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An efficient one-pot oxidative esterification of aldehydes to carboxylic esters using $B(C_6F_5)_3$–TBHP

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ABSTRACT

A simple and efficient protocol for oxidative esterification of diverse aldehydes with alcohols was accomplished with *tert*-butyl hydroperoxide and 1 mol % of tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] to generate the corresponding esters in good to excellent yields. The present protocol represents compatibility with wide range of functional groups as well as exceptional tolerance toward acid labile protecting groups such as TBDPS, TBDMS, acetonide, and Boc.

The ester functional group is omnipresent in organic molecules and is a prevalent structural motif found in an array of drugs, dyes, polymers, agrochemicals, and natural products.[1] Traditionally, esters are prepared by the reaction of acids, acyl chlorides or anhydrides, and nitriles[2,3] with alcohols. In addition, palladium-catalyzed carbonylation of aryl halides to give carboxylic acid derivatives is another strategic and reliable tool.[4] However, these methodologies have certain limitations.[5] Recently, a potentially powerful transformation which has regained attention is oxidative esterification of aldehydes with alcohols under mild reaction conditions.[6] The traditional methods require stoichiometric amounts of heavy-metal oxidants such as $KMnO_4$,[7] CrO_3,[8] hydrogen peroxide,[9a] ozone,[9b] oxone,[9c] *N*-iodosuccinimide,[10a] sodium hypochlorite,[10b] silver carbonate on celite®,[10c] 2,3-dichloro-5,6-dicyanobenzoquinone in the presence of amberlyst,[11a] sodium metaperiodate,[11b] 1,2-dimethylindazolium,[11c] and mixtures of methane sulfonic acid and aluminum oxide[12] or transition-metal catalysts such as vanadium,[13] rhenium,[14] silver,[15] palladium,[16] ruthenium,[17] rhodium,[18] copper,[19] titanium,[20] iridium,[21] iron,[22a] nickel,[22b] zinc.[23] Also, electrochemical oxidations are utilized for the same purpose.[24] Very recently, calcium and magnesium chloride have also been used for the transformation of aldehydes to their corresponding esters.[25]

Tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] has received prominence as non-conventional, nontoxic, air-stable, water-tolerant, and thermal abiding Lewis acid.[26,27] Numerous research groups are engaged in exploring the potential of $B(C_6F_5)_3$ in modern organic synthesis, such as ring-opening of epoxides,[28a] aza-Ferrier glycosylation,[28b] hydrosilylation of imines,[29a] reduction of alcohols with silane,[29b] and hydrogenation of imines,[29c] Friedel–Crafts alkylation of activated arenes and heteroarenes,[30a] α-amidosulfones,[30a] and Sakurai allylation.[30b] Recently, $B(C_6F_5)_3$ has been exploited as the Lewis acid component in frustrated Lewis pair (FLP) chemistry to promote catalysis or to activate small molecules.[31,32]

In continuation of our research in exploiting the efficiency of $B(C_6F_5)_3$ as Lewis acid catalyst,[33] we disclose herein an oxidative esterification of a variety of aldehydes with alcohols in the presence of a catalytic amount of $B(C_6F_5)_3$ (Scheme 1).

Initially, the reaction of benzaldehyde (1 mmol) in methanol (6 mL) was carried out with 1 mol % $B(C_6F_5)_3$ and various oxidants. Table 1 reveals that when 30% w/v H_2O_2, and *m*-CPBA (1 equiv) were used as oxidants (Table 1, entries 1 and 2), the desired ester was obtained in low yields along with benzoic acid and (dimethoxymethyl) benzene as by-products. Further, we noticed that the reaction proceeded with significant yields and negligible by-products with 1 mol % $B(C_6F_5)_3$ and TBHP in decane (5.5 M) in comparison to TBHP in 90% water (Table 1, entries 3 and 4). Other oxidants benzoquinone and sodium hypochlorite (NaClO) were found ineffective for oxidative esterification with 1 mol % $B(C_6F_5)_3$ catalyst (Table 1, entries 5 and 6).

Further optimization of the oxidative esterification utilized benzaldehyde (1 mmol) in methanol (6 mL) using $B(C_6F_5)_3$ (1 mol %) as catalyst and TBHP (1 equiv) as oxidant, which yielded 25% of the corresponding ester after 30 h (Table 2, entry 1). With

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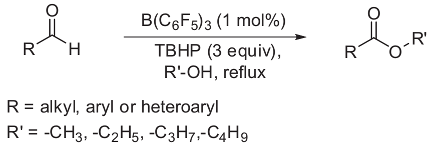


Scheme 1. General scheme for oxidative esterification of aldehydes with alcohols.

