

Alcohol Esterification

Efficient and Simple Approaches Towards Direct Oxidative Esterification of Alcohols

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Abstract: The present article describes novel oxidative protocols for direct esterification of alcohols. The protocols involve successful demonstrations of both “cross” and “self” esterification of a wide variety of alcohols. The cross-esterification proceeds under a simple transition-metal-free condition, containing catalytic amounts of TEMPO (2,2,6,6-tetra-

methyl-1-piperidinyloxy)/TBAB (tetra-*n*-butylammonium bromide) in combination with oxone (potassium peroxo monosulfate) as the oxidant, whereas the self-esterification is achieved through simple induction of Fe(OAc)₂/dipic (dipic = 2,6-pyridinedicarboxylic acid) as the active catalyst under an identical oxidizing environment.

Introduction

Ester groups are ubiquitous in various natural products, agrochemicals, and in commonly used synthetic scaffolds. They constitute the backbone of several drugs as well as function as the building blocks of various polymers, such as polyethylene terephthalate (PET) (Figure 1). The characteristic odors of esters have made them useful constituents for artificial fragrances

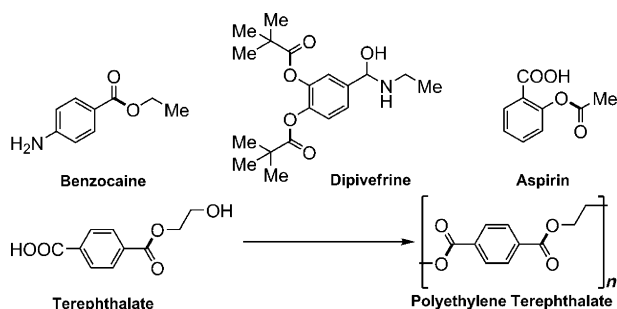


Figure 1. Ester moieties in commercially available drugs and polymers.

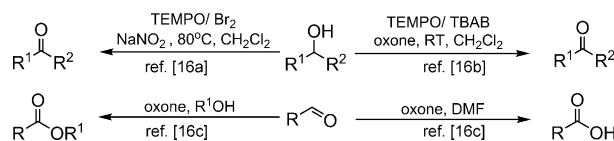
and flavoring agents of numerous products.^[1]

Traditional esterification strategies involving reactions of carboxylic acids or their derivatives with alcohols^[2] and carbonylation of aryl halides^[3] lack eco-friendliness.^[4] Though one-pot oxidative esterification of aldehydes with alcohols has gained considerable attention in the recent past,^[5] a more convenient

and straightforward approach would be the direct esterification of alcohols primarily due to their easy availability and cost-effectiveness.^[6–15] In this context, the initial approach by Milstein^[6a–c] followed by Beller^[6d] of acceptorless dehydrogenation of primary alcohols to esters by Ru-pincer complexes are commendable.^[7] Precious metals such as Ru^[8] and Rh^[9]-catalyzed esterification of primary alcohols in the presence of hydrogen acceptors^[10] were also reported. A few Ir complexes were also shown to catalyze this type of reaction.^[11] Palladium-catalyzed esterification of primary alcohols in the presence of O₂ as the terminal oxidant was reported by Lei^[12] and Beller.^[13] However, these methods made use of either an expensive Ag additive^[12a] or a combination of an expensive additive and a ligand.^[13] Very recently, Beller also demonstrated esterification of alcohols using reusable heterogeneous Co₃O₄-N@C catalysts.^[14] However, development of more sustainable reaction protocols under homogeneous conditions demand further exploration.^[15]

In this regard TEMPO-catalyzed oxidation of alcohols to aldehydes and ketones in the presence of either NaNO₂ or oxone as the oxidant was reported by Hu^[16a] and Bolm (Scheme 1).^[16b] Furthermore, Borhan^[16c] reported oxidation of aldehydes to esters and acids using oxone as the sole oxidant (Scheme 1).^[17]

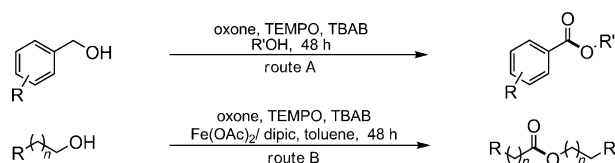
These studies have been the incentive for the present article, in which we demonstrate a catalytic system under transition-metal-free conditions for the direct esterification of a wide variety of alcohols in the presence of oxone and catalytic amounts of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy)^[18–20] and TBAB



Scheme 1. Previous reports on metal free oxidation of alcohols and aldehydes.

