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Temperature-controlled acyloxylations and hydroxylations of bromoarene by a silver salt

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ABSTRACT

Temperature-controlled selective acyloxylations and hydroxylations of bromoarene were achieved using a silver salt. Various aryl esters were synthesized at 100 °C, and the hydroxylated arene was obtained at 150 °C from silver-mediated conditions. Mechanistically, a two-step acyloxylation–hydrolysis pathway was revealed for hydroxylation of bromoarene.

The carboxylic ester is a fundamental functional group used in organic synthesis, pharmaceutical molecules, and material sciences.[1,2] Esters are prepared via direct reactions with carboxylic acids and alcohols. However, harsh conditions are required for this traditional method due to the low nucleophilicity of carboxylic acids. Various activated intermediates or catalytic conditions have been studied for the synthesis of esters from carboxylic acids and alcohols, including Mitsunobu-type azopyridine catalysts[3] and iron catalysts.[4] In addition, different types of coupling partners have been developed. The coupling reaction between carboxylic acids and aryl boronic acid molecules were first studied with copper-catalyzed Chan-Lam reactions.[5] The diaryliodonium salt was also used for the O-arylation of carboxylic acids. Olofsson and co-workers contributed significantly in this field, using metal-free coupling reactions in mild reaction conditions.[6] Aryl halides are also good reaction partners for the synthesis of aryl esters with the carboxylate anion functioning as a nucleophile to attack the carbon–halogen bond. Several catalytic conditions have been studied for this acyloxylation.[7] Lastly, acyloxylation through the sp^2 C–H bond activation has been extensively studied using various precious late transition metals.[8] Herein, we present silver-mediated acyloxylation and hydroxylation of a bromoarene molecule, which is controlled by temperature. Various aryl esters and 10-hydroxy benzo[*h*]quinoline are selectively synthesized from 10-brombenzo[*h*]quinoline with moderate to high yields.

We started our investigations with 10-bromobenzo[*h*]quinoline (**1**) as the model substrate, and it reacted with benzoic acid in the presence of various silver salts, bases, and solvents (Table 1). No reactivity was observed with various silver salts such as silver acetate, silver chloride, silver cyanide, and silver hexafluorophosphate (Table 1, entries 1–4). However, silver carbonate in the presence of potassium fluoride provided increased reactivity (entry 5). Among the various alkali fluorides, lithium fluoride and potassium fluoride displayed good yields for benzo[*h*]quinoline-10-yl-benzoate (**3a**) (Table 1, entries 5–9). In addition, the usage of potassium carbonate showed moderate yield (Table 1, entry 10), and not surprisingly the absence of either the silver salt or base resulted in no conversion for benzoxylation (Table 1, entries 11 and 12). Non-polar aromatic solvents showed moderate yields, and among them benzene provided the best result (entries 13 and 14). Lastly, the combination of silver fluoride and potassium carbonate displayed lower yields than the original combination of silver carbonate and potassium fluoride (entry 15). Finally, by replacing the combination of benzoic acid and silver carbonate to only silver benzoate, only 39% yield of **3a** was observed.

Under the optimized reaction conditions, a range of carboxylic acids were tested with 10-bromobenzo[*h*]quinoline (**1**, Scheme 1). Interestingly, the steric hindrance of carboxylic acids did not diminish the reactivity of acyloxylation. For example, 2-methylbenzoic acid (e.g., *o*-toluic acid) showed better yield than *p*-toluic acid (**3b** for 79% and **3d** for 16% in Scheme 1). Additionally, other *ortho*-substituted benzoic acids (MeO, Cl, and Br series) showed better yield than *para*-substituted benzoic acids for the acyloxylation of **1**

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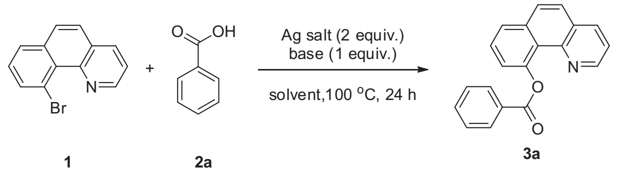
Table 1
Catalytic condition screening for acyloxylation[a]



