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Cobalt-Promoted Dimerization of Aminoquinoline Benzamides

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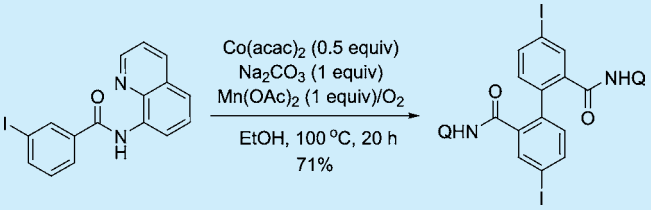
Supporting Information

ABSTRACT: A method for aminoquinoline-directed, cobalt-promoted dimerization of benzamides has been developed. Reactions proceed in ethanol solvent in the presence of $Mn(OAc)_2$ cocatalyst and Na_2CO_3 base and use oxygen as a terminal oxidant. Bromo, iodo, nitro, ether, and ester moieties are compatible with the reaction conditions. Cross-coupling of electronically dissimilar aminoquinoline benzamides proceeds with modest yields and selectivities.

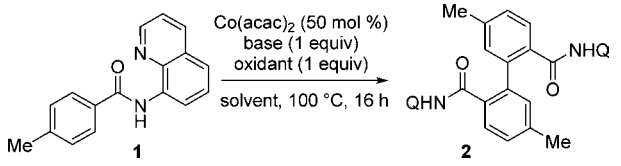


Direct dehydrogenative arene coupling is the most efficient method for the formation of biaryls.[1] However, most of the methods for arene homocoupling use polyfluorobenzene, five-membered-ring heterocycles, or phenol starting materials.[2] Cross-coupling of heterocycles and acidic arenes with each other or simple benzene derivatives is also possible.[3] In rare cases when simple arenes such as toluene are coupled, isomer mixtures of products are usually obtained.[4] Furthermore, reactions often require either palladium or rhodium catalysts or several equivalents of silver salt additives. Few reports describe dimerization of directing-group-containing arenes. In a notable exception, Yu has described copper-promoted 2-arylpyridine dimerization.[5] Methods for palladium- or ruthenium-catalyzed dimerization of 2-arylpyridines, phenylacetamides, and aryloxazolines have been reported by Sanford, Greaney, and Oi.[6] Miura has recently reported a method for aminoquinoline-directed homocoupling of thiophenes mediated by copper.[7] Thus, directed arene homocouplings are still rare. Furthermore, very few reports describe dehydrogenative arene couplings that do not require second-row transition metals as catalysts or additives.[2f,3d,e,9g]

We have reported that 8-aminoquinoline, picolinamide, and 2-pyridinylmethylamine auxiliaries can be used for palladium-, copper-, and cobalt-catalyzed C−H bond functionalization.[8,10a−c] Other research groups have extensively used these auxiliaries for palladium-, ruthenium-, iron-, and copper-catalyzed reactions.[9] The aminoquinoline auxiliary can direct cobalt-catalyzed C−H activation/alkene, alkyne, and CO migratory insertion sequences, leading to *ortho*-functionalized benzoic acid derivatives.[10a−c] We report here cobalt-promoted, aminoquinoline-directed dimerization of arenes that affords biphenyldicarboxylic acid derivatives, uses oxygen as a terminal oxidant, and does not require second-row transition metal additives.

On the basis of previous results,[10a−c] we decided to use $Co(acac)_2$ catalyst in an alcohol solvent. The reaction optimization was carried out with respect to solvent, oxidant, and base (Table 1). In contrast with previous cobalt-catalyzed reactions, trifluoroethanol is an inferior solvent compared to ethanol (entries 1 and 2). Sodium carbonate base afforded higher yield than sodium pivalate (entries 2 and 3). Reaction under oxygen gives higher yield than the reaction under air (entries 2 and 4). Manganese(III) acetate is an inferior co-oxidant compared with $Mn(OAc)_2$ (entry 5). Use of 10 mol % of catalyst affords lower yield (entry 6), while the presence of cobalt is essential (entry 7). Temperatures less than 100 °C afford lowered yields (entry 8).

