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Na_2CO_3-Catalyzed *O*-Acylation of Phenols for the Synthesis of Aryl Carboxylates with Use of Alkenyl Carboxylates

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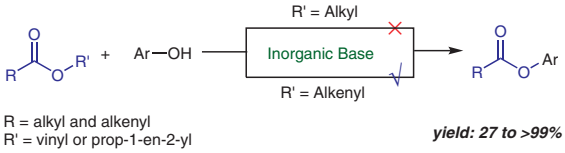

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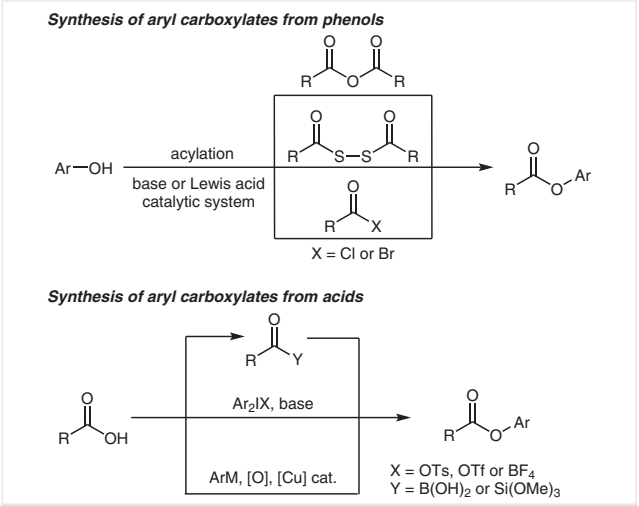
Abstract Inorganic base-catalyzed *O*-acylation of phenol and its derivatives has been developed. The procedure provides an efficient catalysis system for the preparation of aryl carboxylates with alkenyl carboxylates as acyl reagents. The reaction proceeded smoothly by using Na_2CO_3 as the catalyst in MeCN to produce the corresponding aryl carboxylates in good to excellent yields.

Key words acylation, phenols, aryl carboxlates, alkenyl carboxylates, catalysis

Acylation has been employed as one of the most ubiquitous and significant technologies in organic synthesis, which further have a great value for the preparation of natural products, pharmaceuticals, and other fine chemicals. Equally important, it plays an important role in protecting group chemistry, especially in terms of amino and hydroxyl group protection.[1] Therefore, the development of convenient and efficient methods for the selective acylation of amines and alcohols has attracted considerable attention.

In the last decades, many efforts have been made in the preparation of aryl carboxylates. The normal and direct methods to obtain aryl carboxylates are acylations of phenols using acyl halides, anhydrides, and carboxylic acids as acyl reagents (Scheme 1). However, these methods have many limitations, such as poor functional group compatibility, low regioselectivity, and harsh reaction conditions. In addition, transition-metal-catalyzed C–O bond formation,[2] carbonylation,[3] C–H bond activation,[4] and esterification of arene carboxylic acids[5] are relatively new methods for the synthesis of esters. In contrast to those methods, the transesterification is also a traditional method, in which an iron catalyst and *N*-heterocyclic carbene (NHC) present the most popular catalysis systems, such as neutral and nucleophilic iron-catalyzed transesterification for the acylation of primary and secondary alcohols and thiols.[6] In 2002, Nolan's group[7] reported an NHC-catalyzed transesterification/acylation reaction of alcohols. In this work, the NHC showed excellent catalytic activity in the transesterification reaction of vinyl acetate with alcohols. However, the acylation of phenols was difficult for the synthesis of aryl carboxylates because of the low reactivity.

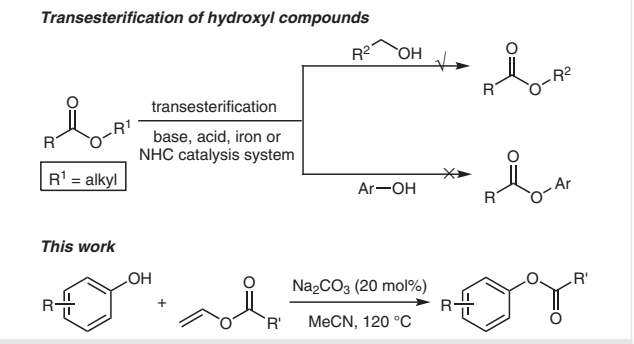


Scheme 1 The synthesis of carboxylates

The development of acylation agents is of high interest in the research on acylation reactions. Early studies on the acylation reaction using vinyl and isopropenyl acetates as acyl agents were provided by Bram and his co-workers.[8a] And Ishii's group demonstrated that $Cp^*_2Sm(THF)_2$-catalyzed acylation of alcohols and amines could be achieved under ambient conditions.[8b] Subsequently, isopropenyl acetate was utilized as an efficient acyl agent in the acylation