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Scheme 2. Present protocols on direct oxidative esterification of primary alcohols.

(tetra-*n*-butylammonium bromide), leading to selective “cross” esterification products (Scheme 2, route A). The “self” esterification of alcohols can however be achieved in the presence of $\text{Fe}(\text{OAc})_2$ in combination with 2,6-pyridinedicarboxylic acid (dipic) as the active catalytic species (Scheme 2, route B)^[21–23] under a suitable oxidizing environment.

To the best of our knowledge, the present article highlights the first example of a transition-metal-free direct “cross” esterification, as well as iron-mediated “self” esterification of alcohols using cheap, non-toxic, and stable oxone as the oxidant. This, in essence, makes the present protocols more appealing from both ecological and economical points of view.

Results and Discussion

To optimize the transformation of benzyl alcohol to methylbenzoate in methanol as a model system for the direct oxidative esterification (“cross”), a variety of oxidants was initially tested (Table 1, entries 1–8). It was established that oxone in combination with a catalytic amount of TEMPO (3 mol%) and TBAB (10 mol%) resulted in the desired methylbenzoate in 90% yield (Table 1, entry 4). The presence of TEMPO and TBAB was rather crucial because the same reaction in their absence afforded methylbenzoate in only 20% yield (Table 1, entry 1). Oxone in particular played a key role in this direct oxidative transformation because, in its absence, benzyl alcohol remained completely unreacted under the present reaction conditions (Table 1, entry 2).

Toluene was employed as a solvent for the initial optimization of the “self” esterification process, that is, oxidative homocoupling of benzyl alcohol. Unlike the cross esterification process, catalytic amounts of TEMPO (2 mol%) and TBAB (8 mol%) in conjunction with a stoichiometric amount of oxone (2.2 mmol) in toluene afforded benzaldehyde as the major product (60%) along with a minor quantity of benzyl benzoate (20%) (Table 1, entry 9). Even the addition of a base (Na_2CO_3) failed to improve the yield of desired benzyl benzoate (Table 1, entry 10). Finally, transition-metal catalyzed ($\text{Fe}(\text{OAc})_2/\text{dipic}$) esterification of benzylic alcohol was realized, which led to the formation of benzyl benzoate in 86% yield (Table 1, entry 11).

Attempts of further optimization of the “self” esterification process using various metal salts in combination with bi- and tridentate ligands revealed the suitability of the $\text{Fe}(\text{OAc})_2/\text{dipic}$ system (Table 2,

entry 11) for benzyl benzoate formation (Table 2). Additionally, systematic survey of oxidants and solvents for the “self” esterification process (Table 1, entries 11–21) indicated oxone/toluene to be the best combination for this transformation (Table 1, entry 11).

Subsequently, the scope and limitations of these two protocols were evaluated using a wide variety of primary alcohols. Unsubstituted benzyl alcohol reacted smoothly with MeOH and EtOH as well as with less reactive long chain aliphatic alcohols, such as *n*-propanol, *n*-butanol, and *n*-pentanol, to give the respective esters in good to excellent yields (Table 3, **2a–2e**).

Notably, reaction of benzyl alcohol with sterically demanding and less reactive secondary alcohol (*iso*-propanol) also resulted in the respective ester in appreciable yield (**2f**). However, when the same reaction was performed in 1:1 mixture of *n*-propanol and *iso*-propanol, *n*-propyl benzoate (60%) was produced preferentially over *iso*-propyl benzoate (40%). This indicates the affinity of benzyl alcohol to react faster with a more nucleophilic primary alcohol (*n*-propanol) rather than a secondary alcohol (*iso*-propanol) under identical reaction conditions. As expected, the present reaction protocol also facilitated the

Table 1. Optimization of the critical reaction parameters.

