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Rhodium-Catalyzed Decarbonylative C−H Arylation of 2-Aryloxybenzoic Acids Leading to Dibenzofuran Derivatives

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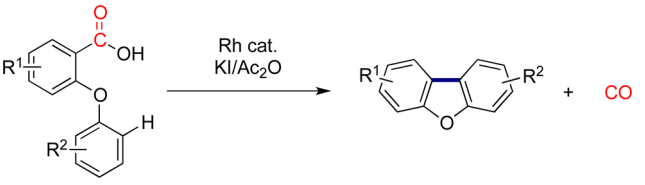
ABSTRACT



Rhodium-catalyzed intramolecular C−H arylation of 2-aryloxybenzoic acids proceeded accompanied by decarbonylation to give dibenzofuran derivatives in high yields. The present reaction is widely applicable to substrates bearing various functionalities.

Dibenzofurans have attracted considerable attention in biological and material sciences with wide ranging pharmaceutical activities as well as optical and electronic properties.[1] Thus, a number of synthetic strategies have been reported for the construction of these ring systems.[2] Among the repertoire of methods for the synthesis of dibenzofurans, palladium-catalyzed intramolecular cyclization reactions have emerged as promising methods for the synthesis of structurally diverse dibenzofurans, including intramolecular C−H arylation of 1-halo-2-phenoxybenzenes,[3] dehydrogenative cyclization of diphenyl ethers,[4] and oxidative C−O cyclization of 2-arylphenols.[5]

The use of carboxylic acids as a carbon source for transition-metal-catalyzed reactions is a rapidly growing area of research.[6,7] Recently, Crabtree[8] and Glorius[9] independently reported the palladium-catalyzed *decarboxylative* C−H arylation of *ortho*-aryloxybenzoic acids (Scheme 1, eq 1). However, this type of reaction requires large amounts of silver salts as oxidants and high loadings (15 mol %) of the palladium catalyst.[9] A recent report from the Shen group also employed a palladium-catalyzed *decarboxylative* cyclization. In this case, bromoarenes are used for the secondary reaction site and bromine serves as the leaving

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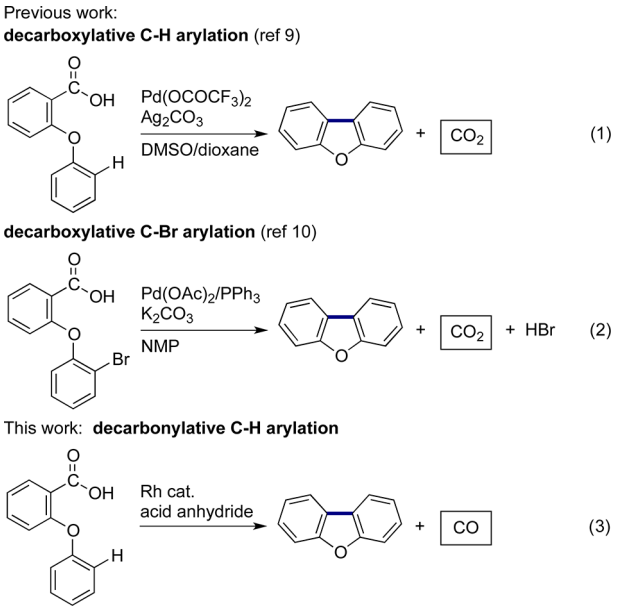
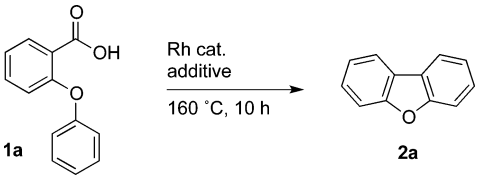
functionality (Scheme 1, eq 2).[10] Our approach uses *ortho*-aryloxybenzoic acids for the synthesis of dibenzofurans, but relies upon a *decarbonylative* C−H arylation, and gives the desired product in high yield, with a low catalyst loading, without the need for other oxidants.[11] Thus herein, we report the first example of *decarbonylative* intramolecular C−H arylation of 2-aryloxybenzoic acids, which gives high yields of dibenzofurans using rhodium catalysis (Scheme 1, eq 3).[12] Importantly, the reaction takes place with high chemoselectivity and functional group compatibility including aryl halogen bonds.

