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Assessing the effectiveness of oxidative approaches for the synthesis of aldehydes and ketones from oxidation of iodomethyl group

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Abstract

Owing to excellent selectivity, high yield and stability towards over-reduction and over-oxidation, one of the impressive approaches to synthesize aldehydes and ketones is the oxidation of halomethyl groups. Numerous halomethyl oxidationbased methodologies to afford aldehvdes and ketones are disclosed in the literature. Mostly, chloromethyl or bromomethyl group containing substrates have been used in the literature for performing oxidation. There are negligible data available in the literature that addresses the use of iodomethyl group containing substrates for transformation to aldehydes and ketones. In this research work, 110 reactions have been carried out to construct aldehydes and ketones from oxidation of iodomethyl group in benzylic iodides and allylic iodides using numerous well-known approaches reported in the literature. The classical approaches under observation include Sommelet oxidation, Kröhnke oxidation, sodium periodate-mediated oxidative protocol, manganese dioxide-based oxidative approach, Kornblum oxidation and Hass-Bender oxidation. The eco-friendly approaches under observation include periodic acid-based IL protocol, periodic acid in vanadium pentoxide-mediated IL method, hydrogen peroxide in vanadium pentoxide-based approach and bismuth nitrate-promoted IL technique. In this investigation, yield, recyclability, cost-effectiveness, eco-friendliness and over-oxidation are the main parameters which are under observation. Among all these investigated techniques, periodic acid-based IL protocol, periodic acid in vanadium pentoxide-mediated IL method and hydrogen peroxide in vanadium pentoxide-based approach (aka. Chunbao oxidation protocol) were found to be highly efficient due to the following reasons: these approaches (1) provide excellent yields, (2) do not lead towards over-oxidation, (3) show good recyclability, (4) demonstrate high thermal stability and negligible flammability, and (5) require no special handling.

Keywords Aldehydes · Ketones · Sommelet · Kröhnke · Iodide · Iodomethyl

Introduction

Aldehydes and ketones comprise a number of most versatile and powerful building blocks that are available for various synthetic transformations (Porcheddu et al. 2017; LoPachin and Gavin 2014; Stellman 1998). The carbonyl group of aldehydes and ketones is highly reactive and undergoes a number of chemical conversions to form key industrial products as well as intermediates for other molecules used in important reactions of industrial preparations. Common

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methods used for the preparation of aldehydes and ketones are oxidation of alkenes (Wang and Jiang 2010), alcohols (Marko et al. 1996) and Wacker's process (Backvall et al. 1979), etc. General methods for the preparation of aromatic aldehydes are Gattermann-Koch reaction (Benington et al. 1954), the Reimer-Tiemann reaction (Wynberg and Meijer 1982) and the Vilsmeier reaction (Marson 1992). Formyl group can also be introduced from different precursors such as a hydroxymethyl, a halomethyl, an acid chloride or a methyl group present at aromatic nucleus. However, the preparation of aldehydes and ketones from alkenes and aryl alcohols is difficult due to over-oxidation of carboxylic acids. The other methods have also drawbacks, for example, some of them are rather aggressive, need comparatively high or low temperature, provide unnecessary by-products and involve acidic reaction conditions that restrict the selection of suitable substrate. Therefore, to avoid complications,

many synthetic approaches have been developed in the literature. The most attractive route for the preparation of aromatic aldehydes and ketones is the oxidation of halomethyl groups on aromatic rings by different methods. This approach is known to be very promising, because it requires no special reaction conditions such as high pressure, temperature and catalysts.

The common approaches for conversion of halomethyls to carbonyl compounds are Hass-Bender reaction (Hass and Bender 1949), Sommelet reaction (Larock 1989), Krohnke oxidation (Krohnke 1963) and Kornblum oxidation (Kornblum et al. 1959). Other methods for the preparation of aldehydes from halomethyls involve oxidation of benzyl chlorides or bromides by the action of MnO₂ in chloroform (Goswami et al. 2005), H_5IO_6 in ([C_{12} mim][FeCl₄]) (Hu et al. 2010a, b), mercury-ethanolic alkali (McKillop and Ford 1974), the Masaki photo-oxidation (Itoh et al. 2000), H_2O_2/V_2O_5 and Aliquat 336 in boiling water (Li et al. 2003), 4-dimethylaminopyridine-N-oxide (Mukaiyama et al. 1981), pyridine N-oxide under microwave irradiations (Barbry and Champagne 1996), K_2CrO_4 in HMPA in the presence of a crown ether (Cardilo et al. 1976), quinolinium chlorochromate in an aqueous medium (Gupta et al. 2014), montmorillonite K₁₀-HIO₃ (Barbry and Champagne 1996), NaIO₄ (Das et al. 2003) and selenium compounds (Syper and Mlochowski 1984). 30% H₂O₂ in ethanol by molybdate-based heterogeneous magnetic catalyst has been used as an oxidant in the oxidation of halomethyls to carbonyl compounds (Bayat et al. 2105).

