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Transition metal free oxidative esterification of alcohols with toluene

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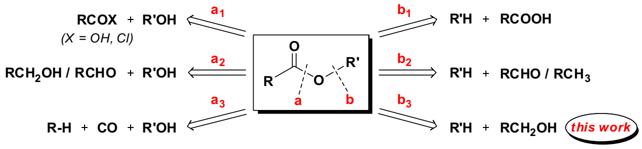
ABSTRACT

Using Bu_4NI as the catalyst and *tert*-butyl hydroperoxide as the oxidant, direct esterification of alcohols with toluene derivatives was achieved. Mechanistic investigations indicate that the alcohols are sequentially oxidized to aldehydes, carboxylic acids, and then to benzyl esters. Bu_4N^+ functions as a phasetransfer reagent and iodide catalyzes the reaction.

Carboxylic acid esters are not only among the most abundant chemicals in nature but also serve as important building blocks in organic transformations and chemical industry. They are traditionally prepared by a reaction of alcohols with carboxylic acids or activated carboxylic acid derivatives (Scheme 1, a_1) which requires multiple procedures and produces unwanted by-products.[1] Direct selective esterification of alcohols,[2] aldehydes,[3] (Scheme 1, a_2) or CO with hydrocarbons[4] (Scheme 1, a_3) by homogeneous or heterogeneous catalysts provides a promising alternative and many efforts have been devoted to achieve this transformation. Recently, several groups have reported fine works on oxidative esterification of carboxylic acids (Scheme 1, b_1)[5] with hydrocarbons via C–H bond activation. As is the same concern, it will be more attractive yet challenging to start with aldehydes,[6] alcohols, or hydrocarbons[7] (Scheme 1, b_2–b_3).

On the other hand, after the pioneering work reported by Ishihara's group,[8] where quaternary ammonium iodide was used as a highly active catalyst for oxidative cycloetherification of ketophenols, Bu_4NI catalyst combined with green oxidants (H_2O_2 or ^{t}BuOOH) has attracted extensive attention[9] for the construction of C–O,[10] C–N,[11] and C–C[12] bonds through cross-dehydrogenation coupling (CDC) reaction.[13] Herein we report on the synthesis of benzyl esters by oxidative esterification of alcohols with benzylic C–H bonds using Bu_4NI as the catalyst.

Heating a mixture of 1-naphthalenemethanol, six equivalents of oxidant *tert*-butyl hydroperoxide (TBHP, 70% aqueous solution) and 20 mol % of Bu_4NI in toluene gave 43% yield of benzyl 1-naphthoate (**1c**, Table 1, entry 1). Obviously, ester **1c** was generated from the oxidative cross-coupling reaction between the alcohol substrate 1-naphthalenemethanol and toluene solvent. No reaction occurred under one bar of oxygen and only 2% yield of 1-naphthaldehyde was observed using di-*tert*-butyl peroxide (DTBP) as the oxidant (Table 1, entries 2 and 3). The yield of the esterification product dramatically increased to 60% by adding 1.2 equiv of NaH_2PO_4 (Table 1, entry 4) and 68% yield was obtained when acetonitrile was used as the solvent (Table 1, entry 5). Prolonging the reaction time to 36 h led to a decent yield (79%; Table 1, entries 6 and 7). However, only 1–11% yields of ester **1c** were formed if Bu_4NI was replaced by Bu_4NBr or KI (Table 1, entries 8 and 9) and **1c** was not observed when iodine was used (Table 1, entry 10). In order to explore the potential application of this method, a scale-up experiment was performed and 83% isolated yield was obtained using 5 mmol of 1-naphthalenemethanol where the ester product was one gram scale (Table 1, entry 11).



Scheme 1. Pathways for synthesis of esters.