Table 1
Initial survey for oxidants[a]

Entry	Oxidant (1 equiv)	Yield[b] (%)
1	H_2O_2 aq (30%w/v)	12
2	*m*-CPBA	16
3	TBHP (5.5 M)	25
4	TBHP (90% water)	20
5	Benzoquinone	—
6	NaClO	—

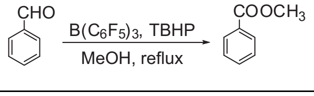
[a] $B(C_6F_5)_3$ (1 mol %), benzaldehyde (1 mmol), MeOH (6 mL), 30 h.
[b] Isolated yields.

further increase in concentration of TBHP led to an improved yield (Table 2, entry 2). By using 3 equiv of oxidant, the desired product was obtained in 86% yield in 18 h (Table 2, entry 3). No improvement in relation to yield or reaction time was observed on increasing the concentration of TBHP or catalyst (Table 2, entries 4 and 5). As a consequence, $B(C_6F_5)_3$ (1 mol %) and TBHP (3 equiv) were selected as optimized reaction conditions for oxidative esterification of aldehydes (Table 2, entry 3).

We also examined the use of different alcohols such as ethanol, propanol, butanol, 2-propanol, and *tert*-butanol in the reaction (Table 3). Under the optimized reaction conditions ethanol, propanol, and butanol all gave the corresponding esters in very good yields (Table 3, entries 2–4). 2-Propanol gave unsatisfactory yields even after longer reaction time while *tert*-butanol and benzyl alcohol gave no products (Table 3, entries 5–7). These observations are consistent with the decreased nucleophilicity or increased steric barriers of the corresponding alcohols.

With the optimized reaction conditions in hand,[34] we examined the scope and generality of present methodology using functionally diverse aldehydes. In general, both electron withdrawing and electron donating groups on the substituted aldehydes (Table 4, entries 1–8) gave excellent yields of the corresponding esters. However, as shown in Table 4, electron withdrawing groups generally increased the rate of reaction. The hydroxyl group substituted aldehydes (Table 4, entries 9 and 10) were transformed into the corresponding esters without affecting the hydroxyl groups. Further, we applied the present protocol to complex compounds which contains triple bond and ether linkage (Table 4, entries

Table 2
Optimization parameters for the oxidative esterification of benzaldehyde[a]



Entry	$B(C_6F_5)_3$ (mol %)	TBHP (equiv)	Time (h)	Yield[b] (%)
1	1	1	30	25
2	1	2	24	58
3	1	3	18	86
4	1	4	18	85
5	2	3	18	85

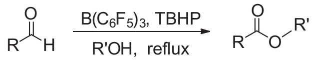
[a] $B(C_6F_5)_3$, TBHP (5.5 M in decane), benzaldehyde (1 mmol), MeOH (6 mL).
[b] Isolated yields.

Table 3
Solvent screening for oxidative esterification of benzaldehyde[a]

Entry	Solvent	Time (h)	Yield[b] (%)
1	Methanol	18	86
2	Ethanol	24	82
3	1-Propanol	30	78
4	1-Butanol	30	75
5	2-Propanol	48	20
6	*tert*-Butanol	48	—
7	Benzyl alcohol	48	—

[a] $B(C_6F_5)_3$ (1 mol %), TBHP (5.5 M in decane) (3 equiv), benzaldehyde (1 mmol).
[b] Isolated yields.

Table 4
Oxidative esterification of aldehydes with simple alcohols[a]



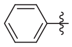
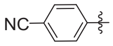
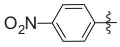
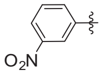
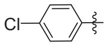
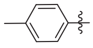
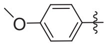
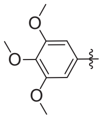
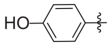
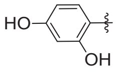
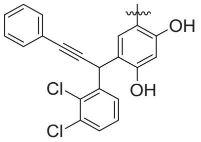
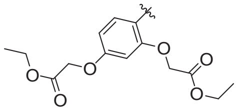
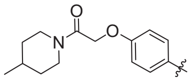
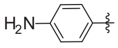
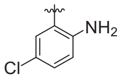
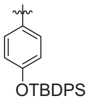
Entry	**R**	R^1	Time (h)	Product	Yield[b] (%)
1		Me	18	**1**	86
2		Me	18	**2**	92
3		Me Pr	14 30	**3a** **3b**	91 65
4		Me Me	14 18	**4a** **4b**	93 85[c]
5		Me Et	22 28	**5a** **5b**	90 76
6		Me Me	32 38	**6a** **6b**	82 75[c]
7		Me Et	32 36	**7a** **7b**	84 85
8		Me	38	**8**	88
9		Me Bu	28 36	**9a** **9b**	83 61
10		Me	36	**10**	79
11[35]		Me	38	**11**	71
12[35]		Me	34	**12**	75
13[35]		Me	24	**13**	83
14		Me	24	**14**	80
15		Me	48	**15**	72
16[35]		Me Et	24 32	**16a** **16b**	81 75

