4c**	MeOH **2a**	 **5c**	42%
4	 **4d**	MeOH **2a**	none	

[a] Reaction conditions: 1a (0.5 mmol), alcohol (12.5 mmol), $Pd(OAc)_2$ (10 mol%), $K_2S_2O_8$ (2 mmol) in DCE (3.0 mL) at 80 °C for 24h. [b] Yield of isolated product. [c] The reaction temperatureo was 105 °C.

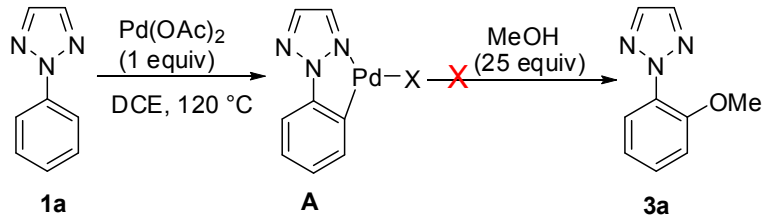
With the optimized conditions in hand, we investigated the directing effect of other heterocycle containing nitrogen in Table 4. For pyridine as the directing group, the dimethoxylated product was obtainded with a 80% yield after 24 h (Entry 1). While for pyrazolone, monomethoxylated product was identified with a lower yield of 45% under identical reaction condition (Entry 2). Interesting, for pyrazole, when the reaction temperature was improved to 105 °C, alkoxylation and hydroxylation both took place (Entry 3). However, other directing group 4d failed to gave the alkoxylated products (entry 4). The reacton conditions were compatible to these chemically active functional groups, which enhanced its practicability in synthesis.

Next, to obtain insight into the reaction mechanism, we conducted kinetic isotope effect (KIE) studies (Scheme 1). As shown in Scheme 1, the KIE was observed to be 3.3, indicating that the C–H bond cleavage at the *ortho*-position of 2-aryl-1,2,3-triazole is most likely involved with the rate-limiting step. We performed additional experiments without $K_2S_2O_8$. In this reaction, **1a** (1 equiv.), $Pd(OAc)_2$ (1 equiv.) and DCE (3 mL) were added in the tube. The reaction mixture was stirred for 10 h, leading the formation of potential intermediate **A**. Then MeOH was added in the tube. After 20 h, we did not find **3a** (Scheme 2). Therefore we can conclude that the mechanism possibily involve a palladium(II)/palladium(IV) pathway in this alkoxylation reaction, but not the palladium(II)/ palladium(0) pathway.

Scheme 1. Intermolecular Kinetic Isotope Effect

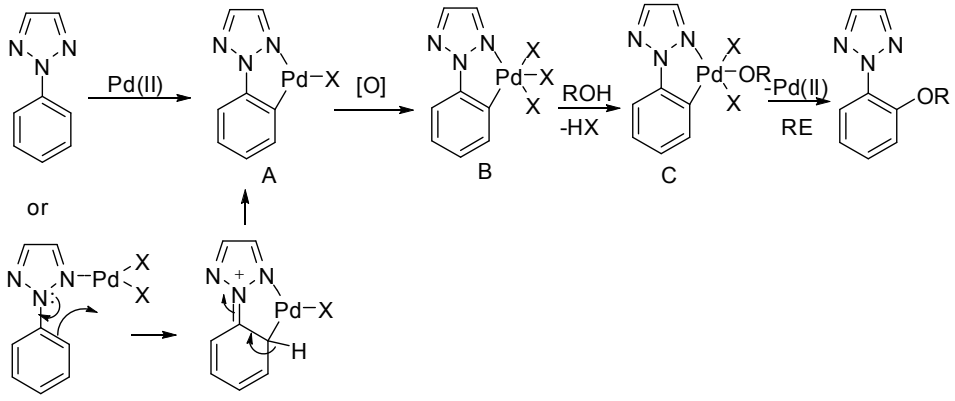


Scheme 2. Formation of Palladacycle A and Attempted Formation of 3a



Although the details of the mechanism of this alkoxylation reaction remain to be elucidated, a possible is outlined based on earlier literature[7,8,9,15] and our preliminary studies(Scheme 3). First, the coordination of nitrogen atom in 1,2,3-triazole **1** with palladium(II) species triggers cyclopalladation to form intermediate A. Next, palladium(II) intermediate was oxidized to palladium(IV) intermediate B by $K_2S_2O_8$[16], which then undergoes ligand exchange to form C. Reductive elimination of C gives the alkoxylated product **3** accompanied by the regeneration of palladium(II) catalyst. There may be another pathway for the formation of intermediate **A** because the 2-(1,2,3-triazole) group is a strong electron-donating group.[17] The first step involves the chelation of palladium with nitrogen atom in 1,2,3-triazole, followed by the intramolecular electronic rearrangement. After two rearrangements, intermediate A is formed. However, the meta-EWG-substituted substrate, which does not form resonance structure, gave a better yield (Tabble 2, entry 8). It should be noted that the bimetallic palladium(II))/palladium(III) pathway could not be excluded.[18]

Scheme 3. Possible Mechanism for the Pd-Catalyzed Alkoxylation Reaction



CONCLUSION

In conclusion, we have described the direct alkoxylation of 2-aryl-1,2,3-triazole with primary and secondary alcohols. The reaction exhibited broad functional group tolerance and was complementary to the previous methods for the synthesis of 1,2,3-triazole derivatives. Some other directing groups of heterocycles containing nitrogen were explored. Further investigations on the mechanism are still in progress.

