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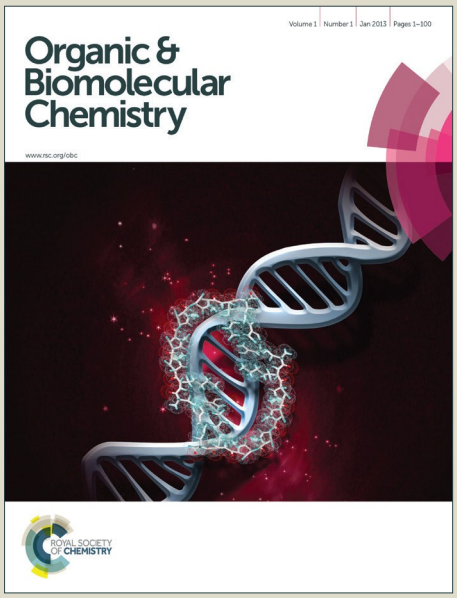

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COMMUNICATION

K_2CO_3-Promoted formation of aryl esters from primary aryl amides by acyl-acyl exchange process

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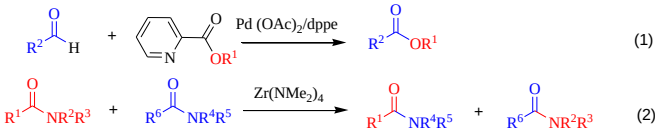
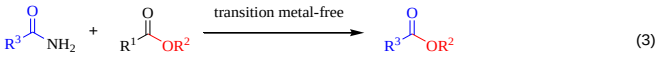
A new acyl-acyl exchange reaction has been developed for the formation of aryl esters from primary aryl amides. The reaction could occur under mild reaction conditions with the catalytic quantities of K_2CO_3, and could afford moderate to good yields of desired products.

Esters are one of the most prevalent and important functional groups abundant in both naturally occurring and synthetic organic compounds.[1] Conventional methods for preparation of the esters use carboxylic acids and their derivatives (mainly acid chloride or acid anhydride) as the acylating reagents through the condensation with alcohols. However, this method is commonly limited due to the unstability of carboxylic acid derivatives. Another protocol is the transesterification between esters and alcohols in the presence of strong acids or bases.[2, 3] Over the past decades, several new Lewis acid catalysts, such as $Y_5(O^iPr)_{13}O$ [4], $Zn_4(OCOCF_3)_6O$ [5], $La(O^iPr)_3$ [6], $Co_2(OCO^tBu)_2$ [7] and NHC (*N*-heterocyclic carbine)[8], were developed for transesterification.[9] Recently, a challenging and underdeveloped methodology has also been explored for the synthesis of esters, in which the notorious stable amides were cleaved by alcohols to give esters. [10, 11] For example, Mashima et al demonstrated Zinc-catalyzed esterification of β-hydroxyethylamides through amide bond cleavage by alcohol. [10a] The acyl-acyl exchange reaction may be a potentially valuable progress for the preparation of esters as well. For example, Huang et al reported Pd-catalyzed acyl-acyl exchange between *N*-heterocyclic aromatic esters and aldehydes for the synthesis of esters. (Scheme 1, Eq 1).[12a, 13] In 2009, Gellman et al achieved acyl-acyl exchange between amides and amides using Zr- and Ha-amido complexes as the catalyst (Scheme 1, Eq 2). [14] These works inspired us to consider acyl-acyl exchange between amides and esters. To the best of our knowledge, no relevant work was reported. Herein, we want to report a acyl-acyl exchange reaction between aryl esters and primary aryl amides (Scheme 1, Eq 3). The reaction is general, efficient, and environmentally benign for the synthesis of various aryl esters.

Previous works:



This work:



Scheme 1 Acyl-acyl exchange reaction

Initially, the inexpensive copper salts were used as the catalysts to attempt the acyl-acyl exchange reactions between aryl esters and primary aryl amides. when a toluene solution containing 0.25mmol of 2-naphthyl pivalate **1a**, 0.5 mmol of 4-methoxybenzamide **2a**, 0.01 mmol of CuI and 0.02 mmol of 1,10-phenanthroline was refluxed in the presence of 2 equiv of $K_3PO_4{\cdot}3H_2O$ for 12 h. (See SI). Pleasingly, a small amount of acyl-acyl exchange product **3aa** was observed. After further screening of various factors, we discovered the base was extremely crucial. If no base was added to the solution, no desired product was generated. Surprisingly, the reaction could be promoted smoothly only using the base without transition metal catalysts. Subsequently, several common bases were screened for the optimal reaction condition in absence of any transition metal, and the results are showed in Table 1(for details, see SI). Among them, K_3CO_3 proved to be best to give the acyl-acyl exchange product **3aa** in 60% yield (Table 1, entry 4). Although, *t*-BuOK and *t*-BuOLi were also effective for this transformation, only the low yields of desired products were isolated (Table 1, entries 1-2). When LiOAc, NaOAc and KF were used as the bases, no product was obtained (Table 1, entries 5-7). Solvents had a very important influence on the reaction. Other solvents, such as 1,4-dioxane or DMF other than toluene, were ineffective on this exchange