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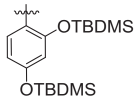
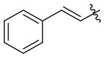
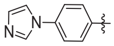
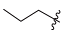
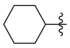
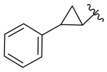
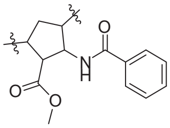
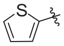
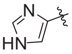
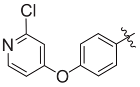
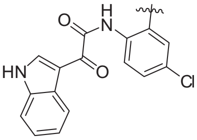
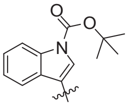
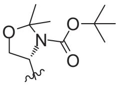
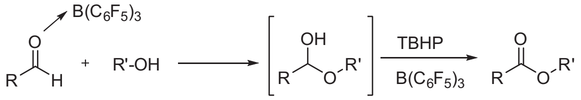
Table 4 (*continued*)

Entry	R	R^1	Time (h)	Product	Yield[b] (%)
17[35]		Me Et	24 30	**17a** **17b**	78 72
18		Me Et	20 28	**18a** **18b**	92 87
19		Me	24	**19**	90
20		Me Et	24 26	**20a** **20b**	72 61
21		Me Et	24 30	**21a** **21b**	63 54
22		Me Et	24 30	**22a** **22b**	67 51
23[35]		Me	34	**23**	68
24		Me Et	24 30	**24a** **24b**	70 62
25		Me	48	**25**	40
26[35]		Me Et	24 28	**26a** **26b**	82 75
27[35]		Me	32	**27**	73
28		Me	30	**28**	74
29		Me	30	**29**	71

[a] $B(C_6F_5)_3$ (1 mol %), TBHP (5.5 M in decane) (3 equiv), aldehyde (1 mmol).
[b] Isolated yield.
[c] Reaction performed in 5 g scale.

11–13) afforded the corresponding esters in good yields. Interestingly, 4-amino benzaldehyde and 5-chloro, 2-amino benzaldehyde (Table 4, entries 14 and 15) provided the desired esters without any observable reactivity with the amino group. The present methodology was applied to the oxidative esterification of TBDPS and TBDMS protected benzaldehydes (Table 4, entries 16 and 17). The anticipated esters were obtained in 72–81% yields without any deprotection of acid sensitive protecting groups. Cinnamaldehyde and 4-(*1H*-imidazol-1-yl) benzaldehyde (Table 4, entries 18 and 19) also afforded the corresponding esters in excellent yields. We also examined various aliphatic aldehydes (Table 4, entries 20–23) which yielded the corresponding esters in moderate yields owing to formation of the corresponding acids as by-product. In an endeavor to investigate the synthetic utility of the methodology, our new catalytic system was applied to heterocyclic aldehydes (Table 4, entries 24–27); the desired esters were afforded in low to moderate yields. To our delight, substrate with acid sensitive protecting groups such as acetonide and Boc were stable under the reaction conditions (Table 4, entries 28 and 29), all of which demonstrate the generality of out methodology.

A plausible mechanism for the oxidative esterification of aldehydes with alcohols may precede through in situ formation of alkoxy(aryl)methanol with the assistance of $B(C_6F_5)_3$, followed by *tert*-butyl hydroperoxide (TBHP) oxidation of the hydroxyl group to generate the corresponding ester (Scheme 2).



Scheme 2. Plausible mechanism.

In summary, the present protocol represents a general, facile, and reproducible strategy for the oxidative esterification of various aromatic, aliphatic, and heterocyclic aldehydes. It is noteworthy that acid sensitive protecting groups such as TBDPS, TBDMS, acetonide, and Boc were amenable to the optimized reaction conditions. The environmentally benign, low catalyst loading, low toxicity, and operationally simple procedure make protocol attractive.

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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.2015.01.033.

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34. *Typical experimental procedure:* $B(C_6F_5)_3$ (1 mol %) was added to a stirring solution of aldehyde (1 mmol) in MeOH (6 mL). After 15 min., 5.5 M TBHP in decane (3 mmol) was added slowly and reaction mixture was refluxed until the complete conversion of starting material (monitored by TLC). After completion of reaction, the methanol was evaporated in vacuo. Later, the reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with cold saturated sodium bicarbonate solution (2 × 20 mL) followed by brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure and products were purified over silica gel column chromatography in ethyl acetate/hexane. All compounds were characterized and confirmed by comparison of their spectral data and physical properties with reported literature.
35. See Supporting information.

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