Experimental Section

General Information

All commercially available reagents and solvent were obtained from the commercial providers and used without further purification. 2-aryl-1,2,3-triazoles **1** were prepared according to known procedures[19].

General procedure for the synthesis of 2-aryl-1,2,3-triazoles:

A reaction mixture containing aryl halide (1.0 eq.), 1,2,3-triazole (1.2 eq.), CuO (0.1 eq.), $Fe(acac)_3$ (0.3 eq.), Cs_2CO_3 (2 eq.) was stirred in DMF in a flask at 100 °C for 24 h under air. After cooling to room temperature, the mixture was diluted with ethyl acetate and washed with water. Organic layers were gathered, dried over Na_2SO_4, filtered and concentrated in vacuum to yield the crude product. The resulting residue was purified on silica gel chromatography to give the starting materials.

General procedure for the alkoxylation of 2-substituted 1,2,3-triazoles: A mixture of 2-substituted 1,2,3-Triazole 1 (0.5 mmol), alcohol 2 (12.5 mmol), $Pd(OAc)_2$ (0.05 mmol), $K_2S_2O_8$(2 mmol) and CF_3COOH (0.5 equiv) in DCE (3.0 mL) was stirred at 80 °C for 24h in sealed tube. The mixture was diluted with CH_2Cl_2 (15 mL) and washed with water (10 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by using a preparative silica gel TLC to give the products **3**.

Determination of intermolecular kinetic isotope effect: MeOH (400mg, 12.5 mmol) was added to an oven-dried, sealed tube charged with 2-phenyl-2H-1,2,3-triazole (1a) (36 mg, 0.25 mmol), 2-phenyl-*d5*-2H-1,2,3-triazole (1a-*d5*) (38 mg, 0.25 mmol), $Pd(OAc)_2$ (11mg, 0.05 mmol), TFA (28mg, 0.25 mmol) and $K_2S_2O_8$ (538 mg, 2 mmol) in DCE (3 mL). The reaction mixture was stirred at 80 ^oC for 24 h. The mixture was cooled to room temperature. The mixture was diluted with CH_2Cl_2 (15 mL) and filtered. The solvent was then evaporated under vacuum. The resulting residue was purified by using a preparative silica gel TLC to yield product. The ratio of 3a / 3a-[D4] was determined to be 2.00 / 0.61 (KIE = 3.3) by ^1H NMR spectroscopy.

Compounds **5a**[20] has been previously reported, and its identities were confirmed by comparison of their spectral data with reported ones.

2-phenyl-2H-1,2,3-triazole (1a)[11b] **:** ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.8 Hz, 2H), 7.84 (s, 2H), 7.51 (t, *J* = 7.9 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H).

2-phenyl-*d5*-2H-1,2,3-triazole (1a-*d5*): ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 2H).

2-o-tolyl-2H-1,2,3-triazole (1b)[21]**:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.55 (d, *J* = 6.9 Hz, 1H), 7.37 – 7.28 (m, 3H), 2.35 (s, 3H).

2-(4-methoxyphenyl)-2H-1,2,3-triazole (1c)[11b]**:** ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 9.1 Hz, 2H), 7.77 (s, 2H), 6.99 (d, *J* = 9.1 Hz, 2H), 3.85 (s, 3H).

Methyl 4-(2H-1,2,3-triazol-2-yl)benzoate (1d)[22]**:** ^1H NMR (400 MHz, CDCl3) δ 8.22-8.13 (m, 4H), 7.86 (s, 2H), 3.95 (s, 3H).

2-(4-chlorophenyl)-2H-1,2,3-triazole (1e)[11a]: ^1H NMR (400MHz, $CDCl_3$) δ 8.03 (d, J = 8.9 Hz, 2H), 7.81 (s, 2H), 7.45 (d, J = 8.9 Hz, 2H).

2-(4-(trifluoromethyl)phenyl)-2H-1,2,3-triazole (1f)[11a]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.5 Hz, 2H), 7.85 (s, 2H), 7.75 (d, *J* = 8.6 Hz, 2H).

1-(4-(2H-1,2,3-triazol-2-yl)phenyl)ethanone (1g)[11b]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.85 (s, 2H), 2.63 (s, 3H).

Methyl 3-(2*H*-1,2,3-triazole-2-yl)benzoate (1h)[11b]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.31 (dd, *J* = 8.1, 1.1 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.87 (s, 2H), 7.60 (t, *J* = 8.0 Hz, 1H), 3.99 (s, 3H).

2-(1-naphthaleneyl)-2H-1,2,3-triazole (1i)[11b]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 6.2, 3.4 Hz, 1H), 8.05-7.93 (m, 4H), 7.82 (d, *J* = 7.4 Hz, 1H), 7.64 – 7.52 (m, 3H).

