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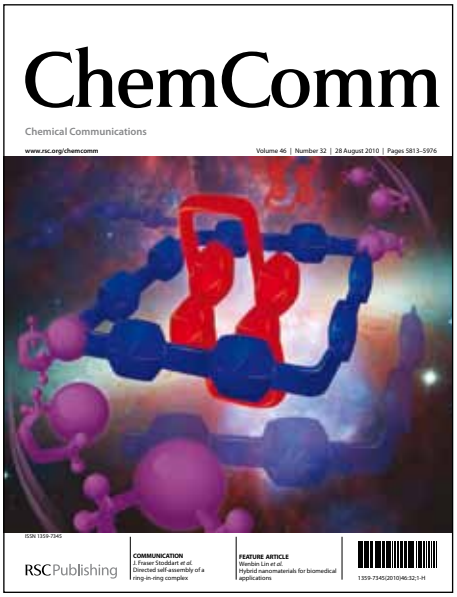

Iodine-catalyzed tandem synthesis of terminal acetals and glycol mono esters from olefins

Macharla Arun Kumar, Peraka Swamy, Mameda Naresh, Marri Mahender Reddy, Chozhiyath Nappunni Rohitha, Sripadi Prabhakar, Akella Venkata Subrahmanya Sarma, Joseph Richard Prem Kumar and Nama Narender*

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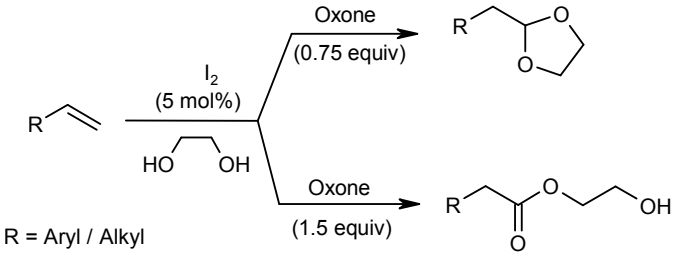

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Iodine-catalyzed tandem synthesis of terminal acetals and glycol mono esters from olefins

Macharla Arun Kumar,[a] Peraka Swamy,[a] Mameda Naresh,[a] Marri Mahender Reddy,[a] Chozhiyath Nappunni Rohitha,[a] Sripadi Prabhakar,[b] Akella Venkata Subrahmanya Sarma,[c] Joseph Richard Prem Kumar[d] and Nama Narender*[a]

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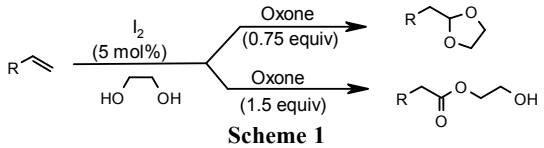
A new metal-free protocol is described for the synthesis of terminal acetals by tandem oxidative rearrangement of olefins using oxone as an oxidant in presence of iodine. Moreover, one-pot procedure for the preparation of glycol mono esters from olefins is also presented first time using the same reagent system.

Protection of carbonyl function as acetol is known to be the widely used synthetic route for the manipulation of various multifunctional organic molecules.[1] Acetals can also be used for C-C bond formations,[2] synthesis of ethers,[3] esters,[4] and cyclization of diynes.[5] Additionally acetals have enormous industrial importance due to their potential utility as flavoring agent in distilled beverages, diesel additives and plastic materials.[6] Classical methods for the synthesis of acetals involve the treatment of aldehydes or ketones with an alcohol by either protic or Lewis acid catalyst.[1] Unfortunately, these procedures have some disadvantages such as use of corrosive and costly reagents or additives, halogenated solvents, large waste and high catalyst loading. The palldium(II)-catalyzed oxidation (wacker process) of terminal olefins in water furnish the methyl ketones[7] and a similar reaction in alcohol gives their corresponding internal acetals[8] and these reactions have been widely studied. Acetalization at the terminal carbon atom of a cheaper terminal olefin instead of a costlier aldehyde as substrate is a challenging task. Consequently some Pd catalyzed protocols have been developed for this important functional group transformation.[9] Recently Lahiri *et al* reported the iron catalyzed synthesis of terminal acetals from olefins.[10] Couple of non-metal catalyzed methods have also been reported for the synthesis of terminal acetals from olefins.[11]

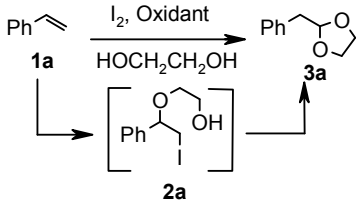
Over the last few years iodine-mediated reactions have been increased dramatically due to its readily availablility, convenient, relatively cheap and environmentally benign characteristics over the toxic heavy metals or complex reagents.[12] The use of oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) in the oxidation reactions is becoming popular due to its high stability, simple manipulation, non-toxic nature and is relatively inexpensive. Moreover, the byproducts associated with oxone are generally recognized as safe.[13]



Scheme 1

In view of the increased attention to design cost-effective, environmentally benign and metal-free chemical transformations. Herein, we report a novel and efficient metal-free protocol for the synthesis of terminal acetals and esters from olefins using oxone as an oxidising agent in presence of catalytic amount of iodine (Scheme 1).

