Tetrahedron 71 (2015) 9388–9395

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Efficient and practical approach to esters from acids/ 2-oxoacids/ 2-oxoaldehydes &/ 2-oxoesters

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ARTICLE INFO

Article history:
Received 30 July 2015
Received in revised form 16 October 2015
Accepted 23 October 2015
Available online 5 November 2015

Keywords:
Esters
Acids
2-Oxoacids
2-Oxoaldehydes
2-Oxoesters

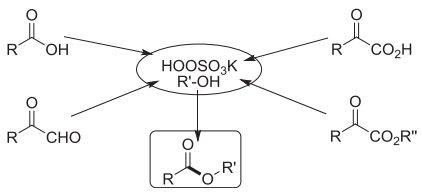
ABSTRACT

An efficient, mild, cost effective and practical method is presented for generation of esters (RCO_2R') from acids (RCO_2H)/ 2-oxoacids ($RCOCO_2H$)/ 2-oxoaldehydes (RCOCHO)/ 2-oxoesters ($RCOCO_2R''$) and alcohols by using oxone as catalyst. In addition to deciphering the scope of our process, we propose a mechanism for esterification through a common intermediate IV. Reaction with 2-oxoacids and 2-oxoaldehydes proceed with initial CO–C cleavage followed by oxone mediated esterification with alcohols. In addition, reaction with 2-oxoesters proceeds through CO–CO bond cleavage and *trans*-esterification.

1. Introduction

Esters are prevalent subunits in various natural products, pharmaceuticals, agrochemicals, and polymers. Besides, they also serve as important building blocks for organic synthesis and have been used as artificial fragrances/flavoring agents. Consequently, plethora of synthetic methods for construction of this important unit has been established.[1] However, in recent times the strategies adopted in the synthesis of molecules and materials have undergone considerable changes. Current strategies lay stress on the use of reagents that are mild, efficient, nontoxic, selective & cost effective and lack production of nonpolluting byproducts. In this direction, we developed an esterification method employing oxone as catalyst.

Oxone, a potassium triple salt containing potassium peroxymonosulfate, is a stable, white crystalline compound, non toxic, water soluble, easy to handle, and above all is economic. Oxone has been used efficiently in numerous transformations. In most of the reactions, anion peroxymonosulfate (HSO_5^-) has been subjected as an active oxidant within the mixture.[2] Even though oxidative potential of oxone has been demonstrated in diverse directions, no studies have been reported till date for its use as esterification catalyst employing acids/ 2-oxoacids/ 2-oxoadlehydes/ 2-oxoesters as reactants. In the course of our continued investigation of the aldehydes, acids, 2-oxoaldehydes, 2-oxoacids and 2-oxoesters,[3] we came across the unique ability of oxone to catalyze the reaction between acids/2-oxoacids/2-oxoaldehydes/2-oxoesters with alcohols. Herein, we present our preliminary results of this reaction, which proved to be tolerant to a wide range of functionalities and avoid the use of co-oxidants/additives. The earlier reports on this transformation utilized aldehydes as substrate of choice.[4] Our method employing acids as substrates belong to conventional esterification reaction, however, with 2-oxoaldehydes and 2-oxoacids, it is a decarbonylative &/decarboxylative esterification reaction, respectively. Surprisingly, the reaction of oxone with 2-oxoesters corresponds to *trans*-esterification reaction (see Scheme 1).



Scheme 1. Summary of this work.

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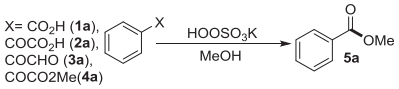
http://dx.doi.org/10.1016/j.tet.2015.10.067
0040-4020/

2. Results and discussion

Our evaluation of the proposed esterifications reactions began with exposure of benzoicacid **1a** with different concentrations of oxone in methanol (Table 1, entry 1–8). To our best, we could isolate require product **5a** with 98% yield in 30 h when **1a** (1 mmol) was treated with 30 mol % of oxone (0.3 mmol) in 2 mL of methanol at 65 °C (entry 7). On the contrary, reaction of 2-oxoacid **2a** generated desired ester **5a** in low yields (20%) when stirred with 30 mol % of oxone in 2 mL of methanol for 36 h at 65 °C (entry 9). In order to improvise the yields of reaction, different test reactions were conducted at varying concentrations of oxone (entry 9–13). To our delight, we isolated **5a** in maximum yield (97%) when **2a** (1 mmol) was treated with 2.5 mmol of oxone in 2 mL of methanol for 30 h at 65 °C (entry 13). The same conditions when tested with phenylglyoxal **3a** and 2-oxoesters **4a** generated the desired product in maximum yields (entry 17 & 20, respectively).