Entry	Oxidant	Catalyst(s)	Additive/base	Solvent	Yield [%]
route A: “cross” esterification ^[a]					2a'' 2a
1	oxone	–	–	MeOH	– 20
2	–	TEMPO	TBAB	MeOH	– –
3	oxone	–	Na_2CO_3	MeOH	– 32
4	oxone	TEMPO	TBAB	MeOH	10 90
5	<i>m</i> -CPBA	TEMPO	TBAB	MeOH	20 –
6	$\text{PhI}(\text{OAc})_2$	TEMPO	TBAB	MeOH	– –
7	PhIO	TEMPO	TBAB	MeOH	30 –
8	O_2 atm	TEMPO	TBAB	MeOH	– –
route B: “self” esterification ^[b]					7a'' 7a
9	oxone	TEMPO	TBAB	toluene	60 20
10	oxone	TEMPO	TBAB/ Na_2CO_3	toluene	55 10
11	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	toluene	14 86
12	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2$	TBAB	toluene	22 20
13	<i>m</i> -CPBA	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	toluene	60 5
14	$\text{PhI}(\text{OAc})_2$	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	toluene	65 –
15	PhIO	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	toluene	58 –
16	O_2 atm	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	toluene	– –
17	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	<i>m</i> -xylene	45 5
18	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	xylene	52 10
19	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	THF	28 –
20	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	1,4-dioxane	13 –
21	oxone	$\text{TEMPO}/\text{Fe}(\text{OAc})_2/\text{L}$	TBAB	1,2-dichloroethane	6 13

[a] Benzyl alcohol (1 mmol), oxone (3 mmol), TEMPO (3 mol%), TBAB (10 mol%), 60 °C, MeOH (2 mL), 48 h. [b] Benzyl alcohol (1 mmol), $\text{Fe}(\text{OAc})_2$ (15 mol%), L (30 mol%), oxone (2.2 mmol), TEMPO (2 mol%), TBAB (8 mol%), 110 °C, toluene (2 mL), 48 h. L = 2,6-pyridinedicarboxylic acid.

Table 2. Optimization with various metal salts/ligands or metal complexes for “self” esterification of alcohols.^[a]

Entry	Metal salts/complexes	Ligands ^[b]	Conversion [%]	Yield [%] ^[c]
1	Ru ₃ (CO) ₁₂	–	95	–
2	Ru(acac) ₃	–	90	–
3	RuCl ₃ ·3 H ₂ O	trpy	90	–
4	Ru(PPh ₃) ₂ Cl ₂	PCy ₃	90	–
5	CuSO ₄ ·5 H ₂ O	dipic	70	–
6	Cu(OTf) ₂	dipic	85	22
7	Cu(OAc) ₂	dppb	30	15
8	Cu(OAc) ₂	dipic	55	40
9	Fe(Pc)	–	90	–
10	Fe(NO ₃) ₃ ·9 H ₂ O	dppb	90	15
11	Fe(OAc) ₂	dipic	> 95	90 (86)
12	Fe(OAc) ₂	pic	70	20
13	Fe(OAc) ₂	dppb	90	25
14	Fe(OAc) ₂	dppe	75	36
15	Fe(OAc) ₂	PPh ₃	76	40
16	Fe(OAc) ₂	PCy ₃	73	13
17	Fe(NO ₃) ₃ ·9 H ₂ O	PCy ₃	90	5
18	Fe(BF ₄) ₂ ·6 H ₂ O	dipic	92	–
19	Fe(SO ₄) ₂ ·7 H ₂ O	dipic	88	–
20	Fe(ClO ₄) ₂ ·6 H ₂ O	dipic	90	–

[a] Reaction conditions: catalyst (15 mol%), ligand (30 mol%), benzyl alcohol (1 mmol), oxone (2.2 equiv), TEMPO (2 mol%), TBAB (8 mol%) in toluene (2 mL), 110 °C, 48 h. See the Experimental Section for the details.