of tertiary alcohols mediated by an oxime ester and $Cp^*_2Sm(THF)_2$.[8c] In 2013, Toy and his colleagues developed a reusable rasta resin-TBD catalyst for the transesterification with alkenyl carboxylates as agents.[8d] In 2010, Grimme et al developed an NHC-catalyzed approach for the chemoselective acylation of alcohols for the synthesis of esters involving oxidations of aldehydes in the presence of amines.[9] Besides, diaryliodonium salts can be used for the synthesis of carboxylates. In 2011, an efficient arylation of carboxylic acids with diaryliodonium salts was provided by Olofsson's group and aryl carboxylates were obtained in high yields.[10] In 2016, Tan and his co-workers reported a general and excellent acylation reagent, diacyl disulfide, for the synthesis of esters catalyzed by DMAP [4-(*N*,*N*-dimethylamino)pyridine]. This protocol offered a promising synthetic platform on site-selective acylation of phenolic and primary aliphatic hydroxyl groups, which greatly expanded the realm of protecting group chemistry.[11] Quite recently, Bode and his co-workers[12] reported the chemoselective acylation of primary amines and amides using potassium acyltrifluoroborates as acyl agents under acidic conditions and medium to high yields were obtained.

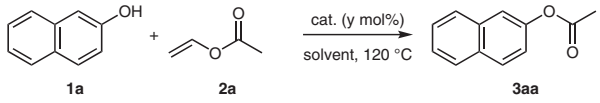
In our current work, we developed an efficient *O*-acylation of phenols using sodium carbonate (Na_2CO_3) and alkenyl carboxylates as catalyst and acyl source, respectively (Scheme 2). The results are presented herein.



Scheme 2 Na_2CO_3-catalyzed *O*-acylation of phenols

The initial experiment began with 2-naphthol (**1a**) and vinyl acetate (**2a**) as the model starting materials and sodium formate ($HCO_2Na{\cdot}2H_2O$) as the base in acetonitrile (MeCN) at 120 °C. The product naphthalen-2-yl acetate (**3aa**) was isolated in 76 and 75% yield (200 and 100 mol% $HCO_2Na{\cdot}2H_2O$, Table 1, entries 1 and 2). This result encouraged us to adhere to our initial hypothesis that vinyl esters could be utilized as acylation agents for the acylation of 2-naphthol under basic conditions. Then, the catalyst, the amount of acylation agent, solvent, and temperature were evaluated to improve the yield of the product **3aa**. The results are shown in Table 1. Triethylamine (NEt_3, entry 3), potassium carbonate (K_2CO_3, entry 4), and sodium carbonate (Na_2CO_3, entry 5) were tested as the bases. Among them, Na_2CO_3 showed a higher catalytic activity than all the others. In order to improve the yields further, the amount of Na_2CO_3 was optimized (entries 5–9), and 20 mol% Na_2CO_3 was found optimal, leading to 99% yield (entry 7). The *O*-acylation of 2-naphthol can be performed under the base-catalyzed reaction conditions; no target product was detected without use of base (entry 9). In order to test whether the use of 4.0 equivalents of **2a** was necessary, 3.0 equivalents of **2a** were added and the yield decreased to 87% (entry 10). This indicated that use of 4.0 equivalents of vinyl ester was the better dosage. Subsequently, other solvents and the temperature were evaluated. Toluene (entry 11), 1,4-dioxane (entry 12), ethanol (EtOH, entry 13), and tetrahydrofuran (THF, entry 14) were chosen as solvents in the Na_2CO_3-(20 mol%) catalyzed acylation of **1a** at 120 °C, and the yields decreased obviously (19, 45, 13, and 40%, respectively). The poor reactivities were considered to be due to the low solubility of Na_2CO_3 in other solvents. At last, the results show that the temperature has a significant effect on the *O*-acylation (entries 15 and 16) and 120 °C proved to be the best choice. Therefore, the subsequent reactions of esters **2a–h**

