Sodium Perborate Catalyzed Selective Transesterification of *β*-Keto Esters under Neutral Conditions

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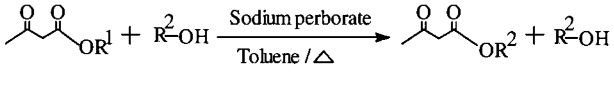
Transesterification of *β*-keto esters with various alcohols has been carried out using sodium perborate as an inexpensive catalyst under neutral conditions. The effectiveness of the protocol is manifested in its selectivity towards *β*-keto esters whereas other esters are found to be unreactive under these reaction conditions.

β-Keto esters represent an important class of organic building blocks and are used for efficient synthesis of a number of complex natural products. Transesterification, one of the effective and important method of ester synthesis has wide applications both in academic and industrial research[2] and in general, it is accelerated by protic acids,[2] Lewis acids and basic catalysts.[3] More recently various catalysts have been reported to effect transesterification.[3,4] Most of the methods of transesterification of *β*-keto esters are not general and are equilibrium driven reactions where usage of excess of one of the reactants is mandatory to obtain good yields. Toxic and expensive DMAP[5] is used for transesterification whereas *tert*-butyl acetoacetate[6] is restricted to *tert*-butyl esters, thus lacking generality. Distannoxanes[7] gave good yields of *β*-keto esters; however the catalysts are difficult to prepare. Although many methods are available for the preparation of alkyl benzoylacetates, there are very few reports[4a,4d] for the synthesis of *β*-keto esters which are required for the synthesis of lignans including podophyllotoxin. *α*-Disubstituted *β*-keto ester enolates underwent efficient 1,3-ester shift under basic conditions.[8] Very few examples are reported on transesterification of *β*-keto esters with propargylic alcohols[2,9] even though several of the reported methods were effective with allylic alcohols. Transesterification of simple esters with stoichiometric amount of iron(III) perchlorate[10] is also reported without selectivity.

Sodium perborate has gained a lot of importance as an inexpensive versatile reagent for effecting organic transformations under neutral conditions.[11] Thus development of a method which allows transesterification under neutral conditions should heighten the synthetic potentiality of the reaction. We report here for the first time sodium perborate as an efficient catalyst for selective transesterification of *β*-keto esters under neutral conditions (Scheme).



Treatment of methyl, ethyl, or propyl *β*-keto ester with alcohols along with a catalytic amount of sodium perborate in toluene at 90–100 °C afforded *β*-keto esters in excellent to good yields.[12] Various alcohols (primary, secondary, tertiary, benzylic, allylic and progargylic) underwent smooth transesterification reaction.

Table 1. $NaBO_3$ catalyzed transesterification of *β*-keto esters

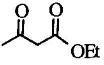
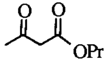
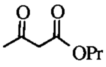
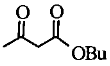
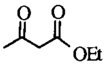
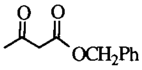
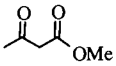
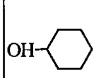
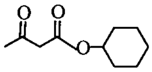
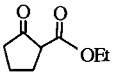
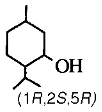
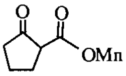
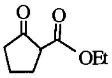
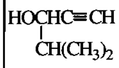
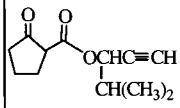
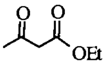
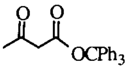
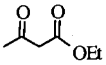
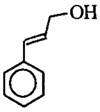
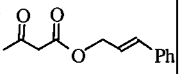
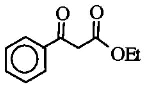
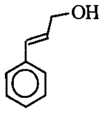
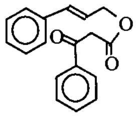
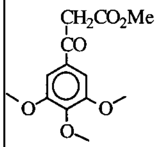
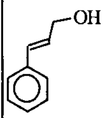
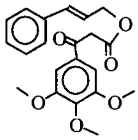
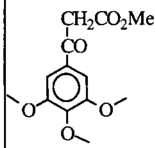
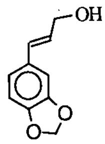
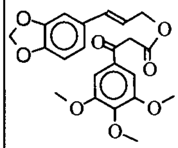
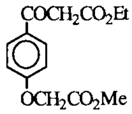
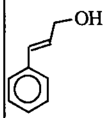
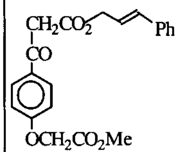
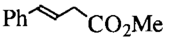
Entry	Ester	Alcohol	Product	Time/h	Yield/[a,b] %
1		$CH_3(CH_2)_2OH$		2	90
2		$CH_3(CH_2)_3OH$		2	88
3		$PhCH_2OH$		2	91
4				3	85
5				3.5	82
6		 $HOCHC{\equiv}CH$ / $CH(CH_3)_2$		2.5	88
7		Ph_3COH		8	58
8				3	80
9				4	85
10				4	88
11				4	87
12				3.5	81
13	$CH_3(CH_2)_4CO_2Me$	BuOH	NR	10	--
14	CH_3COCO_2Me	BuOH	NR	10	--