2-p-tolyl-2H-1,2,3-triazole (1j) [11b]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.82 (s, 2H), 7.28 (d, 2H), 2.43 (s, 3H).

2-phenyl-2H-1,2,3-triazole-4-carbaldehyde (1k)[23]**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.29 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.6 Hz,2H), 7.47 (t, *J* = 7.1 Hz, 1H).

methyl 2-phenyl-2H-1,2,3-triazole-4-carboxylate (1l) [23]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.14 (d, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 4.00 (s, 3H).

2-phenyl-2H-benzo[d][1,2,3]triazole (1m)[19]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.7 Hz, 2H), 7.94 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.50 – 7.39 (m,3H).

2-(2-methoxyphenyl)-2H-1,2,3-triazole (3a): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.30) to give **3a** (58.6 mg, 66 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.12-7.01 (m, 2H), 3.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 135.1, 130.4, 129.8, 127.1, 120.7, 112.8, 56.3. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_9H_9N_3O$: 175.0746;

found: 175.0743. IR:$_{max}$(thin film) (cm $^{-1}$) = 3409, 3237, 3010, 2982, 2876, 2362, 1513, 1450, 1412, 1308.

2-(2-methoxy-6-methylphenyl)-2H-1,2,3-triazole (3b): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 8/1, Rf =0.35) to give **3b** (72.8 mg, 77 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.32 (t, *J* = 8.0 Hz, 1H), 6.86 (m, 2H), 3.71 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 137.8, 134.9, 130.7, 129.2, 122.4, 109.5, 56.0, 17.0. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{10}H_{11}N_3O$: 189.0902; found: 189.0906. IR:$_{max}$(thin film) (cm $^{-1}$) = 3415, 3299, 2962, 2939, 2841,2360, 2342, 1687, 1604, 1590, 1495,1356

2-(2,4-dimethoxyphenyl)-2H-1,2,3-triazole (3c): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 4/1, Rf =0.41) to give **3c** (63.5 mg, 62 %) as a white solid, mp 62.4-62.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 2H), 7.40 (d, *J* = 8.7 Hz, 1H), 6.60 (s, 1H), 6.55 (d, *J* = 8.7Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 154.8, 134.9, 127.9, 123.5, 104.4, 99.8, 56.2, 55.6. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{10}H_{11}N_3O_2$: 205.0851; found: 205.0856. IR:$_{max}$(thin film) (cm $^{-1}$) = 3473, 3416, 3409, 2922, 2847, 2359, 2341, 1616, 1558, 1472, 1457.

methyl 3-methoxy-4-(2H-1,2,3-triazol-2-yl)benzoate (3d): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 4/1 , Rf =0.32) to give **3d** (66.4 mg, 57 %) as a white solid, mp 74.6-75.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 2H), 7.83-7.77 (m, 2H), 7.66 (d, *J* = 8.1 Hz, 1H), 4.03-3.93 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 152.9, 135.7, 133.0, 131.6, 126.5, 122.1, 114.0, 56.6, 52.5. HRMS (ESI-TOF): m/z [M + Na^+] calcd for

$C_{11}H_{11}N_3O_3$: 233.0800; found: 233.0802. IR:$_{max}$(thin film) (cm $^{-1}$) = 3564, 3235, 2920, 2849, 2359, 2341, 2065, 1717, 1637, 1616, 1457,1237.

2-(4-chloro-2-methoxyphenyl)-2H-1,2,3-triazole (3e): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1 , Rf =0.45) to give **3e** (56.4 mg, 54 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 2H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.10 – 7.02 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 135.9, 135.42, 128.4, 127.8, 120.8, 113.4, 56.6. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_9H_8ClN_3O$: 209.0356; found: 209.0359. IR:$_{max}$(thin film) (cm $^{-1}$) = 3564, 3482, 3416, 3237, 2929, 2872, 2360, 2341, 1616, 1507, 1456.

2-(2-methoxy-4-(trifluoromethyl)phenyl)-2H-1,2,3-triazole (3f): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 4/1 , Rf =0.48) to give **3f** (54.8 mg, 45 %) as a white solid, mp 73.3-73.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.32 (s, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 135.8, 132.2, 132.2 (q, *J* = 32.7 Hz), 127.2, 123.5 (q, *J* = 271 Hz), 117.7 (q, *J* = 3.9 Hz), 110.0 (q, *J* = 3.7 Hz), 56.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.7. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{10}H_8F_3N_3O$: 243.0619; found: 243.0621. IR:$_{max}$(thin film) (cm $^{-1}$) =3496, 3464, 3404, 3025, 2921, 2864, 2331, 1638, 1617, 1491.