Table 1 Conditions Optimization for Base-Catalyzed Synthesis of Aryl Carboxylates[a]



1a 2a 3aa

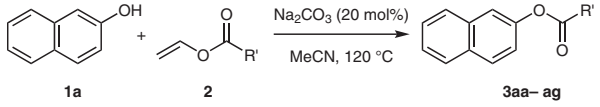
Entry	**2a** (x equiv)	Cat. (y mol%)	Solvent	Yield (%)[b]
1	4.0	$HCO_2Na{\cdot}2H_2O$ (200)	MeCN	76
2	4.0	$HCO_2Na{\cdot}2H_2O$ (100)	MeCN	75
3	4.0	NEt_3 (200)	MeCN	64
4	4.0	K_2CO_3 (100)	MeCN	74
5	4.0	Na_2CO_3 (100)	MeCN	78
6	4.0	Na_2CO_3 (50)	MeCN	88
7	4.0	Na_2CO_3 (20)	MeCN	99
8	4.0	Na_2CO_3 (10)	MeCN	82
9	4.0	–	MeCN	n.a.
10	3.0	Na_2CO_3 (20)	MeCN	87
11	4.0	Na_2CO_3 (20)	toluene	19
12	4.0	Na_2CO_3 (20)	1,4-dioxane	45
13	4.0	Na_2CO_3 (20)	EtOH	13
14	4.0	Na_2CO_3 (20)	THF	40
15[c]	4.0	Na_2CO_3 (20)	MeCN	95
16[d]	4.0	Na_2CO_3 (20)	MeCN	72

[a] Reaction conditions: **1a** (72 mg, 0.50 mmol), **2a** (x equiv), cat. (y mol%), solvent (3.0 mL), 120 °C, 24 h.
[b] Isolated yields.
[c] Carried out at 100 °C.
[d] Carried out at 80 °C.

and phenols **1a–n** were performed in the presence of Na_2CO_3 (20 mol%) and vinyl ester (4.0 equiv) as the catalyst and acylation agent, respectively, in MeCN at 120 °C.

The reactions of 2-naphthol (**1a**) and the esters **2a–h** (Table 2, entries 1–8) were conducted to screen the scope of carboxylates **2** under the optimal conditions. The results show that the alkenyl carboxylates **2a–g** can react smoothly, and moderate to high isolated yields (79–>99% yield, entries 1–7) of products **3** were obtained. When ethyl acetate was used as the acylation agent, there was no product detected and the starting materials were recovered (entry 8). The alkyl carboxylate was not applicable to the *O*-acylation of phenols, which was considered to be due to the stability of alkyl carboxylates.

Table 2 Scope of Substrate **2**[a]



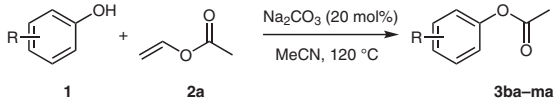
1a **2** **3aa– ag**

Entry	2	3aa–ag	Yield (%)[b]
1	**2a**	**3aa**	99
2	**2b**	**3aa**	>99
3	**2c**	**3ac**	82
4	**2d**	**3ad**	>99
5	**2e**	**3ae**	>99
6	**2f**	**3af**	86
7[c]	**2g**	**3ag**	79
8	**2h**	**3aa**	n.a.

[a] Reaction conditions: **1a** (72 mg, 0.50 mmol), **2** (2.0 mmol, 4.0 equiv), Na_2CO_3 (10.6 mg, 0.10 mmol, 20 mol%), MeCN (3.0 mL), 120 °C, 24 h.
[b] Isolated yields.
[c] 1.1 equiv **2a** was added.

Subsequently, the *O*-acylations of phenols **1b–n** with vinyl acetate (**2a**) were conducted under the optimal reaction conditions, as shown in Table 3, and the phenols **1b–k** were compatible with these reaction conditions for the preparation of aryl acetates (47–>99%, entries 1–10). In especial, the optimal conditions can be applied to the *O*-acylation of naphthalene-1,5-diol (**1c**, entry 2), pyrocatechol (**1f**, entry 5), hydroquinone (**1i**, entry 8), but with relatively lower yields (47, 77, and 79%, respectively). In order to test whether the *O*-acylation can be suitable for alcohols, 4-(hydroxymethyl)phenol (**1l**) and naphthalen-2-yl methanol (**1m**) with alcohol hydroxyl groups were subjected to the reaction conditions, and the products **3la** and **3ma** were obtained in 27 and 63% yield, respectively (entries 11 and 12). The results indicate that the optimal conditions were not suitable enough for the *O*-acylation of alcohols.