[b] Dipic = pyridine-2,6-dicarboxylic acid, pic = pyridine-2-carboxylic acid, dppb = 1,4-Bis(diphenylphosphino)butane, dppe = 1,4-Bis(diphenylphosphino)ethane, PPh₃ = triphenylphosphine, PCy₃ = Tricyclohexylphosphine, trpy = 2,2':6',2''-Terpyridine. [c] Determined by GC using *n*-decane as an internal standard. Isolated yield is given in parenthesis.

formation of cyclohexyl benzoate in a preparatively useful yield (**2g**). Excellent yields of the corresponding methyl esters with *para*- and *meta*-alkyl substituted benzyl alcohols (**2h** and **2k**) were also obtained. Reactions of *para*-alkyl substituted benzyl alcohols with higher alcohols also resulted in the respective esters in appreciable yields (**2i**, **2j**, and **2l**).

Various halogenated benzylic alcohols consistently afforded the corresponding methyl and ethyl esters in good yields without any dehalogenation process (**2m–2s**). Furthermore, the present reaction conditions successfully tolerated benzyl alcohols containing strongly electron withdrawing –NO₂ and –CF₃ groups (**2t–2v**). Though a benzyl alcohol-containing, strongly electron-donating –OMe group at the *para*-position failed to yield the desired ester^[16c], the –OMe group at the *meta*-position of the phenyl ring afforded the corresponding ester in moderate yield (**2w**). Complete conversion was observed for biphenylmethanol, producing methyl biphenyl-4-carboxylate in 92% yield (**2x**).

Notably, under the present reaction conditions aliphatic alcohols, with MeOH as solvent, also underwent direct oxidative esterification in moderate to good yields (Table 4, **4a–4c**). Reports on direct “cross” esterification of aliphatic alcohols even in the presence of metal catalysts are rather limited. This fur-

Table 3. Transition-metal-free direct oxidative “cross” esterification of alcohols.

1	2

Reaction conditions: benzylic alcohol (1 mmol), oxone (3 mmol), TEMPO (3 mol%), TBAB (10 mol%), 60 °C, MeOH (2 mL), 48 h. [a] ROH (2 mL, R = Et, *n*Pr, *i*Pr), 48 h, 75 °C. [b] R'OH (2 mL, R' = *n*Bu, *n*Pent, C₆H₁₁), 110 °C. [c] GC yields.

Table 4. Transition-metal-free direct oxidative “cross” esterification of aliphatic alcohols.^[a]

3	4

[a] Aliphatic alcohol (1 mmol), oxone (4 mmol), TEMPO (10 mol%), TBAB (20 mol%), 60 °C, MeOH (2 mL), 48 h. [b] GC Yield.

ther emphasizes the broader applicability of the present methodology.

Another intriguing feature of the present methodology was the formation of 2-hydroxyethyl benzoates and allyl benzoates from benzyl alcohol, from reactions in which ethane-1,2-diol (Table 5, **5a**) and allyl alcohol (Table 6, **6a**) were employed as solvents. Substituted benzylic alcohols (Table 5, **5b** and **5c**;

Table 5. Transition-metal-free direct oxidative “cross” esterification of benzylic alcohols with ethane-1,2-diol as the solvent.^[a]

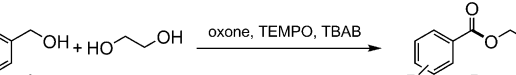
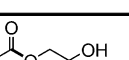
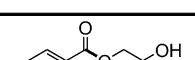
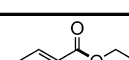
		
 5a, 92%	 5b, 95%	 5c, 88%
[a] Benzylic alcohol (1 mmol), oxone (4 mmol), TEMPO (10 mol%), TBAB (20 mol %), 110 °C, ethane-1,2-diol (2 mL), 60 h.		

