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Transition-metal- and organic-solvent-free: a highly efficient anaerobic process for selective oxidation of alcohols to aldehydes and ketones in water†

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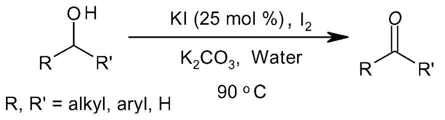
A new system, I_2–KI–K_2CO_3–H_2O, selectively oxidized alcohols to aldehydes and ketones under anaerobic condition in water at 90 °C with excellent yields. The process is green, mild and inexpensive.

In recent years, the search for environmentally benign chemical processes or methodologies has received much attention from chemists, because they are essential for the conservation of the global eco-system.[1] On the other hand, the selective oxidation of alcohols to aldehydes and ketones is a pivotal transformation in organic chemistry.[2] In particular, the controlled oxidation of primary alcohols to aldehydes, without forming over-oxidized product is a challenging task for chemists. A number of oxidizing methods using variety of reagents and conditions have been developed, they involve transition metals,[3] which are associated with waste disposal problems, use of oxygen-containing oxidants[4] and organic solvents[2b,3a–f,4b–f] in the reaction mixture. Also, despite the industrial importance of these processes and ever growing environmental concerns, only a few efficient and environmentally benign catalytic processes[3d,3g,3j,5] are known till today, which involve organic solvents, transition metals, O_2–air, O_3, TEMPO *etc.* as the ultimate stoichiometric oxidants, and this reaction awaits further development of high yielding, clean, safe and inexpensive methods for the oxidation of alcohols. In recent years, I_2 has been used extensively as a synthetic reagent due to its inherent properties of low toxicity, electrophilicity, and easy handling.[6] Recently, we described Brønsted acid catalysed selective oxidation of alcohols to aldehydes and ketones using DMSO as a nucleophilic oxidant, where the catalyst HI was generated in a redox process of N_2H_4 and I_2 in hydrated acetonitrile.[7] Very recently, we reported the deprotection of oximes and imines to the corresponding aldehydes or ketones catalysed by I_2 in presence of a surfactant (SDS) in water.[8]

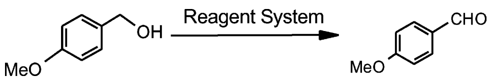
Herein, we want to report a new, efficient and an environment friendly system *i.e.* I_2–KI–K_2CO_3–H_2O for the selective oxidation of alcohols to aldehydes and ketones in water. In a typical experimental procedure, a mixture of alcohol, potassium carbonate, iodine and a catalytic amount of potassium iodide, dissolved in water, was stirred at 90 °C and after work-up produced high to excellent yields of aldehydes and ketones. Although the oxidation of alcohols with I_2 in presence of base, K_2CO_3 in water produced a trace amount of oxidized products, the addition of a catalytic amount of KI in the reaction mixture led to the formation of aldehyde and ketones at 90 °C with very good to excellent yields (Scheme 1). The catalytic amount of potassium iodide was optimised and 25 mol% was established to be sufficient for the oxidation process.



Scheme 1 Oxidation of alcohols to aldehyde and ketones.

To investigate the scope and the general applicability of the oxidation process under the optimised conditions, we examined several different reagent systems (Table 1). Using these different reagent systems the oxidation process successfully could be performed. Among the systems under study, the system I_2–KI–K_2CO_3–H_2O was the best, because it is efficient and cost effective in comparison to the other systems. In a demonstration of the practicality of this selected system (Table 1, entry 2), the oxidation of 4-methoxybenzyl alcohol was carried out on a 13 g scale,[9] the product (anisyldehyde) was isolated by fractional distillation without using any chromatographic techniques with 95% yield.

Table 1 Oxidation of 4-methoxybenzyl alcohol to anisyldehyde using different reagent systems[a]



Entry	Reagent system	Time/min or h	Product	Yield (%)[b]
1[c]	Na_2CO_3–NaI–I_2–H_2O	20 min	*p*-Anisaldehyde	93
2[c]	K_2CO_3–KI–I_2–H_2O	20 min	—	96
3[c]	$CsCO_3$–CsI–I_2–H_2O	18 min	—	98
4[d]	K_2CO_3–I_2–acetonitrile	1 h	—	50
5[d]	K_2CO_3–KI–I_2–acetonitrile	1 h	—	55
6[d]	K_2CO_3–I_2–acetone	1.5 h	—	47
7[e]	K_2CO_3–I_2–toluene	6 h	—	50
8[d]	$CsCO_3$–I_2–acetonitrile	1 h	—	55
9[d]	Na_2CO_3–I_2–acetonitrile	1 h	—	50
10[c]	K_2CO_3–I_2–H_2O	2 h	—	Trace

[a] The reactions were carried out using 1 mmol of 4-methoxybenzyl alcohol with 1.5 mmol of base, 25 mol% of iodate and 1 mmol of iodine in 4 ml water–organic solvent. [b] Isolated yield. [c] Stirred at 90 °C. [d] Stirred at refluxed temperature. [e] Stirred at room temperature.