1-(3-methoxy-4-(2H-1,2,3-triazol-2-yl)phenyl)ethanone (3g): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 4/1 , Rf =0.25) to give **3g** (62.9 mg, 58 %) as a white solid, mp56.7-61.2°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H), 7.71 – 7.65 (m, 2H), 7.62 (d, *J* = 8.1, 1H), 3.94 (s, 3H), 2.63 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.8, 153.2, 138.3, 135.7, 133.1, 126.6, 121.3, 112.1, 56.6, 26.7. HRMS (ESI-TOF): m/z [M + Na^+] calcd for

$C_{11}H_{11}N_3O_2$: 217.0851; found: 217.0848. IR:$_{max}$(thin film) (cm $^{-1}$) =3461, 3437, 3230, 2962, 2877, 2360, 2339, 1702, 1616, 1501,1334,1240.

methyl 4-methoxy-3-(2H-1,2,3-triazol-2-yl)benzoate (3h): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 6/1 , Rf =0.41) to give **3h** (79.2 mg, 68 %) as a white solid, mp 67.9-68.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.15 (d, *J* = 8.7, 1H), 7.88 (s, 2H), 7.13 (d, *J* = 8.7 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 157.0, 135.4, 132.2, 129.4, 128.7, 122.9, 112.1, 56.5, 52.2. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{11}H_{11}N_3O_3$: 233.0800; found: 233.0803. IR:$_{max}$(thin film) (cm $^{-1}$) =3454, 3469, 3417, 2953, 2920, 2850, 2360, 2341, 1717, 1615, 1516,1363, 1269.

2-(8-methoxynaphthalen-1-yl)-2H-1,2,3-triazole (3i): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1 , Rf =0.30) to give **3i** (84.4 mg, 75 %) as a brown solid, mp 83.8-84.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.84 (s, 2H), 7.54 (t, *J* = 5.2 Hz, 1H), 7.52-7.48 (m, 2H), 7.43 (t, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 3.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0, 136.1, 135.9, 134.0, 130.6, 127.0, 126.3, 125.2, 121.5, 120.7, 107.1, 56.3. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{13}H_{11}N_3O$: 225.0902; found: 225.0906. IR:$_{max}$(thin film) (cm $^{-1}$) =3473, 3417, 3234, 2958, 2932, 2838, 2360, 2341, 1652, 1636, 1616, 1404, 1260.

2-(2-ethoxyphenyl)-2H-1,2,3-triazole (3j): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.37) to give **3j** (57.6 mg, 61 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.49 (d, *J* = 7.8, Hz, 1H), 7.43-7.38 (m, 1H), 7.13-7.00 (m, 2H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.31 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 135.0, 130.4, 127.2, 120.6, 114.2, 65.0, 14.6. HRMS (ESI-TOF): m/z [M + Na^+] calcd for

$C_{10}H_{11}N_3O$: 189.0902; found: 189.0907. IR:$_{max}$(thin film) (cm $^{-1}$) =3648, 3566, 2981, 2927, 2851, 2359, 2341, 1600, 1506, 1456, 1412, 1286.

2-(2-ethoxy-6-methylphenyl)-2H-1,2,3-triazole (3k): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.38) to give **3k** (68.0mg, 67 %) as a yellow solid, mp 46.0-46.4°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.30 (t, *J* = 8.0 Hz, 1H), 6.91 – 6.81 (m, 2H), 3.97 (q, *J* = 7.0 Hz, 2H), 1.97 (s, 3H), 1.19 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 137.7, 134.7, 130.5, 129.6, 122.2, 110.8, 64.6, 17.0, 14.5. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{11}H_{13}N_3O$: 203.1059; found: 203.1062. IR:$_{max}$(thin film) (cm $^{-1}$) =3481, 2978, 2929, 2872, 2359, 1605, 1589, 1491, 1475, 1414, 1373.

2-(2-butoxyphenyl)-2H-1,2,3-triazole (3l): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 20/1, Rf =0.29) to give **3l** (42.3mg, 39 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.10-7.00 (m, 2H), 4.01 (t, *J* = 6.5 Hz, 2H), 1.72 – 1.61 (m, 2H), 1.34-1.29 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 134.9, 130.4, 130.3, 127.1, 120.5, 114.1, 69.1, 31.0, 19.0, 13.7. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{12}H_{15}N_3O$: 217.1215; found: 217.1217. IR:$_{max}$(thin film) (cm $^{-1}$) =3457, 3010, 2924, 2851, 2358, 2341, 1601, 1505, 1457, 1484, 1410, 1371, 1263.

2-(2-(2H-1,2,3-triazol-2-yl)phenoxy)ethanol (3m): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 2/1, Rf =0.31) to give **3m** (45.1mg, 44 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 2H), 7.67 – 7.60 (m, 1H), 7.40 (t, *J* = 8.6 Hz, 1H), 7.16 – 7.09 (m, 2H), 4.30 (t, *J* = 8.0 Hz, 2H), 3.86 (t, *J* = 8.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 135.2, 130.5, 130.0, 126.1, 121.9, 116.5, 72.7, 61.0. HRMS (ESI-

TOF): m/z [M + Na^+] calcd for $C_{10}H_{11}N_3O_2$: 205.0851; found: 205.0847. IR:$_{max}$(thin film) (cm^{-1}) =3469, 3408, 2925, 2874, 2359, 1601, 1506, 1455, 1416, 1357, 1289, 1252.