Table 1 Optimization for acetal and ester formation[a]



Entry	I_2 (mmol)	Oxidant (mmol)	Time	Yield[b] (%)	
				2a	**3a**
1	0.1	Oxone (0.5)	24 h	10	49
2	0.1	Oxone (1)	24 h	10	84
3	**0.1**	**Oxone (1.5)**	**1.3 h**	**-**	**95**
4	0.1	Oxone (2.5)	24 h	-	12 (70)[c]
5	**0.1**	**Oxone (3)**	**24 h**	**-**	**- (94)[c]**
6	1	Oxone (0.5)	1.3 h	92	-
7	0.5	Oxone (1.5)	1.3 h	12	85
8	1	Oxone (1.5)	1.3 h	35	61
9	0.1	H_2O_2 (1.5)	24 h	10	-
10	0.1	O_2	24 h	-	-
11	0.1	TBHP (1.5)	24 h	-	-
12	0.1	-	24 h	-	-

[a] Styrene (2 mmol), Ethylene glycol (2 ml). [b] Products were characterized by NMR, mass spectra and quantified by GC. [c] 2-Hydroxyethyl-2-phenylacetate (**4a**).

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† Electronic Supplementary Information (ESI) available: Experimental procedures, ^1H and ^{13}C NMR spectra of all compounds. See DOI: 10.1039/b000000x/

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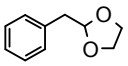
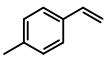
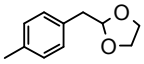
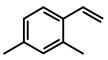
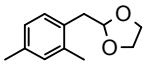
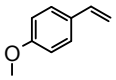
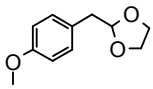
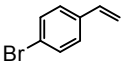
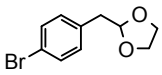
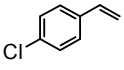
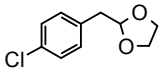
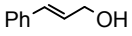
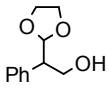
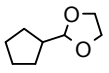
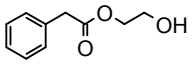
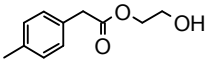
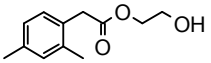
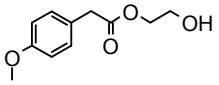
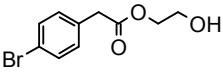
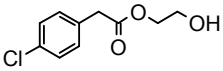
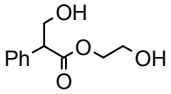
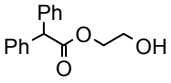
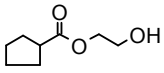
Table 2 Synthesis of acetals form various olefins[a]

Entry	Olefin	Time (h)	Product	Yield[b] (%)
1	 **1a**	1.3	 **3a**	95
2	 **1b**	3.3	 **3b**	90
3	 **1c**	3	 **3c**	76
4	 **1d**	3.3	 **3d**	89
5	 **1e**	5	 **3e**	95
6	 **1f**	6	 **3f**	94
7	 **1g**	2.3	 **3g**	95
8	 **1h**	7	 **3h**	80
9	 **1i**	1.3	 **3i**	64

[a] Olefine (2 mmol), I_2 (0.1 mmol), Oxone (1.5 mmol), Ethylene glycol (2 ml), r.t. [b] Products were characterized by NMR, mass spectra and quantified by GC.

Table 3 Synthesis of esters from various olefins[a]

Entry	Olefin	Product	Yield[b] (%)
1	**1a**	 **4a**	94
2	**1b**	 **4b**	90
3	**1c**	 **4c**	51
4	**1d**	 **4d**	60
5	**1e**	 **4e**	88
6	**1f**	 **4f**	90
7	**1g**	 **4g**	65
8	**1h**	 **4h**	-
9	**1i**	 **4i**	60

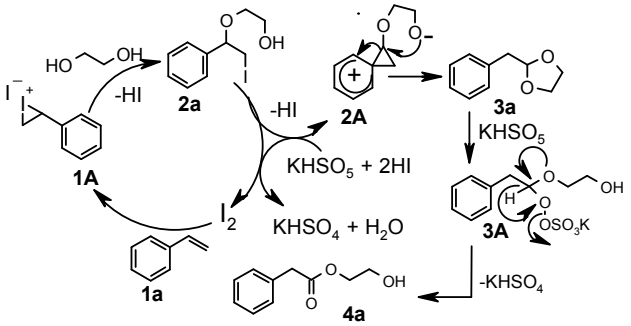
[a] Olefine (2 mmol), I_2 (0.1 mmol), Oxone (3 mmol), Ethylene glycol (2 ml), 24 h, r.t. [b] Products were characterized by NMR, mass spectra and quantified by GC.