Entry	Silver salt	Base	Solvent	Yield[b] (%)
1	AgOAc	KF	Benzene	<1%
2	AgCl	KF	Benzene	<1%
3	AgCN	KF	Benzene	<1%
4	$AgPF_6$	KF	Benzene	<1%
5	Ag_2CO_3	KF	Benzene	75
6	Ag_2CO_3	LiF	Benzene	75
7	Ag_2CO_3	NaF	Benzene	32
8	Ag_2CO_3	RbF	Benzene	55
9	Ag_2CO_3	CsF	Benzene	35
10	Ag_2CO_3	K_2CO_3	Benzene	57
11		KF	Benzene	<1%
12	Ag_2CO_3	—	Benzene	<1%
13	Ag_2CO_3	KF	Toluene	62
14	Ag_2CO_3	KF	*p*-Xylene	55
15	AgF	K_2CO_3	Benzene	44

[a] The reaction of 10-bromobenzo[*h*]quinoline (**1**, 0.15 mmol) with benzoic acid (**2a**, 0.3 mmol) was carried out in a specified solvent (0.5 mL) in the presence of silver salt (0.3 mmol) and base (0.15 mmol) at 100 °C for 24 h.

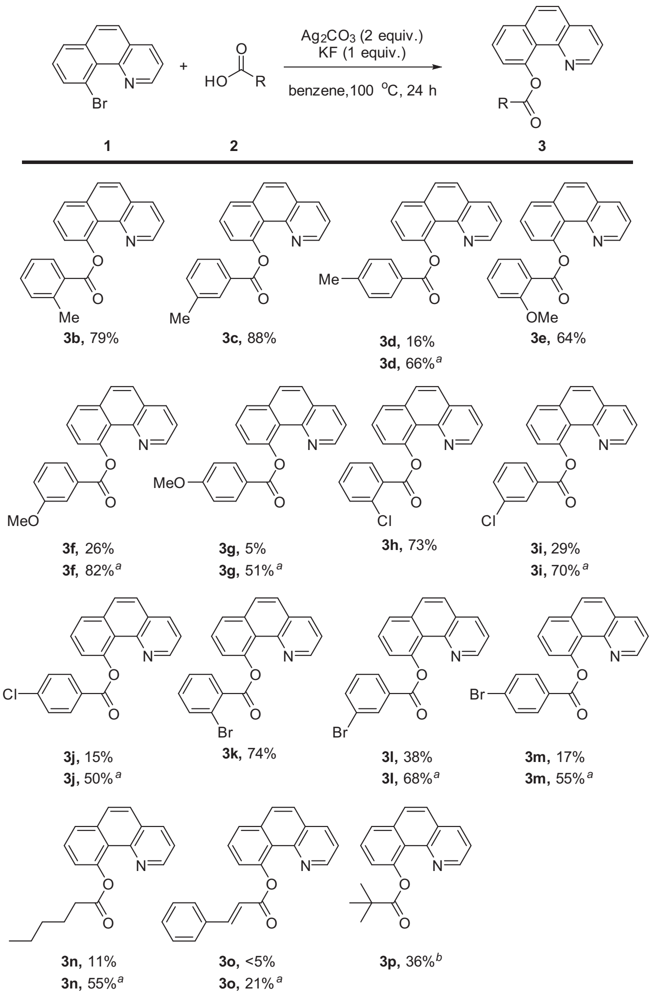
[b] Yield of isolated product is reported as an average number from at least two independent measurements.