2-(2-isopropoxyphenyl)-2H-1,2,3-triazole (3n): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.39) to give **3n** (68.0mg, 67 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 2H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 4.49 – 4.38 (m, 1H), 1.23 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 134.9, 131. 6, 130.3, 127.3, 120.9, 116.9, 72.6, 22.0. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{11}H_{13}N_3O$: 203.1059; found: 203.1056. IR:$_{max}$(thin film) (cm^{-1}) =3551, 3475, 3408, 3235, 2978, 2920, 2849, 2359, 2341, 1652, 1637, 1616, 1558, 1505.

2-(2-isopropoxy-6-methylphenyl)-2H-1,2,3-triazole (3o): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.35) to give **3o**(92.2mg, 82 %) as a yellow solid, mp 39.3-41.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.29 (t, *J* = 8.0 Hz, 1H), 6.93-6.82 (m, 2H), 4.46 – 4.35 (m, 1H), 1.96 (s, 3H), 1.15 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 137.8, 134.6, 130.9, 130.4, 122.4, 113.0, 72.0, 21.9, 17.1. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{12}H_{15}N_3O$: 217.1215; found: 217.1220. IR:$_{max}$(thin film) (cm^{-1}) =3481, 2978, 2929, 2872, 2359, 1605, 1589, 1491, 1475, 1414, 1373.

2-(2-isopropoxy-4-methoxyphenyl)-2H-1,2,3-triazole (3p): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 4/1, Rf =0.39) to give **3p**(69.9mg, 60 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 2H), 7.36 (d, *J* = 8.7 Hz, 1H), 6.61 (s, 1H), 6.56 (d, *J* = 8.7Hz, 1H), 4.45 – 4.34 (m, 1H), 3.84 (s, 3H), 1.22 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 153.7, 134.7, 128.0, 125.2, 105.1, 103.2, 72.5, 55.6, 21.9. HRMS

(ESI-TOF): m/z [M + Na^+] calcd for $C_{12}H_{15}N_3O_2$: 233.1164; found: 233.1158. IR:$_{max}$(thin film) (cm $^{-1}$) =3367, 2982, 2848, 2360, 2341, 2065, 1683, 1637, 1616, 1519, 1457, 1315.

2-(4-chloro-2-isopropoxyphenyl)-2H-1,2,3-triazole (3q): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.39) to give **3q**(61.6mg, 52 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.07 (s, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 4.52-4.41 (m, 1H), 1.26 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 135.7, 135.2, 129.9, 128.1, 120.9, 116.7, 72.9, 21.8. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{11}H_{12}ClN_3O$: 237.0669; found: 237.066. IR:$_{max}$(thin film) (cm $^{-1}$) =3480, 3471, 3239, 2980, 2921, 2850, 2359, 2341, 1652, 1636, 1617, 1558, 1500.

2-(2-(cyclopentyloxy)-4-methylphenyl)-2H-1,2,3-triazole (3r): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.41) to give **3r**(86.3mg, 71 %) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 6.87 (s, 1H), 6.83 (d, *J* = 8.1 Hz, 1H), 4.77 – 4.71 (m, 1H), 2.40 (s, 3H), 1.77 (m, 4H), 1.66 – 1.43 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 140.6, 134.7, 128.8, 126.9, 121.0, 116.4, 81.0, 32.7, 23.6, 21.7. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{14}H_{17}N_3O$: 243.1372; found: 243.1375. IR:$_{max}$(thin film) (cm $^{-1}$) = 3478, 3329, 2970, 2913, 2839, 1621, 1614, 1491, 1435, 1421, 1373, 1254, 1223.

2-(2-(cyclohexyloxy)-6-methylphenyl)-2H-1,2,3-triazole (3s): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 15/1, Rf =0.35) to give **3s**(100.2mg, 78 %) as a pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 2H), 7.30 (t, *J* = 8.0 Hz, 1H), 6.91-6.84 (m, 2H), 4.26 – 4.17 (m, 1H), 1.99 (s, 3H), 1.64 – 1.18 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 137.7, 134.5, 130.8, 130.4, 122.2, 112.9, 76.2, 31.2, 25.5, 22.9, 17.1. HRMS

(ESI-TOF): m/z [M + Na^+] calcd for $C_{15}H_{19}N_3O$: 257.1528; found: 257.1530. IR:$_{max}$(thin film) (cm $^{-1}$) =3456, 3369, 2984, 2925, 2864, 1626, 1610, 1502, 1446, 1435, 1421, 1373, 1254, 1223.