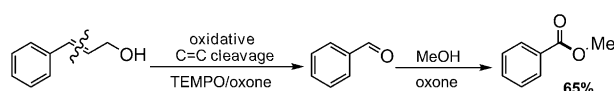
Table 6. Transition-metal-free direct oxidative “cross” esterification of benzyl alcohols with allyl alcohol as the solvent.^[a]

[a] Benzylic alcohol (1 mmol), oxone (4 mmol), TEMPO (10 mol%), TBAB (20 mol%), 90 °C, allylic alcohol (2 mL), 60 h. [b] GC yield.	

Table 6, **6b**) were also well-tolerated under the respective reaction conditions.

Interestingly, the C=C bond in the allylic position remained completely intact (Table 6, **6a** and **6b**) even under a strong oxidizing environment, which highlights the novelty of the present strategy.

The reaction of cinnamyl alcohol with MeOH as solvent afforded methyl benzoate in 65% yield instead of the expected methyl cinnamate; this can be attributed to an oxidative C=C bond cleavage process in the presence of TEMPO/oxone, leading to the initial formation of benzaldehyde, followed by esterification in a methanolic medium (Scheme 3).^[24]



Scheme 3. Oxidative C=C bond cleavage in the presence of TEMPO/oxone.

The Fe(OAc)₂/dipic-catalyzed oxidative homocoupling of primary alcohols to the corresponding “self” esters was also found to be effective for both the benzylic (Table 7, **7a–7h**) and aliphatic alcohols (Table 7, **7i–7l**).

Clean conversions to the respective esters were observed for various alkylated and halogenated benzylic alcohols (**7b**, **7c**, and **7d–7f**). In addition, *para*-substituted benzyl alcohol containing the strongly electron-withdrawing –CF₃ group was also tolerated (**7g**). Similar to the “cross” esterification process, the corresponding homocoupled ester was obtained for the *meta*-

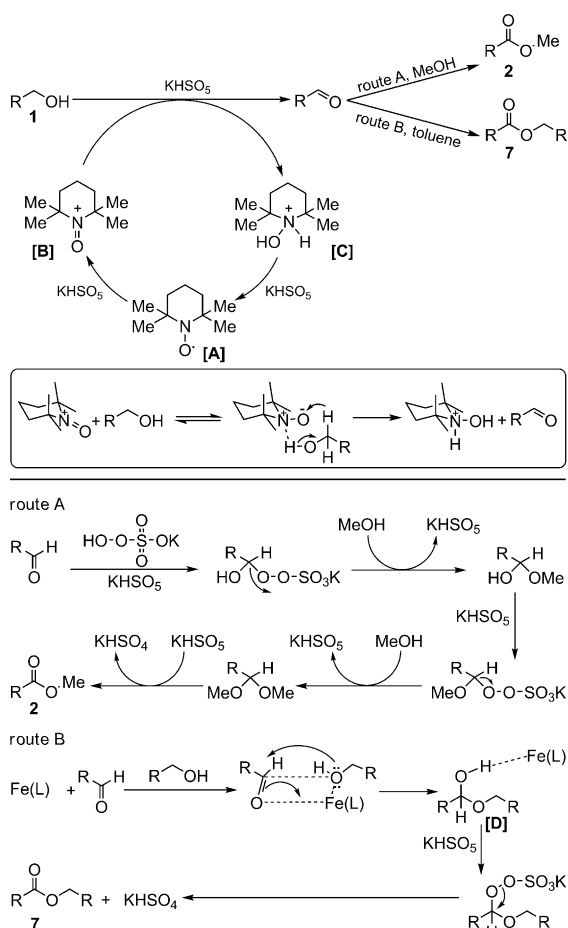
Table 7. Metal-catalyzed direct oxidative “self” esterification of alcohols.^[a]

7a, 86%	7b, 78%	7c, 80%
7d, 72%	7e, 65%	7f, 55%
7g, 75%^[b]	7h, 55%	7i, 62%^[b]
7j, 81%	7k, 51%^[b]	7l, 70%^[b]
[a] Benzylic alcohol (1 mmol), Fe(OAc)₂ (15 mol%), dipic (30 mol%), oxone (2.2 mmol), TEMPO (2 mol%), TBAB (8 mol%), 110 °C, toluene (2 mL), 48 h. [b] GC yields.		