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† Electronic supplementary information (ESI) available: Experimental details. See http://dx.doi.org/10.1039/b509527a

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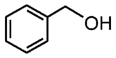
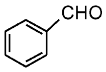
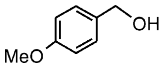
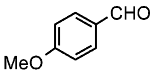
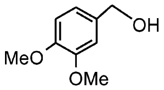
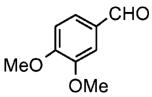
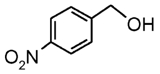
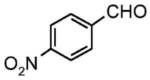
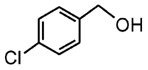
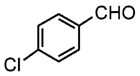
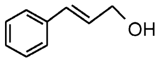
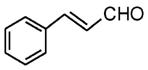
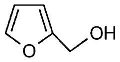
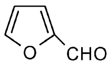
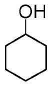
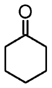
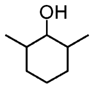
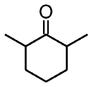
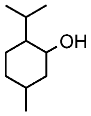
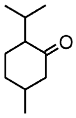
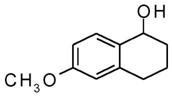
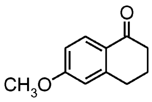
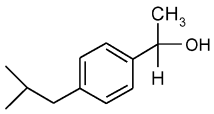
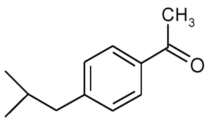
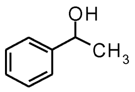
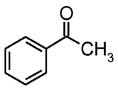
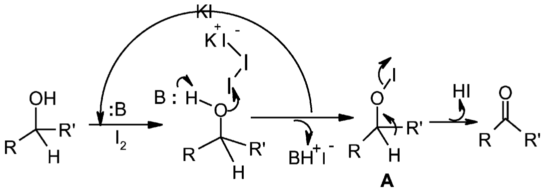
Table 2 Anaerobic oxidation of alcohols to aldehyde and ketones[a]

Entry	Substrate	Time/min	Product	Method	Yield (%)[b]
1		20		A	95
2		20		A	96
3		25		A	90
4		20		A	92
5		20		A	90
6		20		A	80
7		20		A	80
8	1-$C_7H_{15}OH$	50	1-$C_6H_{13}CHO$	B	50
9	1-$C_{10}H_{21}OH$	50	1-$C_9H_{19}CHO$	B	40
10		30		B	75
11		35		B	64
12		45		B	70
13		30		B	75
14		30		B	76
15		30		B	80

[a] Reaction conditions: alcohol (1 mmol), KI (25 mol%), I_2 (1 mmol), 90 °C (oil bath temperature with magnetic stirring). Method A: K_2CO_3 (1.5 mmol), water (4 ml). Method B: K_2CO_3 (2 mmol), water (5 ml). [b] All the yields are pure and isolated products. [c] All the products are known and compared with authentic data.[13]

The system was applicable for the oxidation of a wide variety of primary and secondary alcohols to the corresponding aldehydes and ketones. During the oxidation of the alcoholic (primary and secondary) group, the other functionality, such as ether, nitro, halo, alkyl, aryl *etc.* survived intact under the oxidation process. In this oxidation process, the aromatic primary alcoholic groups (Table 2, entry 1–7) were oxidized with faster rate and higher yields than the secondary aromatic/aliphatic and primary aliphatic alcoholic (Table 2, entry 8–15) groups. In the case of the cinnamyl (Table 2, entry 6) and furfuryl (Table 2, entry 7) alcohols, the system produced neither *cis* nor *trans* iodinated products during the oxidation process. This system did not produced any α-iodinated aryl ketones in the case of the secondary alcohols.[10] On the other hand, this anaerobic oxidation process is simply a subsequent deprotonation of alcohols, therefore we did not get over-oxidized products of the primary alcohols *i.e.* acids during this oxidation process. After separating the organic product layer from the reaction mixture, the catalyst-cum-promoter, KI could be kept as such in solution for further use or, the I_2 may be regenerated by passing O_2 through the acidified inorganic end product.[4b,11]

Regarding the mechanism of the oxidation reaction, it is proposed that the nucleophile alkoxide (formed by abstracting acidic proton of alcoholic group by base) reacts with KI_3 (generated *in situ* from I_2 and KI),[12] forms an intermediate state **A**,[10a] which eliminates HI to generate aldehyde or ketones in the reaction mixture, and finally the generated acid (HI) is being scavenged by inorganic base to produce KI in water (Scheme 2).



Scheme 2 Proposed mechanism and tentative intermediates for the anaerobic oxidation of alcohol.

In conclusion, we have discovered a highly efficient, mild and inexpensive system that selectively oxidizes a wide range of alcohols into aldehydes and ketones and it is free from oxygen-containing oxidants, transition metals, and organic solvents in the oxidation process. The system is applicable to a large-scale production of aldehydes and ketones, and it is a green, and economically viable anaerobic process for the oxidation of alcohols to aldehydes and ketones.

Acknowledgements

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