Table 1. Optimization of Reaction Conditions[a]



entry	solvent	oxidant	base	yield of **2**, %
1	CF_3CH_2OH	$Mn(OAc)_2/O_2$	Na_2CO_3	12
2	EtOH	$Mn(OAc)_2/O_2$	Na_2CO_3	97
3	EtOH	$Mn(OAc)_2/O_2$	NaOPiv	53
4	EtOH	$Mn(OAc)_2$/air	Na_2CO_3	70
5	EtOH	$Mn(OAc)_3{\cdot}2H_2O$/air	Na_2CO_3	40
6[b]	EtOH	$Mn(OAc)_2/O_2$	Na_2CO_3	49
7[c]	EtOH	$Mn(OAc)_2/O_2$	Na_2CO_3	NR
8[d]	EtOH	$Mn(OAc)_2/O_2$	Na_2CO_3	8
9[e]	EtOH	$Mn(OAc)_2$	Na_2CO_3	NR

[a]Amide (0.1 mmol), oxidant (0.1 mmol), $Co(acac)_2$ (0.05 mmol), base (0.1 mmol), solvent (1 mL), Q = quinolin-8-yl. Yields determined by NMR of crude reaction mixtures, with 1,1,2-trichloroethane as internal standard. [b]$Co(acac)_2$ (10 mol %). [c]No $Co(acac)_2$. [d]Reaction temperature = 60 °C. [e]Deoxygenated EtOH.

Reaction scope is presented in Table 2. Aminoquinoline benzamide (entry 1) affords dimerization product in 83% yield. Amides possessing electron-withdrawing (entries 4−8, 10, and 11) as well as electron-releasing substituents (entries 2, 3, 9, and 12) are reactive. While amides substituted at 3- and 4-positions afford products in high yields, substitution at the 2-position results in lower yields (entries 3 and 7). Similar to other high-valent cobalt-catalyzed C−H functionalization reactions,[10a−c]

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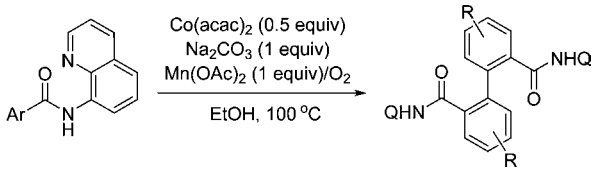
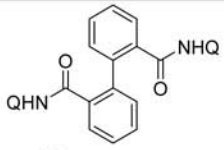
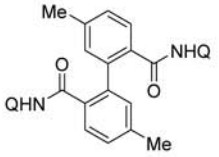
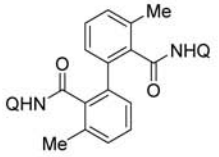
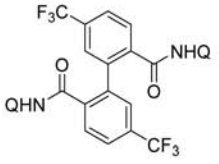
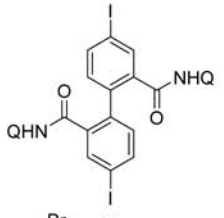
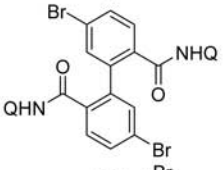
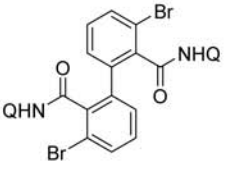
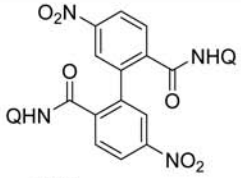
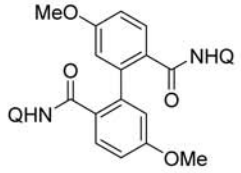
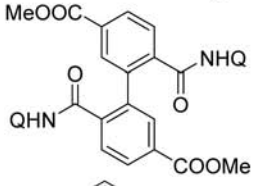
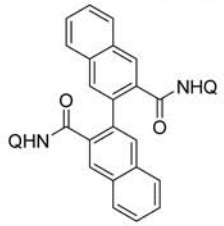
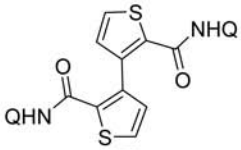
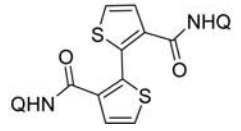
Table 2. Dimerization of Aminoquinoline Benzamides[a]



entry	Ar	product	yield, %
1	C_6H_5		83
2	4-MeC_6H_4		76
3	2-MeC_6H_4		37
4	4-$CF_3C_6H_4$		80
5	3-IC_6H_4		71
6	4-BrC_6H_4		71
7	2-BrC_6H_4		54
8[b]	4-$NO_2C_6H_4$		83
9	4-$MeOC_6H_4$		91
10	4-$CF_3OC_6H_4$		46
11[c]	4-$MeO_2CC_6H_4$		73
12	2-Naphthyl		73
13	2-Thiophenyl		71
14	3-Thiophenyl		75

[a]Amide (1 mmol), $Co(acac)_2$ (0.5 mmol), $Mn(OAc)_2$ (1 mmol), Na_2CO_3 (1 mmol), EtOH (5 mL). Yields are isolated yields. Please see Supporting Information for details. [b]Reaction under air. [c]Reaction was performed in MeOH (5 mL).

high functional group tolerance is observed. Iodo (entry 5), bromo (entries 6 and 7), nitro (entry 8), and ester (entry 11) substituents are tolerated. Heterocyclic substances, such as aminoquinoline thiophenecarboxylic acid amides, are reactive and afford bithiophenedicarboxylic acid derivatives in high yields (entries 13 and 14). In all cases, only one isomer of product was obtained.