alkoxy-substituted benzyl alcohol (**7h**) but the same reaction failed to occur for similar substitution at the *para*-position.^[16c] Under the present reaction conditions, aliphatic alcohols such as 2-phenethyl alcohol, 1-octanol and its isomer, 2-ethyl-hexanol, consistently afforded the desired homocoupled esters (**7i**, **7k**, and **7l**) in conjunction with a benzoate derivative in each case (see the Supporting Information). The unusual formation of the benzoate derivatives can be attributed to the partial oxidation of the solvent toluene to benzyl alcohol and/or benzaldehyde^[25] followed by condensation with the respective aliphatic alcohols, as mentioned above. However, 3-phenyl propanol produced 3-phenylpropyl 3-phenylpropanoate in 81% yield (**7j**) without any such unexpected esterification.

The probable mechanistic pathways for both “cross” and “self” esterification processes have been depicted in Scheme 4. It is logical to believe that the present reaction conditions lead to the initial formation of an aldehyde intermediate, which subsequently undergoes the “cross” and “self” esterification processes in alcohol (Scheme 4, route A) and toluene (Scheme 4, route B), respectively.

Under aerobic reaction conditions, the oxidation of alcohol to aldehyde is catalyzed by TEMPO in the presence of a stoichiometric amount of oxone as the terminal oxidant.^[18–20] Oxone (acting as the secondary oxidant) initially converts TEMPO (nitroxide) **[A]** to its corresponding oxoammonium cation **[B]**, which essentially acts as the active catalytic species in the oxidation of alcohol to aldehyde. In the role of secondary oxidant, oxone is crucial because the same reaction in its absence led to no desired product formation. The alcohol oxidation occurs with an initial hydrogen bond formation between the hydroxyl group and the oxoammonium nitrogen, followed by simultaneous proton transfer and hydride abstraction. Subsequently, the hydroxyammonium cation **[C]**, so formed again, undergoes oxidation to **[A]**, followed by the formation of **[B]**, and the catalytic cycle involving alcohol oxida-



Scheme 4. Probable pathways for "cross" and "self" esterification processes.

tion thereby follows. The involvement of an aldehyde intermediate in the reaction cycle is corroborated by its detection as a minor product on all occasions (5–30%). The "cross" esterification then proceeds by a Baeyer–Villiger oxidation pathway, as reported earlier.^[16c]

Although TEMPO-catalyzed aerobic oxidation of alcohol to aldehyde in presence of oxone is also operational for the "self" esterification process, the active involvement of the metal catalyst, that is, $\text{Fe}(\text{OAc})_2/\text{dipic}$, is imperative for the desired product formation as established by the optimization reactions (Table 1, entry 11). Therefore, it can be proposed that for homocoupled oxidative esterification, the nucleophilic attack on the aldehyde by the second alcohol molecule is promoted by the Lewis-acidic character of the active $\text{Fe-dipic}^{[5e]}$ complex, which in turn facilitates the formation of hemiacetal intermediate **[D]** (Scheme 4).^[13] The hemiacetal **[D]** thereby undergoes further oxidation in the presence of oxone by a Baeyer–Villiger oxidation pathway to give the desired ester **7** (route B in Scheme 4).^[16c]

The controlled experiment comprising of the reaction of a unimolar mixture of benzoic acid and *p*-tolualdehyde in methanolic solvent, under optimized reaction conditions for "cross" esterification (Table 1, entry 4), as expected, resulted in simultaneous formation of methyl benzoate and methyl 4-

Table 8. Control experiments.