Scheme 1. One Carbon Degradation Strategies for the Synthesis of Dibenzofurans from 2-Aryloxybenzoic Acids



After a survey of a variety of transition-metal catalysts for the conversion of 2-phenoxybenzoic acid (**1a**) to dibenzofuran (**2a**), we found that the catalyst system employing rhodium complexes could attain the envisaged transformation (Table 1). No reaction took place, when **1a** was heated at 160 °C for 10 h in the presence of a catalytic amount (2.5 mol %) of $[RhCl(CO)_2]_2$ (entry 1). However, the use of Ac_2O (300 mol %) as an additive gave the desired dibenzofuran (**2a**) in 20% yield (entry 2). Although addition of KI alone did not promote the reaction (entry 3), the addition of both Ac_2O and KI dramatically improved the product yield to 74% (entry 4).[7] When $[RhI(CO)_2]_2$ was used as a catalyst without the addition of KI, a similarly good result was obtained (entry 5), suggesting that KI caused the in situ ligand exchange on rhodium between Cl and I.[13] $[RhCl(cod)]_2$ (cod = 1,5-cyclooctadiene), $Rh(acac)(CO)_2$ (acac = acetylacetonate), and Rh(acac)(cod) also showed good catalytic activity (entries 6−8). Among them Rh(acac)-(cod) exhibited the highest catalytic activity, affording **2a** in 91% yield (entry 8). The decarbonylative arylation reaction proceeded smoothly even with a 1 mol % catalyst with a longer reaction time (entry 9).

Table 1. Optimization of Reaction Conditions[a]



entry	Rh cat. (mol %)	additive (mol %)	yield (%)[b]
1	$[RhCl(CO)_2]_2$ (2.5)	none	0
2	$[RhCl(CO)_2]_2$ (2.5)	Ac_2O (300)	20
3	$[RhCl(CO)_2]_2$ (2.5)	KI (50)	0
4	$[RhCl(CO)_2]_2$ (2.5)	Ac_2O (300), KI (50)	74
5	$[RhI(CO)_2]_2$ (2.5)	Ac_2O (300)	79
6	$[RhCl(cod)]_2$ (2.5)	Ac_2O (300), KI (50)	77[c]
7	$Rh(acac)(CO)_2$ (5)	Ac_2O (300), KI (50)	87
8	$Rh(acac)(cod)]_2$ (5)	Ac_2O (300), KI (50)	91[c]
9[d]	$Rh(acac)(cod)]_2$ (1)	Ac_2O (300), KI (10)	81

[a] Conditions: 2-Phenoxybenzoic acid (**1a**, 0.5 mmol), Rh cat., additive, 160 °C, 10 h under an argon atmosphere. [b] Yield based on the GC internal standard technique. [c] Yield of isolated product. [d] Reaction time, 20 h.

With the optimized reaction conditions of entry 8 in hand, we examined the conversion of a variety of 2-aryloxybenzoic acids (**1b**−**1p**) to the corresponding dibenzofurans (**2b**−**2p**). Results are shown in Table 2. 2-Phenylbenzoic acids bearing Me or OMe at the *para* position of the phenoxy ring were converted to the desired dibenzofurans **2b** and **2c** in 87% and 90% yield, respectively. Halogen substituents, F, Cl, and Br, on the *para* position of phenoxy ring were all tolerated such that **2d**−**2f** could be obtained in good yield. The presence of a Me substituent at the *ortho* position of the phenoxy group did not affect the decarbonylative cyclization, and **2g** was obtained in 84% yield. A substrate derived from 1-naphthol gave **2h** in a 91% yield. Substrate **1i**, having an *ortho*-bromo phenoxy moiety, also reacted smoothly to afford **2i** in 72% yield. Dimethyl substituted aryloxy substrate **1j** gave the desired dibenzofuran **2j** in 70% yield. For substrates **1k** and **1l** in which there are two nonequivalent *ortho* hydrogen atoms

