C–H Activation

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Cobalt(III)-Catalyzed Aryl and Alkenyl C–H Aminocarbonylation with Isocyanates and Acyl Azides**

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Abstract: *Expedient C–H aminocarbonylations of unactivated (hetero)arenes and alkenes were accomplished with a cobalt(III) catalyst that shows high functional group tolerance. The C–H functionalization occurred with excellent chemo-, site-, and diastereoselectivity and enabled step-economical reactions with isocyanates or acyl azides.*

Transition-metal-catalyzed C–H functionalization reactions have emerged as increasingly powerful tools for the sustainable synthesis of organic compounds.[1] Considerable progress in the assembly of aromatic amides was recently realized through C–H functionalization by isocyanates,[2] with key contributions from the groups of Kuninobu/Takai, Bergman/Ellman, Cheng, Li, and Ackermann, among others.[3] Despite these major advances, all catalyzed C–H activations with isocyanates have thus far been accomplished with complexes of the expensive 4d or 5d transition metals rhenium, rhodium, or ruthenium. In consideration of the cost-effective nature of first-row transition metals, recent focus has shifted towards the use of catalysts based on abundant base metals for C–H functionalization.[4] In this context, Nakamura, Yoshikai, and Ackermann recently utilized low-valent cobalt catalysts for C–H transformations that were until then the domain of precious rhodium, palladium, and ruthenium catalysts.[5,6] Furthermore, high-valent cobalt(III) catalysts were very recently employed for chemoselective C–H functionalization as reported by the groups of Matsunaga/Kanai,[7] Ackermann,[8] Glorius,[9] Ellman,[10] and Chang.[11,12] As part of our research program on base-metal-catalyzed C–H functionalization,[13] we have developed a cobalt-catalyzed C–H functionalization with isocyanates as the electrophiles that provides expedient access to substituted benzamides under mild reaction conditions (Figure 1). Notable features of our strategy include 1) the use of user-friendly cobalt catalysts, 2) the versatile C–H aminocarbonylation of arenes, heteroarenes, and alkenes with ample substrate scope, and 3) expedient amide syntheses that proved viable with isocyanates or azides.

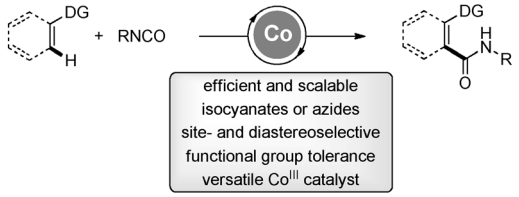
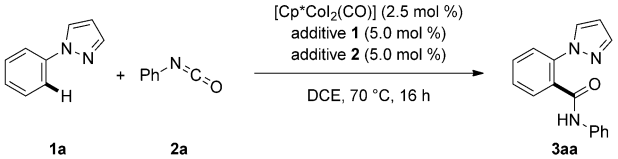


Figure 1. Cobalt-catalyzed C–H aminocarbonylation.

We commenced our studies by exploring reactions conditions for the envisioned cobalt-catalyzed aminocarbonylation of pyrazolylbenzene (**1a**) with isocyanate **2a** (Table 1 and Table S1 in the Supporting Information). The nature of the additive appeared to be critical and the combination of AgOPiv with either $AgSbF_6$ or $AgNTf_2$ gave optimal results (entries 1–11). The molecular complex $[Cp^*CoI_2(CO)]$[14] in particular was highly effective (entry 11) and test reactions verified the crucial importance of the cobalt catalyst and the additives (entries 12 and 13). In contrast, simple cobalt salts failed to give the desired benzamide **3aa** (entries 14–16).