Table 1
Optimization of reaction conditions[a]



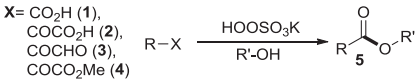
Entry	1a/2a/3a/4a	Oxone (mmol)	Temp (°C)	Time (h)	Yields (%)[f]
					5a
1	**1a**	1.5	rt	24	15
2	**1a**	1.5	65	24	98
3	″	1	″	″	98
4	″	0.5	″	″	96
5	″	0.3	″	″	90
6	″	0.2	″	″	75
7[b]	″	**0.3**	**65**	**30**	**98**
8	″	0.3	60	″	84
9	**2a**	″	65	36	20
10	″	1	″	″	48
11	″	1.5	″	″	69
12	″	2	″	36	89
13[c]	″	**2.5**	″	**30**	**97**
14	**3a**	1	″	36	50
15	″	1.5	″	″	72
16	″	2	″	″	90
17[d]	″	**2.5**	″	**30**	**99**
18	**4a**	1.5	″	″	60
19	″	2	″	″	84
20[e]	″	**2.5**	″	″	**96**

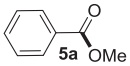
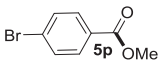
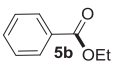
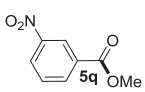
Reaction conditions: [a] 1a (1 mmol), oxone (0.3 mmol) and methanol (2 mL), 65 °C, 30 h; [b,c,d,e] 2a/3a/4a (1 mmol), oxone (2.5 mmol), and methanol (2 mL), 65 °C, 30 h; [f] Isolated yields.
Bold signifies the best suited conditions for different reactions mentioned in this Table.

Next, we investigated the scope of the esterification reaction against different substrates (Table 2). Primarily, it was observed that the reactions of benzoic acid/2-oxo-2-phenylacetic acid/2-oxo-2-phenylacetaldehyde and/methyl-2-oxo-2-phenylacetate with different alcohols under optimized conditions generated desired ester **5** in excellent yields despite the nature of carbon chain length (entries 1–6). In addition, we tested esterification reaction against different substrates with electronic/structural variation in methanol (entry 8–20). In general, we observed our protocol works well in all substrates tested. As an advantage, we observed that a wide range of functional groups were tolerant to our method. Furthermore, we investigated few more substrates against different alcohols (entry 21–30). Interestingly, we observed that our method has wide substrate scope. To highlight the importance of our reaction, alcohols like allyl alcohol, 2-methylprop-2-en-1-ol, benzyl alcohol and (*S*)-(+)-1,2- isopropylideneglycerol were being used against both aromatic and/aliphatic substrates successfully (entry 24, 25, 26, 28). In all the cases, we observed that time consumed for completion of the reaction with aliphatic acids is very less as compared to aromatic. A highlight in our studies toward the esterification of various substrates was the generation of same esters (RCO_2R') in excellent yields under mild conditions from corresponding acid (RCO_2H), 2-oxoacid ($RCOCO_2H$), 2-oxoaldehyde (RCOCHO) and/or 2-oxoester ($RCOCO_2R'$). In case of acids, it was observed to be a simple oxone mediated esterification reaction. However, in case of 2-oxoacid and 2-oxoaldehyde, it was possible through decarboxylative and decarbonylative esterification reaction, respectively. Surprisingly, the reactions with 2-oxoesters can be a good example of *trans*-esterification reaction involving CO–CO bond cleavage as well.

As proof of concept, we conducted few control experiments (Scheme 2). Along with, we also observed our reaction intermediates in each case. In experiment 1, 2 & 3, on reaction of **2r**, **3r** & **4r** with oxone under optimized concentrations, we isolated solely benzoic acid **1r**. This clearly indicates that oxone has potential to cleave CO–C bond in 2-oxoacids, 2-oxoaldehydes and/2-oxoesters through a common intermediate (**IV**). This intermediate is labile enough to get hydrolyzed by moisture in DMF. Along with, our reactions with **2**, **3** and **4** under optimized conditions generated different intermediates. However, in each case, we observed a minute quantity of acid throughout till completion of the reaction. This clearly indicates the presence of common intermediate (**IV**) in each case. Furthermore, in case of reaction with 2-oxo-2-(*m*-tolyl) acetaldehyde, we isolated an intermediate 2,2-dimethoxy-1-(*m*-tolyl)ethan-1-one (**IIr**). This intermediate on treatment with optimized concentration of oxone generated desired product in

Table 2
Substrate scope of esterification reactions[a]



Entry	Product	(Yields %[b], time h)	Entry	Product	(Yields %[b], time h)
1		X=CO_2H–(98%, 30 h) $COCO_2H$–(97%, 30 h) COCHO–(99%, 30 h) $COCO_2Me$-(96%, 30 h)	16		X=CO_2H–(97%, 30 h) $COCO_2H$–(97%, 30 h) COCHO–(98%, 30 h) $COCO_2Me$–(94%, 30 h)
2		X=CO_2H-(97%, 30 h) $COCO_2H$–(96%, 30 h) COCHO–(98%, 30 h) $COCO_2Me$-(95%, 30 h)	17		X=CO_2H–(98%, 30 h) $COCO_2H$–(98%, 30 h) COCHO–(99%, 30 h) $COCO_2Me$–(95%, 30 h)

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