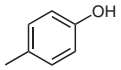
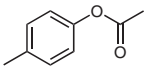
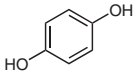
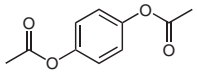
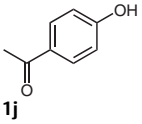
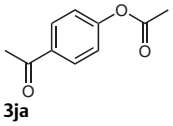
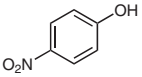
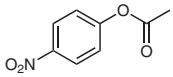
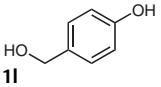
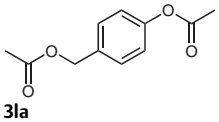
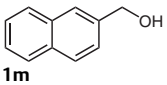
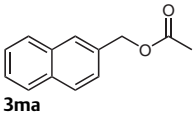
Table 3 Scope of Substrate **1**[a]



1 **2a** **3ba–ma**

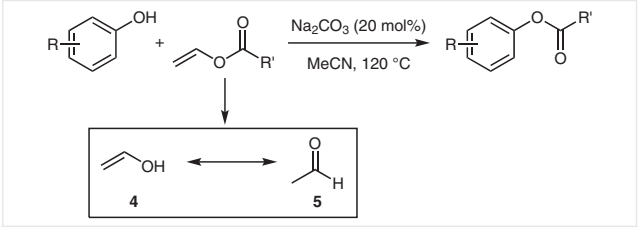
Entry	1	3ba–ma	Yield (%)[b]
1	**1b**	**3ba**	90
2[c]	**1c**	**3ca**	47
3	**1d**	**3da**	>99
4	**1e**	**3ea**	>99
5[c]	**1f**	**3fa**	77
6	**1g**	**3ga**	76

Table 3 (continued)

Entry	1	3ba–ma	Yield (%)[b]
7	 **1h**	 **3ha**	98
8[c]	 **1i**	 **3ia**	79
9	 **1j**	 **3ja**	98
10	 **1k**	 **3ka**	81
11[c]	 **1l**	 **3la**	27
12	 **1m**	 **3ma**	63

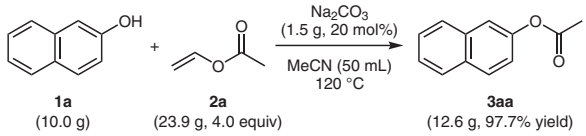
[a] Reaction conditions: **1** (0.50 mmol), **2a** (172 mg, 2.0 mmol, 4.0 equiv), Na_2CO_3 (10.6 mg, 0.10 mmol, 20 mol%), MeCN (3.0 mL), 120 °C, 24 h.
[b] Isolated yields.
[c] 8.0 equiv **2a** was added.

Based on the above results, *O*-acylation of phenols can be achieved by using alkenyl carboxylates as acyl agents but not alkyl carboxylates. The reason presumably is that the formation of by-product acetaldehyde **5** by isomerization of **4** is the driving force for the process with alkenyl carboxylates, as shown in Scheme 3. However, EtOH was produced as a by-product in the case of alkyl carboxylates and the reversed reaction inhibited the formation of aryl carboxylates.



Scheme 3 The speculated reason for *O*-acylation of phenols

To test the effect of Na_2CO_3-catalyzed *O*-acylation of phenols under scale-up conditions, 2-naphthol (**1a**, 10.0 g) was added to the reaction and 12.7 g of **3aa** was obtained with 97.7% yield (Scheme 4). The result indicates that the Na_2CO_3-catalyzed *O*-acylation of phenols for the synthesis of aryl carboxylates may be appropriate for scale-up and industrial production.



Scheme 4 The scale-up conditions for the synthesis of **3aa**

In conclusion, by using alkenyl carboxylates as acylation agents, the Na_2CO_3-catalyzed *O*-acylation of phenols was successfully achieved for the selective synthesis of aryl carboxylates with up to >99% yield.[13] The principle of these reactions provides a new strategy to develop other types of acylation reactions under convenient reaction conditions. To the best of our knowledge, this catalytic *O*-acylation of phenols for the synthesis of aryl carboxylates by using alkenyl carboxylates as acyl sources is the first example reported on such reactions.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610265.