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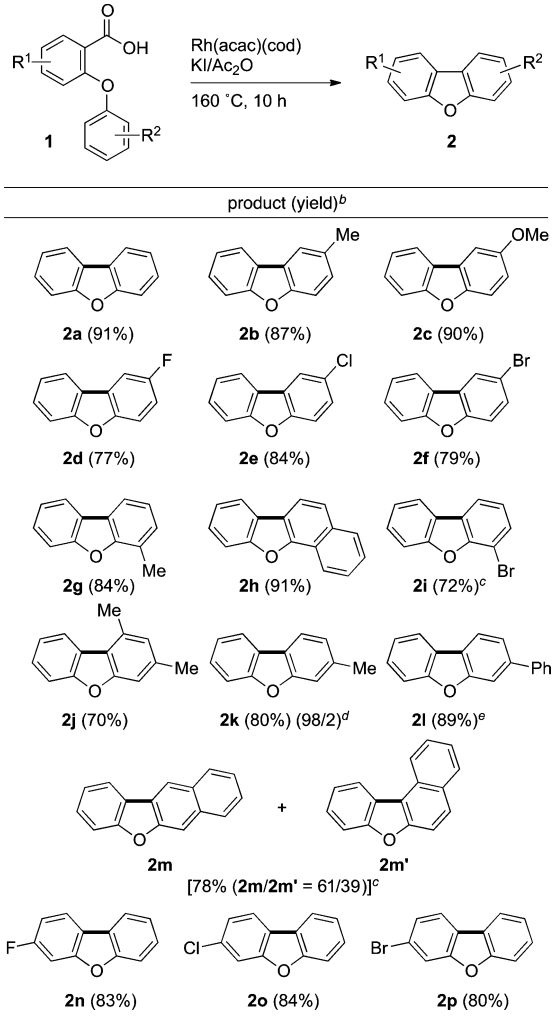
on the phenoxy ring, the reaction took place with high selectivity at the sterically less hindered position (**2k** and **2l**). However, the reaction of 2-naphthol-based benzoic acid **1m** gave a 61/39 mixture of two regioisomers **2m** and **2m′**. Halogen substituents, such as F, Cl, and Br, on the benzoic acid side are also compatible with the process to afford the corresponding dibenzofurans **2n**−**2p** in good yields.

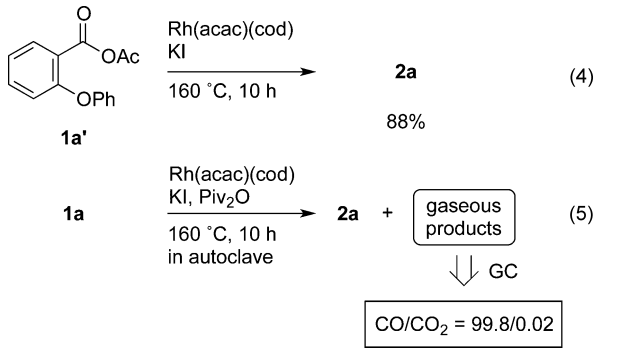
Table 2. Rh-Catalyzed Decarbonylative Intramolecular C−H Arylation of 2-Aryloxybenzoic Acids[a]



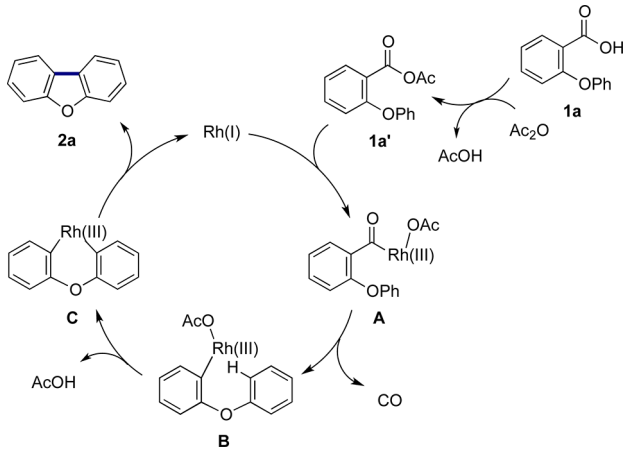
[a] Conditions: **1** (0.5 mmol), Rh(acac)(cod) (5 mol %), KI (50 mol %), Ac_2O (300 mol %), 160 °C, 10 h. [b] Isolated yield. [c] Reaction time, 20 h. [d] Ratio of regioisomers. [e] Only a single regioisomer was formed.