(Scheme 1).[9] Both electron-withdrawing and -donating groups substituted in *ortho*-position of benzoic acid displayed moderate to good yields (**3b** for 79%, **3e** for 64%, **3h** for 73%, **3k** for 74%). During our investigations in this substrate scope, we found solubility issues when low yields were obtained. Some benzoic acids, including *para*-substituted benzoic acids, remained in a solid form after the reaction. Since benzoic acids are generally not highly soluble organic molecules in common non-polar aromatic solvents, aprotic polar solvents were tested. Although *N*,*N*-dimethylformamide (DMF) allowed for greater solubility, the mixture of benzene and DMF was the best combination for the acyloxylation yields. Overall, the yields of non- or less- reactivity benzoic acids were enhanced 2–10 times (Scheme 1, Condition B, benzene/DMF, 1:3, v/v ratio).[9] For examples, the yield of **3d** from *p*-toluic acid was increased from 16% to 66%, and **3g** was improved 10 times (from *p*-anisic acid) in the condition B. Lastly, the reactivity of aliphatic and conjugated carboxylic acids was investigated. Although the simplest, acetic acid showed no conversion, hexanoic acid and *trans*-cinnamic acid showed the acyloxylation product with very low yields in benzene (**3n** and **3o**). In addition, for pivalic acid, the selective conversion for the acyloxylation occurred at a lower temperature (80 °C) than the optimized condition (100 °C), and a low yield for the acyloxylated product (**3p**) was obtained. It was also found that the benzene–DMF mixture solvent enhanced the product yields in the case of long aliphatic chains and conjugated carboxylic acids (**3n** and **3o**).

The scope of the reaction of aryl halides and benzoic acids was then examined. An aryl chloride, 10-chlorobenzo[*h*]quinoline showed no reactivity using this silver-mediated system. Pyridyl-containing compounds 2-(2-bromophenyl)pyridine and 2-(2,6-dibromophenyl)pyridine were tested for acyloxylation, and displayed poor conversion under the present system. In addition to the pyridyl group, furan and thiophene moieties (e.g., 2-(2-bromophenyl)furan and 2-(2-bromophenyl)thiophene) showed no reactivity in the present system. In fact, only 10-bromobenzo[*h*]quinoline showed reactivity for this system. We also tested bromopolyarene substrates such as 1- or 2-bromonaphthalenes, 9-bromoanthracene, and 9-bromophenanthrene. Again these polyaromatic compounds showed no reactivity with this silver system. Thus, we assumed the combination of a pyridine metal binding group and the distinct electronic environment of benzo[*h*]quinoline lead to the good reactivity for acyloxylation using this silver system.

During our further investigations for acyloxylation, 10-hydroxybenzo[*h*]quinoline (**4**) was obtained as a major product when the reaction temperature was elevated (Table S1). When the reaction solvent was changed to *p*-xylene, due to the higher boiling point, only the hydroxylation of aryl bromide was observed using the combination of silver carbonate and potassium fluoride at 150 °C (Table 2). Recently, the synthesis of hydroxylated arenes has been observed using various transition metals.[10] Although palladium, copper, and iron catalysts have been widely studied for the hydroxylation of haloarenes, silver-mediated hydroxylation has not been reported to date. The reactivity of *para*-substituted benzoic acids showed slightly lower reactivities than *ortho*-substituted substrates, and similar trends were observed in the substrate scope tests (entries 1–6, Table 2). Interestingly, the aliphatic carboxylic acid, pivalic acid (e.g., 2,2,2-trimehtylacetic acid) displayed the best conversion for hydroxylation; thus reaction temperature could be decreased to 135 °C with good yield for **4** (95%, entry 7).

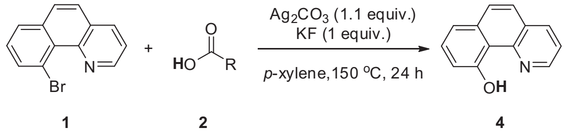
We began our mechanistic investigations with a ^{1}H NMR time study to observe reaction intermediates. At 3 h and 6 h, the



Scheme 1. Carboxylic acid substrate scopes for acyloxylation.[9]

Table 2

Silver-mediated hydroxylation of 10-bromobenzo[*h*]quinoline[a]