2-(2-(benzyloxy)phenyl)-2H-1,2,3-triazole (3t): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.37) to give **3t** (43.9mg, 35%) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 2H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.27 (m, 6H), 7.09 (m, 2H), 5.15 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 136.5, 135.1, 130.6, 130.3, 128.4, 127.8, 127.2, 126.8, 121.2, 115.0, 71.0. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{15}H_{13}N_3O$: 251.1059; found: 251.1056. IR:$_{max}$(thin film) (cm $^{-1}$) = 3478, 3416, 3405, 3109, 3020, 2991, 2923, 1691, 1473,1385, 955

2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carbaldehyde (3ua): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.45) to give **3ua** (38.6 mg, 38 %) as pale yellow solid. mp. 87.6 - 88.2 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.30 (s, 1H), 7.61 – 7.45 (m, 2H), 7.17 – 7.06 (m, 2H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.4, 153.6, 147.8, 135.0, 131.4, 129.1, 127.0, 120.7, 112.9, 56.3. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{10}H_9N_3O_2$: 203.0695; found: 203.0698. IR:$_{max}$(thin film) (cm $^{-1}$) = 3489, 3459, 3412, 3127, 3061, 2918, 2842, 1618, 1507, 1249,1025

dimethoxy(2-(2-methoxyphenyl)-2H-1,2,3-triazol-4-yl)methanol (3ub): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.31) to give **3ub** (53.0 mg, 40 %) as a white solid. mp. 132.2 - 132.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.45 – 7.38 (m, 1H), 7.08 – 7.00 (m, 2H), 5.68 (s, 1H), 3.83 (s, 3H), 3.42 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.63, 146.77, 133.81, 130.53, 129.67, 127.16, 120.55, 112.66, 98.22, 56.21, 53.06. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{12}H_{15}N_3O_4$:

265.1063; found: 265.1068. IR:$_{max}$(thin film) (cm $^{-1}$) = 3554, 3489, 3408, 3231, 3124, 3025, 2923, 2854, 1704, 1611, 1485, 1451, 1309

methyl 2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylate (3v): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.34) to give **3v** (69.9 mg, 60%) as a yellow solid, mp. 67.5 - 68.1°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.53 (d, *J* = 7.7, 1H), 7.50 – 7.43 (m, 1H), 7.11 – 7.03 (m, 2H), 3.98 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 153.7, 140.6, 137.5, 131.3, 129.2, 127.3, 120.6, 112.6, 56.2, 52.4 HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{11}H_{11}N_3O_3$: 233.0080; found: 233.0085. IR:$_{max}$(thin film) (cm $^{-1}$) = 3557, 3420, 3412, 3380, 3127, 2923, 2901, 1726, 1383, 1117.

2-(2-methoxyphenyl)-2H-benzo[d][1,2,3]triazole (3w): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.37) to give **3w** (69.8 mg, 62%) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.66 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.43 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.20 – 7.07 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7, 144.9, 131.2, 130.3, 127. 7, 126.8, 120.7, 118.5, 112.8, 56.4. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{13}H_{11}N_3O$: 225.0902; found: 225.0905. IR:$_{max}$(thin film) (cm $^{-1}$) = 3423, 3234, 2984，2896，2365, 1652, 1488, 1442, 1372, 1285, 1153.

2-(2-isopropoxyphenyl)-2H-benzo[d][1,2,3]triazole (3x): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.41) to give **3x** (73.3 mg, 58%) as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.21 – 7.06 (m, 2H), 4.53 – 4.41 (m, 1H), 1.22 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 144.7, 132.1, 130.9, 127.8, 126.6, 121.0, 118.5, 117.0, 72.8,

22.0. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{15}H_{15}N_3O$: 253.1215; found: 253.1211. IR:$_{max}$(thin film) (cm^{-1}) = 3411, 3227, 3165, 2934, 2864, 1546, 1485, 1423, 1354, 1233, 1186, 1079

2-(2,6-dimethoxyphenyl)pyridine (5a)[20]: According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.32) to give **5a** (94.6mg, 88 %) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.5 Hz, 1H), 7.72 (td, *J* = 7.7, 1.7 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.23 (dd, *J* = 6.9, 5.5 Hz, 1H), 6.65 (d, *J* = 8.4 Hz, 2H), 3.73 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 154.5, 149.2, 135.8, 129.7, 126.3, 121.7, 119.0, 104.2, 56.0.

2-(2-methoxyphenyl)-1,5-dimethyl-1H-pyrazol-3(2H)-one (5b): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (EA/MeOH = 20/1, Rf =0.45) to give **5b** (70.8mg, 65 %) as a yellow solid, mp 101.2-101.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 1H), 7.30 (d, *J* = 7.7Hz, 1H), 7.08 - 7.00 (m, 2H), 5.34 (s, 1H), 3.82 (s, 3H), 3.04 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 156. 6, 151.5, 131.3, 131.1, 123.1, 121.1, 112.7, 95.6, 56.1, 33.2, 12.7. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{12}H_{14}N_2O_2$: 218.1126; found: 218.1135. IR:$_{max}$(thin film) (cm^{-1}) =3002, 2823, 1629, 1565, 1552, 1530, 1483, 1452, 1384.

3-methoxy-2-(1H-pyrazol-1-yl)phenol (5c): According to the General Procedure, a crude product was purified by using a preparative silica gel TLC (Hex/EA = 10/1, Rf =0.34) to give 5c (39.9mg, 42 %) as a yellow liquid. ^{1}H NMR (400 MHz, CDCl3) δ 11.00 (s, 1H), 8.29 (d, J = 2.2 Hz, 1H), 7.75 (s, 1H), 7.15 (t, J = 8.3 Hz, 1H), 6.77 (d, J = 8.3 Hz, 1H), 6.59 (d, J = 8.3 Hz, 1H), 6.506 – 6.458 (m, 1H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 151.5, 151.2, 138.4, 132.9, 127.6, 116.0, 111.3, 105.6, 103.1, 56.1. HRMS (ESI-TOF): m/z [M + Na^+] calcd for $C_{10}H_{10}N_2O_2$: 190.0742 ; found: 190.0747.