(i) ^[a]				
PhCO_2H	$\text{Me-C}_6\text{H}_4\text{-CHO}$	$\xrightarrow[\text{route A (Scheme 2)}]{\text{MeOH}}$	$\text{Me-C}_6\text{H}_4\text{-CO}_2\text{Me}$	$+\text{PhCO}_2\text{Me}$
1 mmol	1 mmol		50%	50% (GC Yields)
(ii) ^[b]				
$\text{PhCO}_2\text{H} + \text{PhCH}_2\text{OH}$	$\text{Me-C}_6\text{H}_4\text{-CHO}$	$\xrightarrow[\text{route B (Scheme 2)}]{\text{toluene}}$	$\text{Me-C}_6\text{H}_4\text{-CO}_2\text{CH}_2\text{Ph}$	$+\text{PhCO}_2\text{H}$
1 mmol	1 mmol		>99% (GC Yield)	(unreacted)

[a] Benzylic alcohol (1 mmol), oxone (3 mmol), TEMPO (3 mol%), TBAB (10 mol%), 60 °C, MeOH (2 mL), 48 h. [b] Benzylic alcohol (1 mmol), $\text{Fe}(\text{OAc})_2$ (15 mol%), dipic (30 mol%), oxone (2.2 mmol), TEMPO (2 mol%), TBAB (8 mol%), 110 °C, toluene (2 mL), 48 h.

methyl benzoate in a 1:1 ratio (Table 8). However, when the same reaction was performed in toluene in the presence of benzyl alcohol (1 mmol) under the optimized reaction conditions for "self" esterification (Table 1, entry 11), benzyl 4-methylbenzoate was formed exclusively, whereas benzoic acid remained completely unreacted (Table 8). It is therefore inferred that, under the present reaction protocols, the reaction preferably proceeds through the aldehyde intermediate instead of an alternate acidic intermediate.^[2]

Conclusion

In conclusion, the present article demonstrates for the first time an operationally simple and sustainable transition-metal-free "cross" esterification, as well as iron-mediated "self" esterification from a wide variety of alcohols, including substituted benzyl alcohols, as well as long chain aliphatic alcohols. The "cross" esterification strategy is rather unique in displaying distinctive tolerance towards the selective formation of allyl benzoates and 2-hydroxyethylbenzoates. The simplicity and broader substrates scope underscore the novelty of the present protocols, which may circumvent the need for the use of precious metals in direct oxidative esterification of alcohols.

Experimental Section

General considerations

Unless otherwise stated, all reactions were carried out under air atmosphere in screw-cap reaction tubes. All solids were weighed in air. Toluene, MeOH, EtOH, *n*PrOH, *i*PrOH, *n*BuOH, *n*Pentanol, and cyclohexanol were purchased from Merck, India and used as received without adding any drying agents. Benzyl alcohol, substituted benzyl alcohols, aliphatic alcohols like phenethyl alcohol, 3-phenyl-1-propanol, 1-octanol, and 2-ethyl-1-hexanol, oxone, tetrabutylammonium bromide, TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy), iron(II) acetate, and 2,6-pyridinedicarboxylic acid were bought from Aldrich, USA and were used as received. For column chromatography, silica gel (100–200 mesh or 230–400 mesh) from Merck, India was used. A gradient elution using petroleum ether and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel 60F254) and visualized by UV (254 nm) lamp or in an iodine chamber depending on the product type.

Analytical methods

Isolated compounds were characterized by ^1H NMR spectroscopy, ^{13}C NMR spectroscopy, and gas chromatography mass spectrometry (GC-MS). In addition, compounds were further characterized by high-resolution mass spectrometry (HRMS). Copies of the ^1H NMR and ^{13}C NMR spectra can be found in the Supporting Information. Nuclear magnetic resonance spectra were recorded on a Bruker 400 and 500 MHz instruments. ^1H NMR experiments were reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. ^{13}C NMR spectra were reported in ppm relative to deuteriochloroform (77.23 ppm), unless otherwise stated, and all were obtained with ^1H decoupling. All GC analyses were performed on a Shimadzu GC-2014 gas chromatograph with a FID detector using a J & W HP-5 column (length 50 m, inner diameter 0.320 mm, film 0.52 μm) with *n*-decane as the internal standard. All GC-MS analyses were done using an Agilent 7890 A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). ESI HRMS spectra were recorded using a BRUKER Maxis Impact mass spectrometer.