It would be useful to selectively cross-couple two different aminoquinoline benzamides. A 1/1 mixture if amides **3** and **4** was reacted in the presence of 1.5 equiv of $Co(acac)_2$. The analysis of the reaction mixture showed that a 0.1/1/0.6 ratio of three possible coupling products **6**, **7**, and **8** was formed, with predominant formation of the cross-coupled product **7** (Scheme 1). Compound **7** was isolated in an acceptable 52% yield. Similarly, *p*-methoxybenzamide **3** was coupled with *m*-iodobenzamide **5** to afford a mixture of three coupling products **9**, **10**, and **8** in 0.2/1/0.5 ratio, with desired cross-coupling product **10** formed predominately. Compound **10** was isolated in 46% yield (Scheme 1). These experiments show that cross-coupling of

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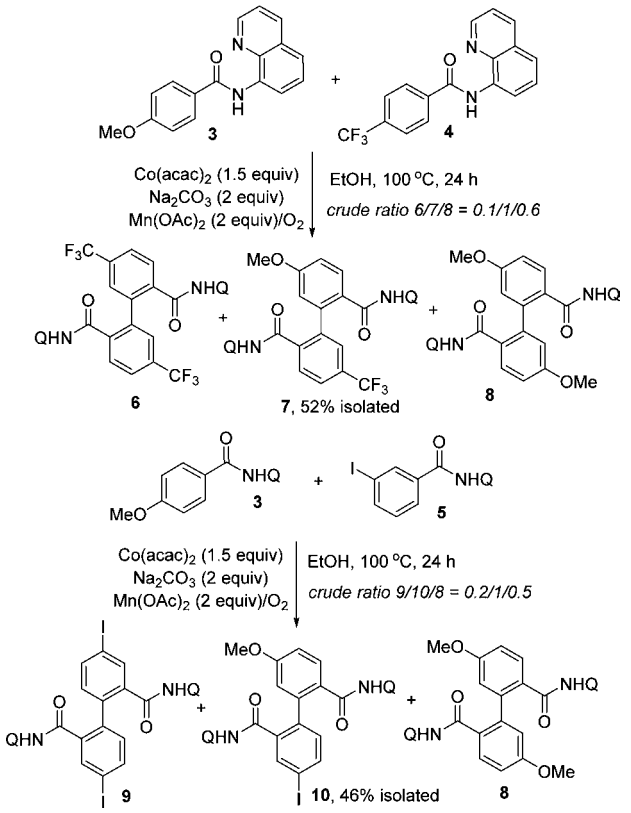
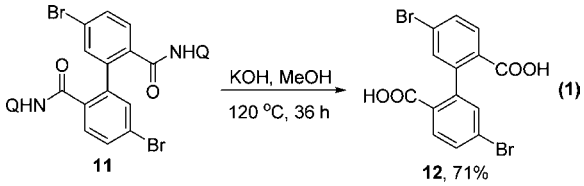
Scheme 1. Cross-Coupling of Aminoquinoline Benzamides



electronically dissimilar aminoquinoline benzamides occurs with some selectivity, and synthetically viable yields of heterocoupling products can be obtained.

The directing group can be removed by base-promoted hydrolysis of the amides (eq 1). Thus, dibromo amide **11** was heated in methanol with KOH to afford a 71% yield of 5,5′-dibromo-[1,1′-biphenyl]-2,2′-dicarboxylic acid.



In conclusion, we have developed a method for directed, dehydrogenative cobalt-promoted dimerization of aminoquinoline benzamides. Reactions proceed in ethanol solvent in the presence of $Mn(OAc)_2$ cocatalyst and Na_2CO_3 base and use oxygen as a terminal oxidant. The reactions are functional-group-tolerant, with bromo, iodo, nitro, ether, and ester moieties compatible with the reaction conditions. Cross-coupling of aminoquinoline benzamides proceeds with modest yields and selectivities if electronically dissimilar amides are used. Future directions of the work involve mechanistic studies of the dimerization and isolation of reaction intermediates.

■ ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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