With the optimized cobalt catalyst in hand, we tested the scope of the reaction with a representative set of decorated

Table 1: Optimization of cobalt(III)-catalyzed C–H aminocarbonylation.[a]



1a 2a 3aa

Entry	[Co]	Additive 1	Additive 2	Yield [%][c]
1	$[Cp^*CoI_2(CO)]$	$AgPF_6$	CsOAc	–
2	$[Cp^*CoI_2(CO)]$	$AgPF_6$	KOPiv	–
3	$[Cp^*CoI_2(CO)]$	$AgPF_6$	NaOPiv	–
4	$[Cp^*CoI_2(CO)]$	$AgNTf_2$	AgOAc	35
5	$[Cp^*CoI_2(CO)]$	$AgPF_6$	AgOAc	23
6	$[Cp^*CoI_2(CO)]$	$AgPF_6$	KOAc	24
7	$[Cp^*CoI_2(CO)]$	$AgPF_6$	AgOPiv	42
8	$[Cp^*CoI_2(CO)]$	$AgSbF_6$	AgOPiv	46
9	$[Cp^*CoI_2(CO)]$	$AgNTf_2$	AgOPiv	57
10	$[Cp^*CoI_2(CO)]$	$AgPF_6$	AgOPiv	64[b]
11	*$[Cp^*CoI_2(CO)]$*	*$AgSbF_6$*	*AgOPiv*	*67*[b]
12	$[Cp^*CoI_2(CO)]$	$AgPF_6$	–	–
13	–	$AgPF_6$	AgOPiv	–
14	CoI_2	$AgSbF_6$	AgOPiv	–
15	$Co(OAc)_2$	$AgSbF_6$	AgOPiv	–
16	$[Co(acac)_2]$	$AgSbF_6$	AgOPiv	–

[a] General reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), [Co] (2.5 mol%), DCE (2.0 mL), 70°C, 16 h. [b] $[Cp^*CoI_2(CO)]$ (5.0 mol%), additives (10 mol%). [c] Yield of isolated product. Piv = pivalate.

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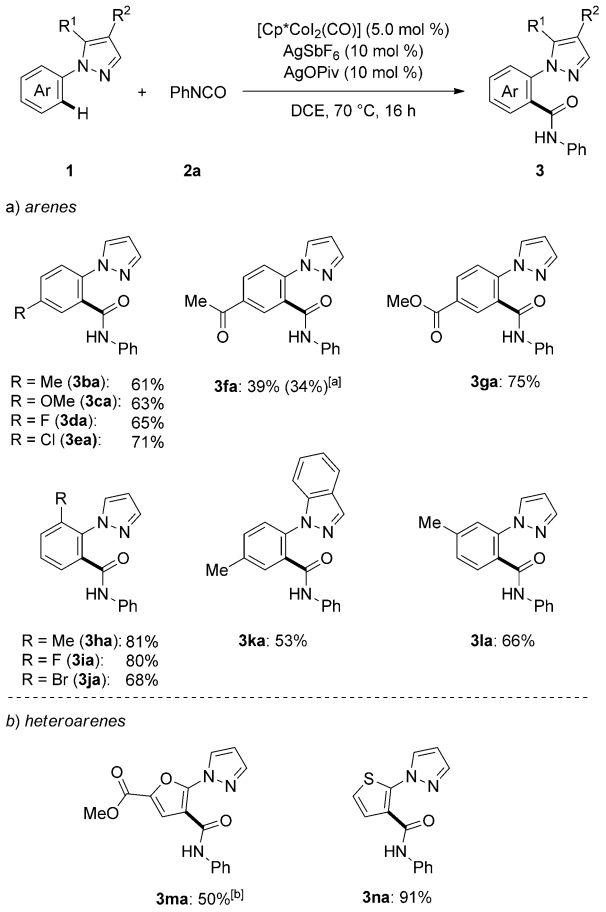
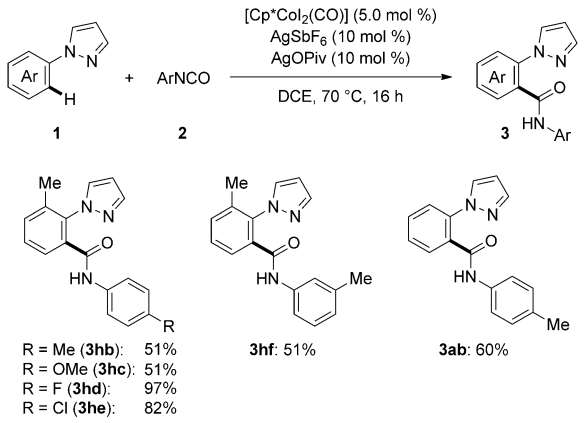
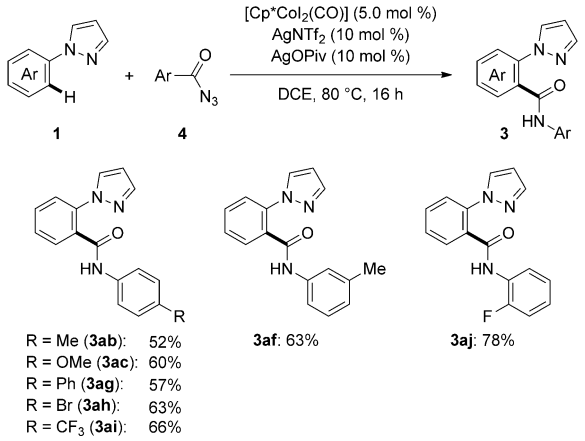