References and Notes

(1) (a) Wuts, P. G. M.; Greene, T. W. *Protection for the Hydroxyl Group Including 1,2- and 1,3-Diols*, In *Greene's Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, **2006**, 4th ed. (b) Pearson, A. L.; Roush, W. J. *Handbook of Reagents for Organic Synthesis: Activating Agents and Protecting Groups*; John Wiley & Sons: Chichester, **1999**. (c) Sartori, G.; Ballini, R.; Bigi, F.; Bosica, G.; Maggic, R.; Righi, P. *Chem. Rev.* **2004**, *104*, 199.
(2) Thasana, N.; Worayuthakarn, R.; Kradanrat, P.; Hohn, E.; Young, L.; Ruchirawat, S. *J. Org. Chem.* **2007**, *72*, 9379.
(3) Watson, D. A.; Fan, X.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 7096.
(4) Ye, Z.; Wang, W.; Luo, F.; Zhang, S.; Cheng, J. *Org. Lett.* **2009**, *11*, 3974.
(5) (a) Wang, W.; Luo, F.; Zhang, S.; Cheng, J. *J. Org. Chem.* **2010**, *75*, 2415. (b) Zhang, L.; Zhang, G.; Zhang, M.; Cheng, J. *J. Org. Chem.* **2010**, *75*, 7472. (c) Luo, F.; Pan, C.; Qian, P.; Cheng, J. *Synthesis* **2010**, 2005.

(6) (a) Magens, S.; Plietker, B. *J. Org. Chem.* **2010**, *75*, 3715. (b) Weng, S.-S.; Ke, C.-S.; Chen, F.-K.; Lyu, Y.-F.; Lin, G.-Y. *Tetrahedron* **2011**, *67*, 1640.
(7) Grasa, G. A.; Kissling, R. M.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 3583.
(8) (a) Barry, J.; Bram, G.; Petit, A. *Tetrahedron Lett.* **1988**, *29*, 4567. (b) Takeno, M.; Kawasaki, Y.; Muromachi, Y.; Nishiyama, Y.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1996**, *61*, 3088. (c) Tashiro, D.; Kawasaki, Y.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 8141. (d) Yang, Y.-C.; Leung, D. Y. C.; Toy, P. H. *Synlett* **2013**, *24*, 1870.
(9) Sarkar, S. D.; Grimme, S.; Studer, A. *J. Am. Chem. Soc.* **2010**, *132*, 1190.
(10) Petersen, T. B.; Khan, R.; Olofsson, B. *Org. Lett.* **2011**, *13*, 3462.
(11) Liu, H.-X.; Dang, Y.-Q.; Yuan, Y.-F.; Xu, Z.-F.; Qiu, S.-X.; Tan, H.-B. *Org. Lett.* **2016**, *18*, 5584.
(12) Gálvez, A. O.; Schaack, C. P.; Noda, H.; Bode, J. W. *J. Am. Chem. Soc.* **2017**, *139*, 1826.

(13) **General Procedure for the Synthesis of Aryl Carboxylates**

A mixture of phenol **1** (0.50 mmol), Na_2CO_3 (10.6 mg, 0.10 mmol, 20 mol%), and alkenyl carboxylate (2.0 mmol, 4.0 equiv) in MeCN (3 mL) was added to a Schlenk flask (25 mL) and stirred at r.t. The mixture was stirred at 120 °C until the reaction was finished. Then, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate 20:1 to 10:1) to afford the product **3**.

Naphthalen-2-yl Acetate (3aa)

Yield: 99%, 92.8 mg, white solid, mp 70–72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.72 (m, 3 H), 7.50 (d, *J* = 2.2 Hz, 1 H), 7.45–7.37 (m, 2 H), 7.19–7.15 (m, 1 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 148.3, 133.7, 131.4, 129.4, 127.8, 127.6, 126.6, 125.7, 121.1, 118.5, 21.2 ppm. HRMS: *m*/*z* calcd for $C_{12}H_{10}O_2Na$ $[M + Na]^+$: 209.0578; found: 209.0582.