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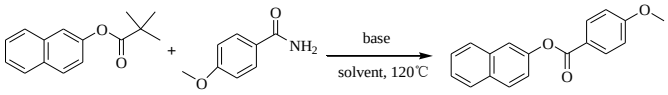
reaction (Table 1, entries 8-9, for details, see SI). In addition, the amount of the base was also investigated. The better result was afforded only using catalytic amount of K_2CO_3, possibly due to the decomposition of 2-naphthyl pivalate **1a** and product ester in the presence of large excess of base (Table 1, compare entries 4 with 11). Obviously, we have developed a new transition metal-free catalytic method for the synthesis of aryl esters.

We also examined the possibility of activating alternative acyl C-O bonds, which have been successfully exchanged in the presence of catalytic amount of K_2CO_3 (Table 2). PA naphthol derivative showed the similar reactive as privalate **1a** under the optimized reaction condition and resulted in a 58% yield of aryl ester **3aa** (Table 2, entry 2). In the reaction of 2-naphthyl acetate and benzoate, 46% and 35% yields of the desired products were obtained, respectively (Table 2, entries 3-4). Furthermore, the benzamide as the corresponding exchange product was isolated in the reaction of 2-naphthyl benzoate with 4-methoxybenzamide, which confirmed that this reaction was accomplished through the acyl-acyl exchange process (for details see SI). Five member heterocyclic 2-furoyl and 2-thenoyl naphthol were also attempted, yields were substantially less than with privalate **1a** (Table 2, entries 5-6). Notably, Sulfonyl naphthol derivative and 2-Napthylmethyl ether were not suitable substrates for this acyl-acyl exchange reaction and failed to react at all (Table 2, entries 7-8).

Under the optimized condition in our hand (Table1, entry 11), the scope of phenolic ester derivatives were explored to examine the generality of this acyl-acyl exchange reaction. Various desired aryl esters were formed in satisfied yields (scheme 1). The results indicated that the reaction could tolerate sorts of functional groups, such as methoxyl, chloro, bromo, fluoro, nitro and acetyl groups. The substituents on the benzene rings of phenolic esters had a certain effect on the yields of the desired products. When The substituents were strong electron-withdrawing groups, the reaction was either difficultly promoted or prevented. For example, when 4-acetylphenyl pivalate **1f** was used as the starting material to react with 4-methoxybenzamide, the desired exchanged product **3fa** was obtained only in 39% yield. Notably, no desired product **3ka** was isolated when 4-nitrophenyl pivalate with a stronger electron-withdrawing group was used. The position of the substituents on the benzene rings of phenolic esters had effects on the reaction yields. When the substituents were located at the meta-position, the yields were decreased significantly (scheme 1, compare **3ca** with **3ea**

Table 1. Optimization of the acyl-acyl exchange Reaction Condition [a]

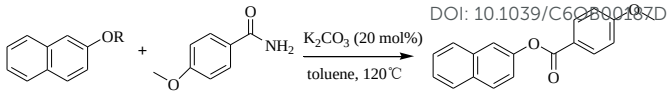


1a 2a 3aa

Entry	Base.	Solvent	Yield (%) [b]
1	*t*-BuOLi	toluene	52
2	*t*-BuOK	toluene	33
3	$K_3PO_4{\cdot}3H_2O$	toluene	18
4	K_2CO_3	toluene	60
5	LiOAc	toluene	trace
6	NaOAc	toluene	0
7	KF	toluene	0
8	K_2CO_3	1,4-dioxane	0
9	K_2CO_3	DMF	< 5
10	K_2CO_3	toluene	72 [c]
11	K_2CO_3	toluene	82 [d]

[a] Condition: **1a** (0.25 mmol), **2a** (0.50 mmol), base (2equiv), solvent (2.0 mL), 120℃, 12h. [b] Isolated yield. [c] 1 equiv of K_2CO_3 was used. [d] 20 mol % of K_2CO_3 was used.