Scheme 1. Scope of the cobalt(III)-catalyzed C–H aminocarbonylation of arenes **1**. [a] Yield of the 2,6-diaminocarbonylated product **3 fa′**. [b] [Cp*CoI_2(CO)] (10 mol%), $AgSbF_6$ (20 mol%), AgOPiv (20 mol%).



Scheme 2. Cobalt(III)-catalyzed C–H aminocarbonylation with isocyanates **2**.



Scheme 3. Cobalt(III)-catalyzed C–H aminocarbonylation with acyl azides **4**.

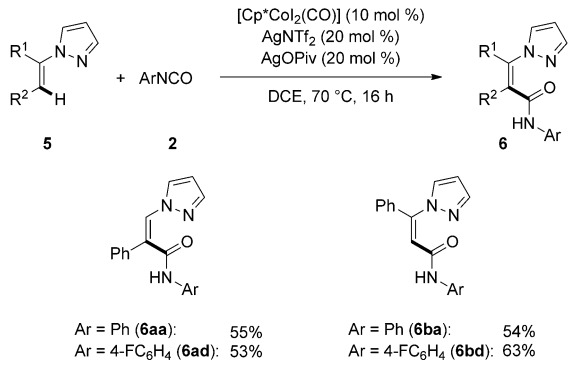
arenes **1** (Scheme 1a). The *para*- and *ortho*-substituted arylpyrazoles **1** were selectively converted into the benzamides **3ba**–**ka**. The catalytic system displayed remarkable chemoselectivity and thus proved tolerant of valuable electrophilic functional groups such as chloro, bromo, ester, and ketone substituents. An intramolecular competition experiment with *meta*-substituted arene **1l** proceeded with excellent site-selectivity under steric control. Importantly, the cobalt(III) catalyst was not limited to aromatic substrates. Indeed, the catalyst showed comparable levels of catalytic efficacy for the C–H aminocarbonylation of heteroarenes **1m** and **1n** (Scheme 1b).

As for the organic electrophiles **2**, the broadly applicable cobalt(III) catalyst enabled the efficient conversion of electron-rich as well as electron-deficient isocyanates (**2b**–**f**; Scheme 2).