IR: $_{max}$ (thin film) (cm -1) =3543, 3378, 3217, 3102, 2827, 1564, 1527, 1522, 1483, 1419, 1374.

Intermediate A: To a stirred solution of 2-phenyl-2H-1,2,3-triazole (1a) (73 mg, 0.5 mmol), $Pd(OAc)_2$ (112 mg, 0.5 mmol) in DCE (3 mL) at 120ºC for 2 h. The solid was collected and washed with EtOAc to give Intermediate A (118mg, 93%) as a black solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.10 (s, 1H), 7.06 – 7.00 (m, 1H), 6.95 (d, J = 3.8 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.5, 141.0, 134.1, 133.4, 131.7, 129.4, 126.6, 125.2, 113.6, 24.5

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ASSOCIATED CONTENT

Supporting Information Available.

Copies of NMR spectra of products **1a-1m, 3a−x**, **5a-c** and intermediate **A.** This material is available free of charge via the Internet at http://pubs.acs. org.

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Reference

(1) (a) Wolter,M.; Nordmann, G.; Job, G. E.; Buchwald, S. L. *Org. Lett*. **2002**, *4*, 973. (b) Marcoux, J.-F.; Doye, S.; Buchwald, S. L. *J. Am. Chem. Soc*. **1997**, *119*, 10539. (c) Vorogushin, A. V.; Huang, X.; Buchwald, S. L. *J. Am.*

Chem. Soc. **2005**, *127*, 8146. (d) Gowrisankar, S.; Sergeev, A. G.; Anbarasan,P.; Spannenberg, A.; Neumann, H.; Beller, M. J. *J. Am. Chem. Soc.* **2010**, *132*, 11592. (e) Wu, X.; Fors, B. P.; Buchwald, S. L. *AngewChem., Int. Ed.* **2011**, *50*, 9943. (f) Li, B.; Dixneuf, P. H. *Chem. Soc. Rev.,* **2013**, *42*, 5744. (g) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.,* **2009**, *48*, 5094

(2) (a) Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Am. Chem. Soc*. **2001**, *123*, 7475. (b) Ferreira, E. M.; Stoltz, B. M. *J. Am. Chem. Soc.* **2001**, *123*, 7725. (c) Kalyani, D.; Sanford, M. S. *Org. Lett.* **2005**, *7*, 4149. (d) Kalberer, E. W.; Whitfield, S. L.; Sanford, M. S. *J. Mol. Catal., A.* **2006**, *251*, 108; (e) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc*. **2004**, *126*, 9542. (f) Zhang, J.; Khaskin, E.; Anderson, N. P.; Zavalij, P. Y.; Vedernikov, A. N. *Chem. Commun.* **2008**, 3625.

(3) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470.

(4) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451.

(5) For selected examples of alternative approaches to synthesize alkyl ethers, see: (a) Molander, G. A.; Colombel, V.; Braz, V. A. *Org. Lett.* **2011**, *13*, 1852. (b) Vo, C.-V. T.; Mitchell, T. A.; Bode, J. W. *J. Am. Chem. Soc.* **2011**,*133*, 14082. (c) Maier, T. C.; Fu, G. C. *J. Am.Chem. Soc.* **2006**, *128* , 4594; (d) Zhang, Y.; Li, C.-J. *J. Am. Chem. Soc*. **2006**, *128*, 4242.

(6) For selected reviews and leading references on C–O bondformation, see: (a) Newhouse, T.; Baran, P. S. *Angew.Chem., Int. Ed.,* **2011**, *50*, 3362. (b) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Sottocornola, S. *Chem. Rev.* **2007**, *107*, 5318. (c) Alonso, D. A.; N´ajera, C.; Pastor, I. M.; Yus, M. *Chem.–Eur. J.* **2010**, *16*, 5274. (d) Stahl, S. S.; Labinger, J. A.; Bercaw, J. E.; *Angew. Chem., Int. Ed.* **1998**, *37*, 2180. (e) Palucki, M.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 10333. (f) Torraca, K. E.; Huang, X.; Parrish, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 10770.

(7) (a) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem.* Soc. **2004**, *126*, 2300. (b) Desai, L. V.; Malik, H. A.;

Sanford, M. S. *Org. Lett*. **2006**, *8*, 1141.

(8) (a) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc*. **2010**, *132*, 12203. (b) Wang, H.; Li, G.; Engle, K. M.; Yu, J. Q.; Davies, H. L. *J. Am. Chem. Soc*., **2013**, *135*, 6774.