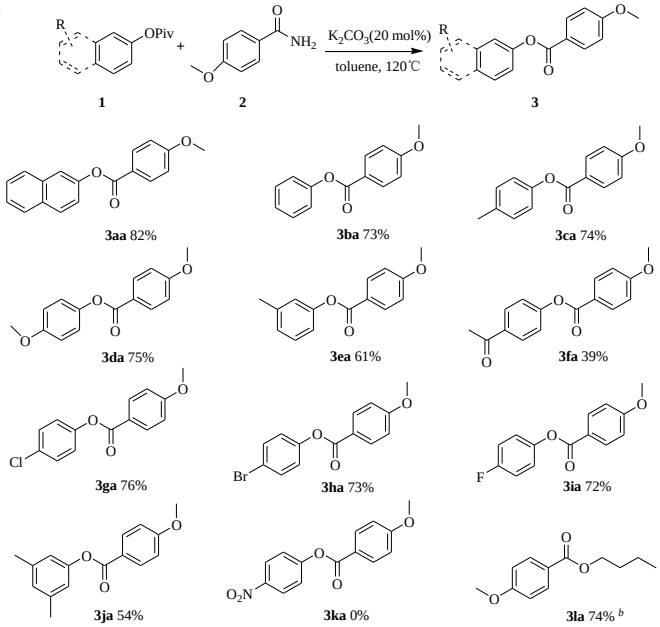
Table 2. Various Oxygen Functional Groups [a]



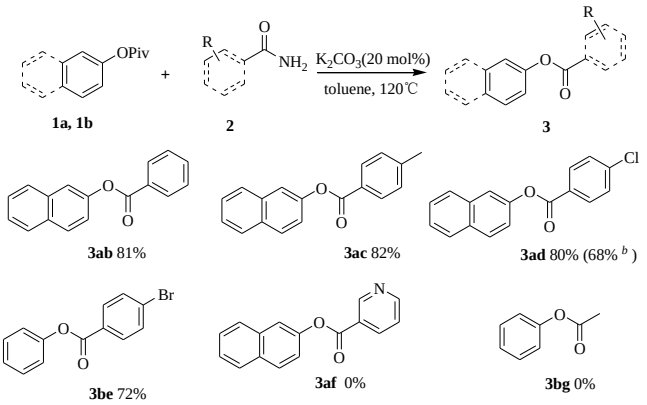
1a, 1A-1G 2a 3aa

Entry	R	Yield (%) [b]
1	Piv (1a)	82
2 [c]	PA (1A)	58
3	Ac (1B)	46
4	Bz (1C)	35
5	2-Furoyl (1D)	53
6	2-Thenoyl (1E)	12
7	Ts (1F)	0
8	Me (1G)	0

[a] Condition: **1** (0.25 mmol), **2a** (0.50 mmol), K_2CO_3 (20 mol %), toluene (2.0 mL), 120℃, 12h. [b] Isolated yield. [c] PA = 2-Pyridinecarboxyl.



Scheme 1. K_2CO_3-Promoted acyl-acyl exchange reaction for the synthesis of the desired products **3**. A mixture of **1** (0.25 mmol), 4-methoxybenzamide **2** (0.50 mmol) and K_2CO_3 (20 mol%) in toluene was stirred at 120℃ for 12 h; Yields of isolated products are given. [b] Butyl picolinate was used as the substrate.



Scheme 2. Scope of the primary amides. Yields of isolated products are given. [b] The naphthalen-2-yl picolinate was used as the substrate.

or **3ja**). The ortho-substituted aryl esters afforded the lower yields of products possibly due to the large steric hindrance. A heterocyclic aromatic ester was also tried and suitable for this acyl-acyl exchange reaction, and could give rise to the desired product **3la** in a satisfied yield. When the unprotected 2-naphthol was used instead of 2-naphthyl pivalate under the standard reaction conditions, no desired product was observed (see SI).

In another set of experiments, we selected various primary amides as the acyl reagents to check this methodology (Scheme 2). Several popular substituents, such as methyl, chloro, and bromo groups, were very well compatible under the optimized condition, and almost had no effect on the yields of the desired acyl-exchanged products. Obviously, when nicotinamide was used as the reactive substrate, no desired product **3af** was obtained possibly because of strong electron-withdrawing nature of the pyridine. In addition, aliphatic amide did not accomplish this transformation (Scheme 2, **3bg**). Other amides, such as secondary and tertiary amides other than primary amides, were not applicable for the current conditions (see SI).

Conclusions

In conclusion, we have explored an effective method for the formation of aryl esters by acyl-acyl exchange reactions only utilizing catalytic quantities of K_2CO_3 without the use of any transition metal catalysts. The reaction could proceed smoothly under mild conditions to give the desired aryl esters in satisfactory yields, and tolerate various functionalities, such as methoxy, fluoro, chloro and bromo groups. Further studies on expanding the scope of the substrates and on detailed reaction mechanism are in progress.

Acknowledgements

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