Having shown that the reaction proceeds with generality, we then turned to mechanistic considerations. It is likely that the present reaction proceeds *via* initial formation of acid anhydrides. Indeed, the reaction of pregenerated acid anhydride **1a′** proceeded smoothly to give **2a** in 88% yield (Scheme 2, eq 4). The formation of CO was confirmed by the GC-TDC analysis of the gas phase after the reaction, which showed CO/CO_2 = 99.8/0.02 (Scheme 2, eq 5). On the basis of these observations we propose a mechanism illustrated in Scheme 3. In the first step, the condensation reaction of carboxylic acid **1a** and Ac_2O would proceed to give the mixed anhydride **1a′**. Oxidative addition of the acyl-O bond of **1a′** into the rhodium(I) catalyst would give acylrhodium species **A**, which would then undergo decarbonylation to produce arylrhodium species **B**.[14] Intramolecular C−H activation from **B** would afford the rhodacycle **C**. Finally, reductive elimination from **C** would give **2a** and regenerate the key rhodium(I) species.

Scheme 2



Scheme 3. Plausible Reaction Mechanism



Under Shen's reaction conditions, **1i** gives dibenzofuran itself via loss of Br (Scheme 1, eq 2).[10] However under our conditions, 4-bromo-dibenzofuran (**2i**) was obtained from **1i** with the *ortho*-bromo functionality still intact. This is a considerable advantage of our procedure, since the carbon−bromine bond in the products can be subsequently converted to carbon-aryl moieties by cross-coupling reactions. For example, **2i** can be converted to **2q** by Suzuki−Miyaura coupling[15] in 95% yield (Scheme 4, eq 6).

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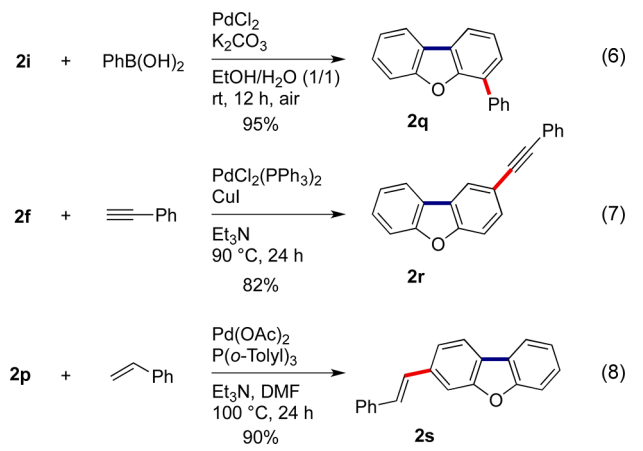
Scheme 4. Transformation of Bromo-Substituted Dibenzofurans



Moreover, **2f** can be converted to the corresponding alkynyl substituted dibenzofuran **2r** in 82% yield via a Sonogashira[16] reaction (Scheme 4, eq 7). Finally, the Mizoroki–Heck reaction of **2p** with styrene gave **2s** in 90% yield (Scheme 4, eq 8).[17]

In summary, we have developed the rhodium-catalyzed decarbonylative intramolecular C–H arylation of 2-aryloxybenzoic acids that gives high yields of dibenzofuran derivatives. The optimized conditions allow the reaction to take place with high chemoselectivity such that potential sites for further reaction, such as halogen substituents, remain unreacted. This provides considerable synthetic flexibility as illustrated in the conversion of C–Br bonds into C–C bonds via a variety of palladium-catalyzed cross-coupling reactions. Further applications of decarbonylative reactions of carboxylic acids in organic synthesis are currently under investigation in our laboratory.

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Supporting Information Available. The experimental procedure and compound characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.