General procedure for the synthesis of esters via oxidative "cross" esterification

Case 1: Cross esterification of benzylic alcohols with ROH (where R = CH_3 , C_2H_5 , nC_3H_7 , iC_3H_7 , nC_4H_9 , nC_5H_{11} , C_6H_{11}): To an oven-dried screw-cap reaction tube charged with a magnetic stir-bar, oxone (3 equiv, 3 mmol), TEMPO (3 mol%, 0.03 mmol) and nBu_4NBr (10 mol%, 0.1 mmol) were added. Depending on the physical state of benzylic alcohols (1 mmol), solid compounds were weighed along with the other reagents, whereas liquid benzylic alcohols and ROH (2 mL) were added by microlitre syringe and laboratory syringe, respectively, under air atmosphere. The reaction tube was closed with a screw cap and kept for vigorous stirring in a preheated oil bath for 48 h. The temperature of the reactions was varied depending on the type of alcohol used as the solvent (see the Supporting Information for details). After completion, the reaction mixture was cooled to room temperature, diluted with water and extracted with 3×10 mL of ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using a mixture of petroleum ether/ethyl acetate as the eluent.

Case 2: Cross esterification of: i) aliphatic alcohols with MeOH, and ii) benzylic alcohols with ethane-1,2-diol and allylic alcohol: To an oven-dried screw-cap reaction tube charged with a magnetic stir-bar, oxone (4 equiv, 4 mmol), TEMPO (10 mol%, 0.1 mmol) and Bu_4NBr (20 mol%, 0.2 mmol) were added. Liquid aliphatic and benzylic alcohols were added by microlitre syringe, whereas the respective solvents, that is, MeOH, ethane-1,2-diol and allylic alcohol (each 2 mL) were added by laboratory syringe under air atmosphere. The reaction tube was closed with a screw cap and kept for vigorous stirring in a preheated oil bath for i) 48 h and ii) 60 h respectively. The temperature of the reactions was varied depending on the type of solvent used (see the Supporting Information for details). After completion, the reaction mixture was cooled to room temperature, diluted with water and extracted with 3×10 mL of ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using a mixture of petroleum ether/ethyl acetate as the eluent.

General procedure for the synthesis of esters by oxidative "self" esterification of benzylic alcohols

To an oven-dried screw-cap reaction tube charged with a magnetic stir-bar, $\text{Fe}(\text{OAc})_2$ (15 mol%, 0.15 mmol, 26.08 mg), 2,6-pyridinedicarboxylic acid (30 mol%, 0.30 mmol, 50.14 mg), oxone (2.2 equiv, 2.2 mmol), TEMPO (2 mol%, 0.02 mmol) and Bu_4NBr (8 mol%, 0.08 mmol) were added. Depending on the physical state of benzylic alcohols (1 mmol), solid compounds were weighed along with the other reagents, whereas liquid benzylic alcohols and toluene (2 mL) were added by microlitre syringe and laboratory syringe, respectively, under air atmosphere. The reaction tube was closed with a screw cap and kept for vigorous stirring in a preheated oil bath at 110°C for 48 h. After completion, the reaction mixture was cooled to room temperature, diluted with water and extracted with 3×10 mL of ethyl acetate. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using a mixture of petroleum ether/ethyl acetate as the eluent.

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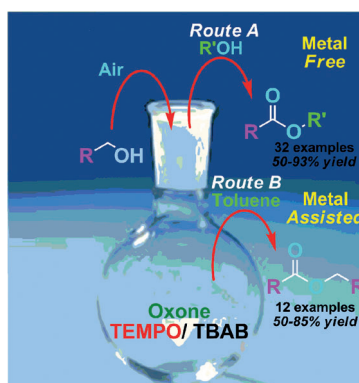
Alcohol Esterification

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Efficient and Simple Approaches
Towards Direct Oxidative Esterification
of Alcohols



One-pot oxidative esterification: A wide variety of alcohols undergo transition-metal-free (in the presence of oxone/2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO)/tetra-*n*-butylammonium bromide (TBAB)) selective “cross” esterification in moderate to excellent yields (see Figure). The “self” esterification process has however been achieved in the presence of $\text{Fe}(\text{OAc})_2$ /2,6-pyridinedicarboxylic acid (dipic) as the active catalytic species under a similar oxidizing environment.