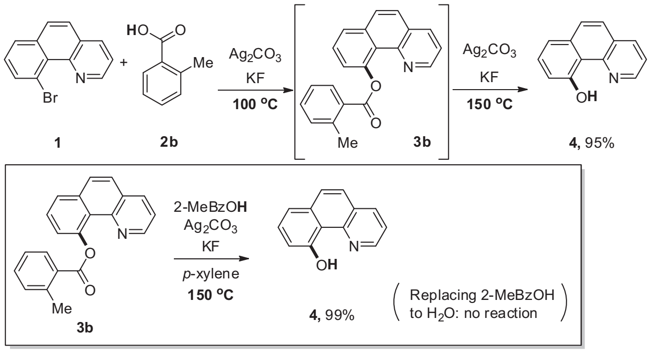
Entry	Carboxylic acids	Yield[b] (%)
1	2-Methylbenzoic acid	95
2	3-Methylbenzoic acid	93
3	4-Methylbenzoic acid	83[c]
4	2-Bromobenzoic acid	95
5	3-Bromobenzoic acid	93
6	4-Bromobenzoic acid	82[c]
7	Pivalic acid	95[d]

[a] The reaction of 10-bromobenzo[*h*]quinoline (**1**, 0.15 mmol) with carboxylic acid (**2**, 0.3 mmol) was carried out in *p*-xylene (0.5 mL) in the presence of silver carbonate (0.165 mmol) and potassium fluoride (0.15 mmol) at 150 °C for 24 h.

[b] Yield of isolated product is reported as an average number from at least two independent measurements.

[c] ^{1}H NMR yield using anisole as a internal standard.

[d] Reaction was performed at 135 °C.



Scheme 2. The 2 step pathways for acyloxylation and hydroxylation of 10-bromobenzo[*h*]quinoline.

significant CH_3 peak of acyloxylated compound **3b** was observed. The ratio between intermediate (**3b**)/final product (**4**) was 6:4 at 6 h. This ratio decreases over time with a ratio of 1:9 (**3b**:**4**) observed at 12 h. In the case of 2-methylbenzoic acid, the hydroxylation was complete at 18 h (Fig. S1 in Supporting information for detail). The kinetic NMR study suggests that acyloxylation is accelerated at high temperatures (150 °C), with benzo[*h*]quinoline fully converted to the acyloxylated product **3b** within 12 h (24 h was required at 100 °C for full conversion), and the hydrolysis of ester only occurred at 150 °C. In addition, when the reaction occurred with isolated compound **3b**, nearly quantitative isolated yield (99% of **4**) was observed under the optimized conditions along with 1.1 equiv of 2-methylbenzoic acid. This hydrolysis step could not be performed in case of water additives. The remaining benzoic acids and recovered benzoate from **3b** could accelerate the hydrolysis step (Scheme 2). Finally, these findings support that a two-step pathway, acyloxylation and following hydrolysis of ester to alcohol pathways, is most ideal. In 2013 Martin and coworkers reported a two-step copper-catalyzed benzoxylation and hydrolysis pathway on their system.[8e] For the present system, the two reactions are controlled by temperature. The lower temperature of 100 °C, only prompted the acyloxylation by the silver salt, and for the higher temperature (150 °C) the hydrolysis of ester is observed.

In summary, we have described temperature-controlled acyloxylations and hydroxylations of 10-bromobenzo[*h*]quinoline by silver salts. The reaction types and products are altered simply by changing the reaction temperature between 100 °C and 150 °C and the solvent. For our mechanistic studies, the hydroxyl compound was synthesized from the hydroxylation of the acyloxylated intermediate in silver-mediated condition. Synthetic applications of the present methodology are underway, which will be reported in due course.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2016.01.022.

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9. *Typical procedure:* The reaction of 10-bromobenzo[*h*]quinoline (**1**, 0.15 mmol) with carboxylic acid (**2**, 0.3 mmol) was carried out in a specified solvent (0.5 mL) in the presence of silver carbonate (0.3 mmol) and potassium fluoride (0.15 mmol) at 100 °C for 24 h. Yields of isolated product are reported as an average number from at least two independent measurements. [a]Condition B: benzene/DMF (1/3; v/v ratio) mixture was used as a solvent (0.5 mL). [b]Reaction was performed at 80 °C.
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