Initially, we investigated the suitable reaction conditions for direct acetalization of olefins (oxidative rearrangement) using styrene as the model substrate. As seen in Table 1, a variety of reaction conditions were employed to achieve the optimal conditions. After screening of several oxidants, oxone is found to have excellent activity and selectivity than other oxidants such as H_2O_2, TBHP and O_2 in the presence of iodine at room temperature. Further styrene (2 mmol) was allowed to react with different mole ratios of oxone (0.5, 1.0, 1.5, 2.5, 3.0) in the presence of I_2 (0.1, 0.5, 1.0). The results revealed that 2:1.5:0.1 mole ratio of styrene, oxone and I_2 at room temperature shown to be optimum reaction conditions for terminal acetalization. Acetal was not observed in the absence of oxone, which indicate that it plays a crucial role in formation of acetal (entry 12, Table 1). With increasing the amount of oxone, formation of ester was observed, 3 mmol of oxone is required for complete conversion of olefin to ester (entry 5, Table 1).

After optimizing the reaction conditions, we explored the scope of this novel transformation with a variety of olefins and results are summarized in Table 2. Various aryl alkenes underwent the oxidative rearrangement to give the corresponding cyclic acetals in good to excellent yields. Styrene produced the respective terminal cyclic acetal with 95% yield in 1.3 h. Whereas, relatively longer reaction time required for activating or deactivating groups present on aromatic ring of styrene to provide excellent yields of corresponding acetals. However, 2, 4-dimethyl styrene gave relatively lesser yield, probably due to steric hindrance. Asymmetric and symmetric olefins also underwent oxidative rearrangement and afforded good yields of the corresponding acetals (entries 7 and 8, Table 2). It is worth mentioning that in the case of cyclic olefin, ring-contraction product was observed (entry 9, Table 2).

After our success with the synthesis of terminal acetals from olefins, we turned our attention to extending the scope of this protocol to preparation of glycol mono esters. Formation of glycol mono esters from variety of olefins (2 mmol) with ethylene glycol (2 ml) using oxone (3 mmol) as an oxidant in

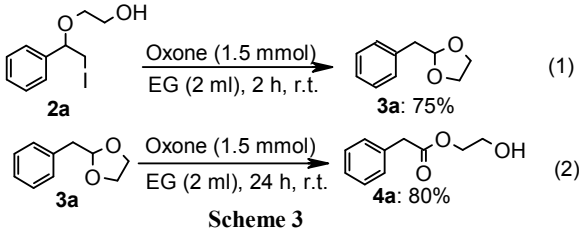
presence of iodine was studied at room temperature (Table 3). Styrene smoothly converted to the corresponding ester with excellent yield in 24 h. Styrene with a moderately activating substituent i.e. methyl and moderately deactivating substituents such as Cl, Br groups also furnished the corresponding esters with high yield in 24 h. Whilst, highly activated styrene i.e. 4-methoxystyrene afforded moderate yield. However, the sterically hindered substrate i.e. 2,4-dimethyl styrene yielded the respective ester comparatively in lesser yield. In case of cis-stilbene ester formation was not observed, probably due to the bulkyness of phenyl groups. Cylohexene provided the ring contraction product i.e 2-hydroxyethyl cyclopentanecarboxylate in 60% yield.



Scheme 2

The plausible reaction mechanism for the formation of acetals/esters is depicted in Scheme 2. It is assumed that electrophilic addition of iodine onto the olefin to give a three-membered cyclic iodonium ion intermediate (**1A**). It then undergoes nucleophilic ring opening by ethylene glycol lead to co-iodo intermediate (**2a**). Further, oxone facilitates the deiodination of **2a** to give phenonium ion intermediate (**2A**) and subsequent cyclization provides the corresponding cyclic acetal (**3a**). Oxone converts the generated HI into I_2 and then the reaction cycle continues.[14] In presence of oxone, **3a** forms a mixed peroxyacetal intermediate (**3A**), which further undergoes rearrangement to yield ester by expelling potassium bisulfate.[15] Initial support for this proposal was obtained by acetalization of styrene-β,β-d_2, which gives a benzylic deuterated product. *In situ* ESI-MS and ^{13}C NMR experimental data also supports the proposed mechanism. Further, computational studies at B3LYP/6-31G* level, clearly demonstrate the propensity for O^- attack on α-C rather than on β-C in the phenonium ion intermediate (see ESI for further details).

The role of oxone in the deiodination of **2a** was confirmed by treating pure **2a** with oxone in EG (Scheme 3, eqn 1).While, formation of **3a** was not observed when pure **2a** stirred in EG or treated with I_2 in EG. Reaction of **3a** with oxone in EG provided the corresponding ester (**4a**) (Scheme 3, eqn 2).



Scheme 3

In conclusion, we have developed a remarkably mild, efficient and selective metal-free method for the synthesis of terminal acetals from olefins using commercially available, safe, stable and inexpensive reagents. A one pot protocol for the preparation of glycol mono esters from olefins has also been introduced using the same reagent system. To our knowledge, this is the first example for direct esterification of olefins at terminal carbon. Interestingly, ring-contraction products were obtained when the process is subjected to cyclic olefins. Further application of this method to prepare acetals and esters using different nucleophiles is currently underway in our laboratory.

M.A.K, M.N and M.M.R thanks the CSIR and P.S for UGC, India for the fellowship.

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