The oxidative esterification of various primary alcohols under optimum conditions is listed in Table 2. A variety of substituted benzyl alcohol derivatives were observed to form benzyl esters in toluene with good to excellent yields. Electronic effects associated

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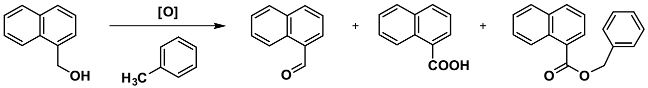
Table 1
Oxidation of 1-naphthalenemethanol[a]

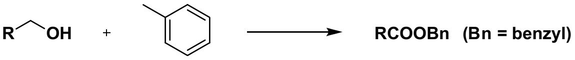


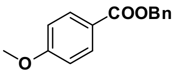
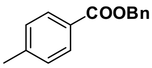
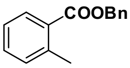
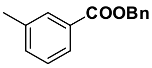
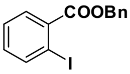
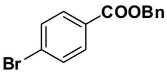
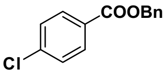
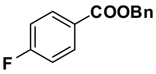
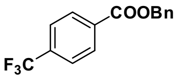
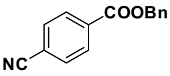
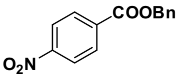
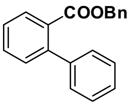
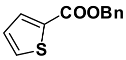
1a 1b 1c

Entry	Catalyst (mol %)	Oxidant (equiv)	Additive (equiv)	Conv[b] (%)	Yield[b] (%)		
					(**1a**)	(**1b**)	(**1c**)
1	Bu_4NI (20)	TBHP (6)	–	100	1	17	43
2	Bu_4NI (20)	O_2 (1 bar)	–	0	–	–	–
3	Bu_4NI (20)	DTBP (6)	–	2	2	–	–
4	Bu_4NI (20)	TBHP (6)	NaH_2PO_4 (1.2)	100	1	7	60
5[c]	Bu_4NI (20)	TBHP (6)	NaH_2PO_4 (1.2)	100	1	8	68
6[c,d]	Bu_4NI (20)	TBHP (6)	NaH_2PO_4 (1.2)	100	1	4	76
7[c,e]	Bu_4NI (20)	TBHP (6)	NaH_2PO_4 (1.2)	100	1	5	79
8[c,e]	Bu_4NBr (20)	TBHP (6)	NaH_2PO_4 (1.2)	91	7	51	1
9[c,e]	KI (20)	TBHP (6)	NaH_2PO_4 (1.2)	83	9	41	11
10[c,e]	I_2 (10)	TBHP (6)	NaH_2PO_4 (1.2)	29	23	6	0
11[f]	Bu_4NI (20)	TBHP (6)	NaH_2PO_4 (1.2)	100	1	2	83[g]

[a] Reaction conditions: 1-naphthalenemethanol (0.50 mmol), toluene (10 mmol), under air atmosphere, 80 °C, 12 h.
[b] GC results.
[c] CH_3CN (2 mL).
[d] 24 h.
[e] 36 h.
[f] 1-Naphthalenemethanol (5.0 mmol), toluene (100 mmol), CH_3CN (20 mL), 36 h.
[g] Isolated yield.

Table 2
Scope of alcohols[a]



 **2a**, 85%	 **2b**, 71%	 **2c**, 78%	 **2d**, 74%
 **2e**, 79%	 **2f**, 84%	 **2g**, 82%	 **2h**, 77%
 **2i**, 86%	 **2j**, 89% (87%)[b]	 **2k**, 86%	 **2l**, 80%
 **2m**, 86%			

[a] Reaction conditions: alcohol (0.50 mmol), toluene (10 mmol), NaH_2PO_4 (0.60 mmol, anhydrous), Bu_4NI (0.10 mmol), TBHP (3.0 mmol, 70% aqueous solution), MeCN (2 mL), air atmosphere, 80 °C, 36 h. GC results.
[b] Isolated yield.

with electron donating and electron withdrawing substituents on the phenyl ring showed little effect on the efficiency of the oxidation reaction. Esters **2a**–**2d** were formed in good yields without over oxidation of the methoxy and methyl groups. Halide groups were well tolerated in the system (**2e**–**2h**). 4-(Trifluoromethyl)benzyl alcohol, 4-cyanobenzyl alcohol, and 4-nitrobenzyl alcohol were all converted to esters **2i**–**2k** with excellent yields and 2-biphenylmethanol also showed pretty good yield (**2l**). The yield of 2-thiophenemethanol was 86%, indicating good tolerance of heteroatoms (**2m**).

Encouraged by the results of Table 2, the scope of hydrocarbons was also examined (Table 3). Mesitylene and xylenes were all converted to esters **3a**–**3d** in moderate to good yields without formation of multi-esters. Halogenated toluenes including 2-iodotoluene, 4-bromotoluene, 4-chlorotoluene, and 4-fluorotoluene all gave good yields of about 85% (**3e**–**3h**). Toluenes with strong