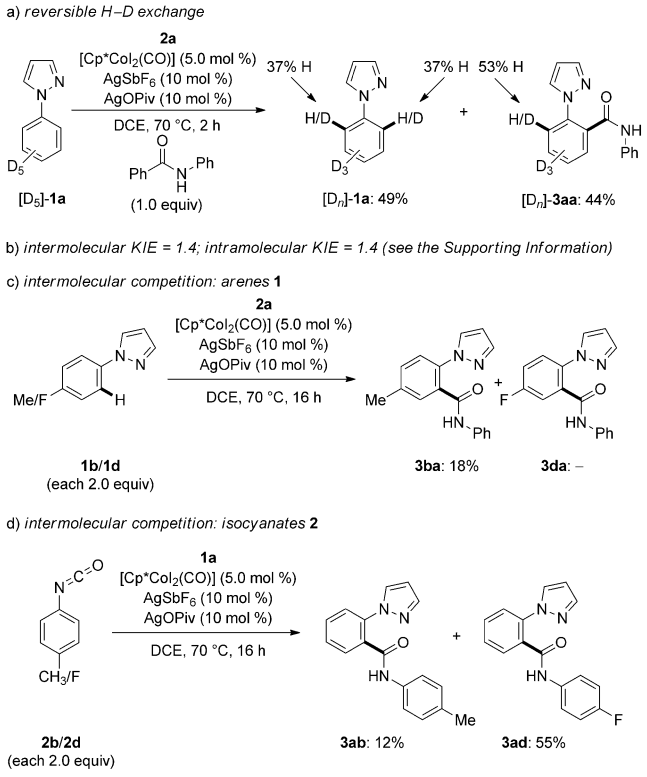
Moreover, the isocyanate electrophiles **2** could be generated in situ from the corresponding acyl azides **4**[15,16], thereby providing step-economical access to the amides **3** through a Curtius[17] rearrangement/C–H activation sequence under cobalt catalysis (Scheme 3). Interestingly, we only observed the formation of amides **3**, while intermolecular C–H nitrogenation[15,16] did not occur. A variety of *para*-, *meta*-, and *ortho*-substituted azides **4** bearing electron-donating or electron-withdrawing groups were efficiently transformed into the desired amide products **3**.

The user-friendly, inexpensive cobalt(III) catalyst was not restricted to the use of (hetero)aromatic substrates **1**. Indeed, with alkenes **5**, diastereoselective C–H aminocarbonylation occurred, thereby furnishing the thermodynamically less stable *Z*-olefins as the sole products (Scheme 4).

Intrigued by the versatility and efficacy of the cobalt(III)-catalyzed C–H activation, we performed mechanistic studies to determine its mode of action. To this end, reactions were conducted with the isotopically labeled substrate $[D]_5$-**1a** and the results indicated a facile C–H metalation (see Scheme 5a and Scheme S1 in the Supporting Information). In good agreement with this observation, we found minor inter- and intramolecular kinetic isotope effects (KIEs) of $k_H/k_D \approx 1.4$ (Scheme 5b), which again suggests that the C–H metalation is not the rate-determining step. Intermolecular competition experiments with differently substituted arenes **1** (Scheme 5c) and isocyanates **2** (Scheme 5d) revealed electron-rich arenes **1** and electron-deficient electrophiles **2** to be inherently more reactive substrates. These findings can be rationalized in



Scheme 4. Diastereoselective cobalt(III)-catalyzed C–H aminocarbonylation of alkenes **5**.

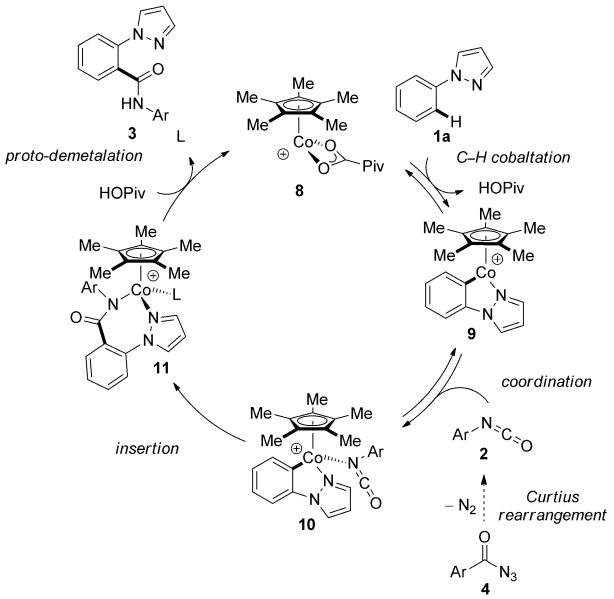


Scheme 5. Mechanistic studies.

terms of a rate-determining nucleophilic attack by a cyclometalated cobalt species on the isocyanate **2**.