(9) (a) Wang, G. W.; Yuan, T. T. *J. Org. Chem.* **2010**, *75*, 476. (b) Jiang, T. S.; Wang, G. W. *J. Org. Chem.* **2012**, *77*, 9504. (c) Li, W.; Sun, P. *J. Org. Chem.* **2012**, *77*, 8362. (d) Xiao, B.; Gong, T. J.; Liu, Z. J.; Liu, L. *J. Am. Chem.* Soc. **2011**. *133*. 9250. (e) Eom, D.; Jeong, Y.; Kim, Y. R.; Lee, E.; Choi, W.; Lee, P. H. *Org. Lett*. **2013**, *15*, 5210. (f) Chen, F. J.; Zhao, S.; Hu, F.; Chen, K. ; Zhang, Q.; Shi, B. F. *Chem. Sci*. **2013**, *4*, 4187. (g) Zhang, S. Y.; He, G.; Zhao, Y.; Wright, K.; Chen, G. *J. Am. Chem. Soc*. **2012**, *134*, 7313.

(10) (a) Crowley, J. D.; McMorran, D. A. *Chem. Asian. J.* **2011**, *6*, 2696. (b) Ackermann, L.; Potukuchi, H. K. *Org. Biomol. Chem.,* **2010**, *8*, 4503. (c) Rozkiewicz, D. I.; Jańczewski, D.; Verboom, W.; Ravoo, B. J.; Reinhoudt, D. N. *Angew. Chem., Int. Ed*. **2006**, *45*, 5292. (d) Heal, W. P.; Wickramasinghe, S. R.; Leatherbarrow, R. J.; Tate, E. W. *Org. Biomol. Chem*. **2008**, *6*, 2308. (e)Chabre, Y. M.; Roy, R. *Curr. Top. Med. Chem.* **2008**, *8*, 1237. (f) Hanselmann, R.; Job, G. E.; Johnson, G.; Lou, R. L.; Martynow, J. G.; Reeve, M. M. *Org. Process Res. Dev.* **2010**, *14*, 152.

(11) (a)Wang, Z.; Tian, Q.; Yu, X.; Kuang, C. *Adv. Synth. Catal.* **2014**, *356*, 961. (b) Tian, Q.; Chen, X.; Liu, W.; Wang, Z.; Shi, S.; Kuang, C. *Org. Biomol. Chem.* **2013**, 11, 7830.

(12) Shabashov, D.; Daugulis, O. *Org. Lett*. **2005**, 7, 3657.

(13) (a)Xiao, B.; Fu, Y.; Xu, J.; Gong, T.-J.; Dai, J.-J.; Yi, J.; Liu, L. *J. Am. Chem. Soc.* **2010**, *132*, 468. (b) Xiao, B.; Gong, T.-J.; Xu, J.; Liu, Z.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 1466. (c) Giri, R.; Lam, J. K.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 686.

(14) (a) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc*. **2002**, *124*, 1586. (b) Wang, G.-W.; Yuan,T.-T.; Wu, X.-L. *J. Org. Chem.*

2008, *73*, 4717. (c) Wang, G.-W.; Yuan, T.-T.; Li, D.-D. *Angew. Chem., Int. Ed.* **2011**, *50*, 1380. (d) Lee, G. T.; Jiang, X.; Prasad, K.; Repic, O.; Blacklock, T. J. *Adv. Synth. Catal.* **2005**, *347*, 1921;

(15) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev*., **2010**, *110*, 1147. (b) Giri, R.; Liang, J.; Lei, J.-G.; Li, J.-J.; Wang, D.-H.; Chen, X.; Naggar, I. C.; Guo, C.; Foxman, B. M.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2005**, *44*, 7420. (c) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (d) Yan, Y.; Feng, P.; Zheng, Q.-Z.; Liang, Y.-F.; Lu, J.-F.; Cui, Y.; Jiao, N. *Angew. Chem., Int. Ed.* **2013**, 52, 5827. (e) Anand, M.; Sunoj, R. B. Org. Lett, **2011**, *13*, 4802. (f) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965.

(16) (a) Xu, L.-M.; Li, B.-J.; Yang, Z.; Shi, Z.-J. *Chem. Soc. Rev.* **2010**, *39*, 712. (b) Powers, D. C.; Ritter, T. *Acc. Chem. Res.* **2012**, *45*, 840. (c) Racowski, J.; Sanford, M. S. *Top. Organomet. Chem.* **2011**, *53*, 61.

(17) Boursalian, G. B.; Ngai, M.-Y.; Hojczyk, K. N.; Ritter, T. *J. Am. Chem. Soc.* **2013**, *135*, 13278.

(18) (a) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, 1, 302. (b) Powers, D. C.; Geibel, M. A. L.; Klein, J. E. M. N.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050.

(19) Taillefer, M.; Xia, N.; Ouali, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 934.

(20) Pignataro, L.; Benaglia, M. *J. Org. Chem.,* **2006**, *71*, 1458.

(21) Oi, S.; Sasamoto, H.; Funayama, R.; Inoue, Y. *Chem. Lett.,* **2008**, *37*, 994.

(22 Ueda, S.; Su, M.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 8944.

(23) El Ashry, E. S. H.; Atta, K. F.; Aboul-Ela, S.; Beldi, R. *J. Carbohydr. Chem*. **2007**, 26, 429.