Table 1. Continued

Entry	Ester	Alcohol	Product	Time/h	Yield[a,b] %
15	$CH_3CO(CH_2)_2CO_2Me$	BuOH	NR	10	--
16	$CNCH_2CO_2Me$	BuOH	NR	10	--
17		BuOH	NR	10	--

[a] Yields of pure isolated products [b] Products are characterized by their spectral analysis.

Even less reactive trityl alcohol afforded corresponding *β*-keto ester in moderate yield (Table 1, entry 7) which is otherwise often problematic in acid catalyzed reaction or failed to undergo transesterification with $Ti(OEt)_4$.[4e] It should be pointed out that transesterification of *β*-keto esters with unsaturated alcohols is rather difficult as it is offset by facile decarboxylated rearrangement.[13] The superiority of this procedure can be clearly visualized in transesterifications leading to the synthesis of *β*-keto esters with an aromatic moiety in good yields (Table 1, entries 9–12). In this connection it should be mentioned that a recent literature report[14] which describes synthesis of alkyl *β*-keto esters employing a tin based supper acid catalyst, failed with aromatic substrates. It is also clear from the Table 1 that the conversion of ethyl ester to higher homologue appears to be efficient by this procedure. It is important to note that chiral integrity of (1*R*,2*S*, 5*R*)-(–)-menthol is mentained under these reaction conditions (chiral alcohol is recovered by base hydrolysis of ester and its optical rotation is checked, Table 1, entry 5). It is noteworthy to mention that the reaction appears to be specific only for transformation of *β*-keto esters. Other esters like *α*-keto esters, *γ*-keto esters as well as normal esters failed to undergo the reaction (Table 1, entries 13–17). After scanning through different catalysts (Table 2), we found that lithium perchlorate and sodium perborate worked remarkably well. However, sodium perborate is superior than lithium perchlorate as a catalyst in terms of cost and its neutral nature.

Table 2. Catalytic effect on transesterification of ethyl acetoacetate (5 mmol) with *n*-butanol (5 mmol)

Entry	Catalyst /mmol	Time/h	Yield[a,b] %
1	None	2	---
2	$NaBO_3$ (0.5)	2	57
3	$NaBO_3$ (1.0)	2	92
4	$NaBO_3$ (1.5)	2	92
5	$NaBO_3$ (2.0)	2	93
6	$LiClO_4$ (0.5)	2	93
7	$MgClO_4$(1.0)	2	80

[a] Yields of pure isolated products [b] Products are characterized by their spectral analysis.

In conclusion, we have developed an efficient and practical method for transesterification of *β*-keto esters using sodium perborate as an inexpensive catalyst. The effectiveness of this protocol is manifested in its selectivity towards *β*-keto esters whereas other esters are found to be unreactive under these reaction conditions.

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Reference and Notes

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12 Typical procedure: A mixture of ethyl 3-(3,4,5-trimethoxyphenyl)-3-oxopropanoate (5 mmol), 3,4-methylenedioxycinnamyl alcohol (5 mmol), sodium perborate (1 mmol) in toluene (20 mL) was heated to 90–100 °C in a round-bottom flask with distillation condenser to remove ethanol. After completion (TLC) the reaction mixture was cooled, filtered and filtrate was concentrated and chromatographed on SiO_2 (hexane:ethyl acetate 9:1) to afford *(E)*-3-(3,4-methylenedioxyphenyl)-2-propenyl 3-(3,4,5-trimethoxyphenyl)-3-oxopropanoate. Yield 87%; IR (neat) cm^{-1} 3322, 1734, 1699; ^1H NMR: (300 MHz, $CDCl_3$), δ 3.98 (d, 9H) 4.12 (s, 2H), 4.7 (dd, *J* = 1.3 and 6 Hz, 2H), 5.90 (s, 2H), 6.0–6.15 (m, 1H), 6.5 (d, *J* = 14 Hz, 1H), 6.7–6.8 (m, 2H), 6.92 (s, 1H), 7.25 (s, 2H); ^{13}C NMR: (60 MHz, $CDCl_3$) δ 45, 55, 60, 65, 85, 102, 106, 107, 108, 121, 122, 131, 131.2, 134, 143, 148, 148.5, 153, 165, 192; Anal. Calcd for $C_{22}H_{22}O_8$ (414.42): C, 63.76; H, 5.35% Found: C, 63.81; H, 5.28%

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