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Cobalt-catalyzed amination of triazoles with dioxazol-5-ones through triazole-directed *ortho* C–H activation

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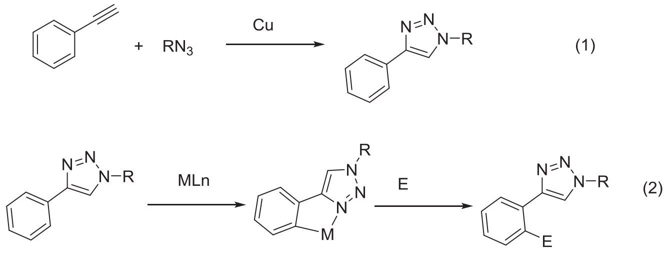
ABSTRACT

Cobalt-catalyzed reactions of triazoles and dioxazol-5-one involving nitrene transfer were described. A number of amidated 1,2,3-trizole derivatives have been obtained in moderate to excellent yields.

1. Introduction

1,2,3-Triazole derivatives are important substructures, which can be used as unique ligands for catalysts[1] and coordination chemistry.[2] Triazole derivatives have found wide applications as photo-active materials,[3] medicine,[4] chemical sensors,[5] and thus synthesis of 1,2,3-trizoles have attracted much attention.[6] 1,2,3-Triazole can be prepared easily via Cu-catalyzed azide–alkyne [3+2] cycloaddition reactions (Eq. 1, Scheme 1).[7] The protocol has been widely applied to the synthesis of various triazoles, which is restricted because the commercially available terminal alkynes are limited. Recently, the construction of C–C and C–N bonds through metal-catalyzed C–H bond activation and functionalization has been made great progress.[8] We envisioned that the C–H activation strategy would also be applicable to the synthesis of triazoles. Functionalization of triazole through triazole-directed C–H bond activation would be an economic synthetic route for complex triazole derivatives (Eq. 2).

1,4,2-Dioxazol-5-ones is known to be a nitrene precursor, which can generate active *N*-acyl nitrenes by losing one molecule of CO_2 when it was heated or illuminated in the presence of metal. 1,4,2-Dioxazol-5-one can be used as a nitrogen source to form C–N bonds by nitrene insertion process.[9] We have previously reported rhodium catalyzed annulation of triazoles and internal alkynes. The reaction proceeded via sequential triazole-directed C–H activation, C–C, C–N, and C–O bond formation affording mesoionic triazolo [5,1-*a*]isoquinoliums.[10] In this paper, we report cobalt-catalyzed directed C–H functionalization of 1,2,3-trizaole leading to amidated triazoles in good to excellent yields.



Scheme 1. Synthesis and functionalization of triazoles.

2. Results and discussion

The experiment results showed that cobalt complex could catalyze the reaction of 1-benzyl-4-(*p*-tolyl)-1*H*-1,2,3-triazole **1a** and 3-phenyl-1,4,2-dioxazol-5-one **2a**. Initially, the reaction conditions were optimized by using the reaction of **1a** and **2a** as the model

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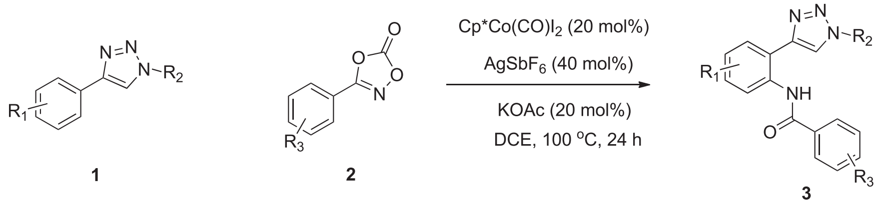
Table 1
Cobalt-catalyzed amidation of 1,2,3-triazole[a]



Entry	**2a** (equiv)	Co (×mol %)	Additive	*T* (C)	Yield (%)
1	2.0	10	—	100	64
2	2.0	10	KOAc	100	69
3	2.0	10	NaOAc	100	65
4	2.0	10	AgOAc	100	42
5	2.0	10	KOAc	80	35
6	2.0	10	KOAc	120	66
7	3.0	10	KOAc	100	60
8	2.0	10	KOAc	100	48[b]
9	2.0	10	KOAc	100	55[c]
10	2.0	15	KOAc	100	80
11	2.0	20	KOAc	100	84
12	2.0	0	KOAc	100	ND[d]
13	2.0	20	KOAc	100	Trace[d]
14	2.0	0	KOAc	100	ND[e]
15	2.0	20	AgOAc	100	ND[d]
16	2.0	20	AgOAc	100	ND[d,f]
17	2.0	20	—	100	73