Based on our mechanistic studies, we propose that the catalytic cycle initiates with a reversible carboxylate-assisted[18] C–H activation, which is followed by coordination of the isocyanate **2** to the thus formed cyclometalated complex **9** (Scheme 6). Thereafter, a rate-determining insertion through nucleophilic attack of the metalated arene **10** on the coordinated isocyanate **2** generates intermediate **11**. Finally protodemetalation liberates the desired product **3** and regenerates the catalytically active complex **8**.

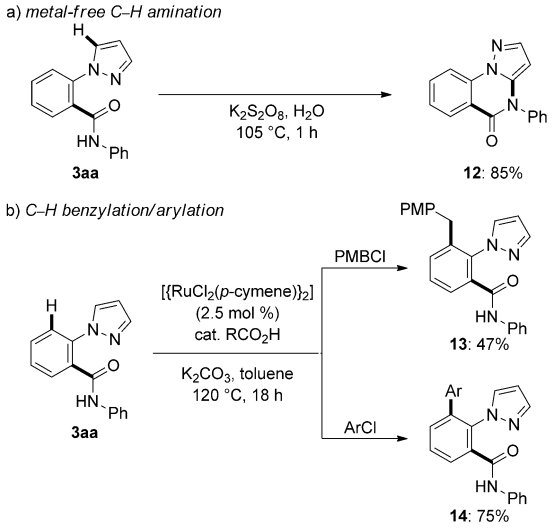
Finally, we demonstrated the synthetic potential of the cobalt(III)-catalyzed C–H activation strategy through the



Scheme 6. Proposed catalytic cycle.

late-stage diversification of the obtained amides **3** through C–H functionalization. A metal-free intramolecular C–H amination provided step-economical access to quinazolinone **12** (Scheme 7a), while ruthenium-catalyzed C–H benzylation[19] or arylation[20] with pyrazole assistance delivered the site-selectively decorated products **13** and **14**, respectively (Scheme 7b).

In summary, we report the first cobalt-catalyzed C–H aminocarbonylation with isocyanates. A versatile cobalt(III) catalyst enabled the C–H functionalization of (hetero)arenes and alkenes with ample scope, as well as excellent chemo-, site-, and diastereoselectivity, under mild reaction conditions.[21,22] This broadly applicable cobalt catalyst also sets the stage for aminocarbonylations with acyl azides, and mecha-



Scheme 7. Late-stage derivatization of amides **3** through C–H functionalization.

nistic studies provided strong evidence for a rate-determining migratory insertion in the carboxylate-assisted C–H functionalization process.

Keywords: amides · azides · C–H activation · cobalt · isocyanates

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Communications

C–H Activation

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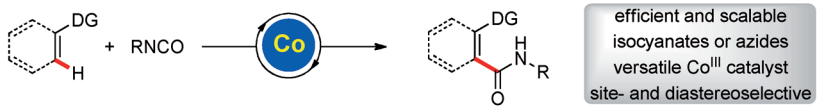
Cobalt(III)-Catalyzed Aryl and Alkenyl C–H Aminocarbonylation with Isocyanates and Acyl Azides



Clever cobalt: C–H aminocarbonylation of (hetero)arenes and alkenes was achieved by means of a user-friendly cobalt(III) catalyst. The reaction shows excellent chemo-, site-, and diastereoselectivity, as well as ample substrate scope.