[a] Reaction conditions: **1a** (0.20 mmol), $AgSbF_6$ (2× mol %), additives (20 mol %), DCE 2 mL, 100 °C 24 h, air; [b]48 h; [c]36 h; [d]No $AgSbF_6$; [e]40 mol % $AgSbF_6$; [f]40 mol % AgOAc.

reaction, and the results were summarized in Table 1. At the loading of 10 mol % [CpCo(CO)I_2] and 20 mol % $AgSbF_6$ at 100 °C using 1,2-dichloroethane as the solvent, the amidation product **3a** was obtained in 64% yield (Table 1, entry 1). Further addition of acetate salts such as KOAc and NaOAc can slightly improve the reaction (entries 2 and 3). However, AgOAc showed negative effect (entry 4). When the temperature was lowered to 80 °C, the yield of the target product was decreased to 35% (entry 5). Further increase of temperature to 120 °C did not show obvious influence on the isolated yield (entry 6). For the triazole-directed amidation reaction, two equivalent of 3-phenyl-1,4,2-dioxazol-5-one **2a** is appropriate, and the use of larger amount of **2a** did not increase the yield (entry 7). Extension of reaction time did not raise the yield of **3a**. Probably longer reaction caused side reactions (entries 8 and 9). When the loading of cobalt catalyst was increased to 15–20 mol %, **3a** could be obtained in up to 84% yield (entries 10 and 11). For comparison, in the absence of cobalt complexes, no desired product was observed (entries 12 and 14). In addition, $AgSbF_6$ is also essential (entry 13). Under the same conditions, only trace amount of desired product was observed without using $AgSbF_6$ (entry 14). $AgSbF_6$ could not be replaced by AgOAc (entries 15 and 16). When 20 mol % of cobalt catalyst was used without KOAc, the yield of **3a** was decreased 73% (entry 17).

After optimization studies, we explored the feasibility of cobalt-catalyzed C–H amidation of other 1,2,3-triazole and dioxazolone derivatives. At the loading of 20 mol % of the cobalt catalyst in 1,2-dichloroethane, the amidation reaction of a number of triazoles bearing electron-withdrawing and electron-donating groups at their aromatic rings were studied. The results were summarized in Table 2. The reaction of **1b** (R_2=H, R_2=CH_2Ph) and **2a** afforded **3b** in 56% yield. Triazole **1c** (R_1=*o*-CH_3, R_2=CH_2Ph) having a *meta* methyl showed lower activity, and the corresponding product was obtained in 64% yield. Fluorine-containing triazole are quite active, and **3d** was obtained in 86% yield in the case of 1-benzyl-4-(4-fluorophenyl)-1*H*-1,2,3-triazole, whereas the chlorine-containing triazole showed relatively lower activity. When *N*-substituent was replaced by an alkyl group, the corresponding triazoles 1**f** (R_1=H, R_2=oct) and 1**g** (R_1=*p*-F, R_2=oct) also reacted with dioxazolone smoothly, especially in the case of 4-(4-fluorophenyl)-1-octyl-1*H*-1,2,3-triazole 1**g** (R_1=*p*-F, R_2=oct), the target product was isolated in nearly quantitative yield. To fully characterize the product, single crystals of **3g** were grown by slow diffusion of hexane into the toluene solution of **3g**. The structure of **3g** determined by X-ray diffraction was given in Fig. 1.

The amidation reactions of triazoles having an *N*-phenylethyl-substituent with dioxazolone were also successful at the loading of 20 mol % of cobalt catalyst at 100 °C, and their corresponding amidated products were isolated in 83, 90, 85, 56, and 60% yields, respectively. Finally, we examined the reactivities of dioxazolone bearing different substituents at their aromatic rings. Although the desired amidated products could be successfully obtained, the yields strongly depend on the substituents including methyl, methoxyl, and fluorine.

On the basis of the previous reports,[10] a plausible catalytic mechanism was proposed and depicted in Fig. 2. The cobalt iodide complexes would generate $[Cp^*Co(Sol)]^+$ species **I** in the presence of $AgSbF_6$ due to halogen abstraction and CO dissociation. Further interaction with a triazole molecule would yield **II** because of the coordination of triazole. Subsequent C–H metalation with the aid of AcO^- and reduction of one molecule of HOAc afforded cobaltacyclic complex **III**. Interaction of 1,4,2-dioxazol-5-one **2** with **III** generates Co(III) amido species **IV** with the release of CO_2 and following nitrene insertion. Protonation of **IV** would yield the target product and regenerate the active cobalt species.

3. Conclusion

In conclusion, we described cobalt-catalyzed amination of various triazoles by using dioxazolones as the nitrogen source. A number of amidated triazole derivatives have been obtained in good to excellent yields. The reaction was believed to proceed via cobalt catalyzed triazole-directed C–H bond activation and subsequent nitrene insertion. The starting materials are easily available and the catalyst is cheap, thus the protocol offers a new method for the direct functionalization of triazoles.