However, most of the above methods suffer from overoxidation, long reaction time, costly reagents, lower conversions, difficulties in work-up, environmental hazards, toxic reagents, harsh reaction conditions, separation difficulties and specially exhibit no selectivity between the halides except few reactions. Hass-Bender method is only satisfactory for *p*-substituted benzylic substrates. Sommelet reaction is limited to active halides such as benzyl/allyl halides and α -halo-ketones (Hass and Bender 1949; Larock 1989; Krohnke 1963; Kornblum et al. 1959; Goswami et al. 2005; Hu et al. 2010a, b). Electron-deficient or ortho-substituted rings are not efficient substrates for this reaction. Selenium compounds are harmful to the environment, and the method of amine N-oxide is not conveniently enough and suffers with variable yields. The use of H_2O_2 is not satisfactory for aliphatic bromides. Potassium nitrate-catalyzed procedure still suffers from harsh reaction conditions. Oxidation of the methyl group on the aromatic ring involves the use of complicated equipments, catalysts and production of side-products. Stoichiometric amounts of oxidants have been used in most of these oxidations. The aliphatic halomethyls were less reactive with H_5IO_6/V_2O_5 , the reactions proceeded slowly and even under more drastic reaction conditions, reactions are still uncompleted (Itoh et al. 2000; Li et al. 2003; Mukaiyama et al. 1981; Barbry and Champagne 1996). Therefore, the need of a convenient and mild reaction procedure still stimulates a continuous research effort and the introduction of new methods for the oxidation of aryl halomethyls is still in demand.

Most of the researchers have been investigated only chloromethyl or bromomethyl group on aromatic rings as substrates for oxidation to carbonyl compounds. There are negligible chemical reactions which address the use of iodomethyl group on aryl nucleus as a reactant for the preparation of aldehydes and ketones. Iodomethyl group containing compounds are particularly interesting synthetic precursors due to the fact that these precursors provide high yield in short amount of time as compared to chloromethyl or bromomethyl group containing compounds. Their better leaving group ability and high reactivity make them very promising reagents, but these features frequently become a significant drawback owing to slowly degradation of these compounds during storage. On account of this, it would be suggested to prepare iodomethyl containing compounds under reaction conditions which enable further synthesis in the similar reaction flask or use them immediately after preparation. Further, in order to store iodide compounds for long period of time, it is recommended to store iodides them in tetrafluoroethylene, stainless steel or glass storage container and keep it over silica gel in a dark vacuum desiccator at - 5 °C (Alvarez-Manzaneda et al. 2005; Armarego et al. 2012; Palamone et al. 2011).

The basic aim of this research study is to investigate the numerous protocols formerly available in the literature for their effectiveness towards synthesis of aldehydes and ketones through oxidation of iodomethyl group. In doing so, we believe that the idea of using benzyl and alicyclic iodides will be effective for the preparation of target carbonyl compounds. Apart from these, important part of our research is concerned with the development of eco-friendly reactions that protect environment from hazards. Our research presents an effective, successful and eco-friendly work for the preparation of aldehydes and ketones in high to excellent yield by substituting the reported substrates with highly efficient substrates. In this investigation, yield, recyclability, cost-effectiveness, eco-friendliness and over-oxidation are the main parameters which are under observation.

Results and discussion

There are numerous popular approaches which are well documented for the syntheses of aldehydes and ketones by oxidation of bromomethyl or chloromethyl group. In this research work, we have investigated these approaches for their efficiency towards construction of aldehyde and ketone skeletons through oxidation of iodomethyl group. Eleven benzyl and alicyclic iodides (reactants) were purchased for this research work (Fig. 1). The results of the different investigations are summarized in Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10.

Oxidative transformation of iodomethyls to carbonyl groups using Sommelet reaction

First of all, Sommelet reaction was selected for the preparation of aldehydes and ketones using library of iodomethyls (Madathil et al. 2006). In this protocol, all the substrates were treated with HMTA in the presence of 50% aqueous acetic acidic at 100 °C for 2.4–4.5 h followed by reaction with 1 M HCl at 100 °C. After carrying out a large number of reactions, we observed that all the substrates led to the syntheses of aldehydes and ketones in reasonable yields (41–71%). Benzaldehyde **2** was obtained from benzyl iodide **1** in 62% yield. Aldehyde **4** was produced from substrate **3** in 64% yield. Similarly, other iodides, *i.e.*, **3**, **4**, **5**, **6**, **7**, **8**, **9**, **10** and **11** led to target compounds in yields of 52, 41, 52, 44, 63, 63, 71, 54 and 54%, respectively. Substrates **21** and

Fig. 1 List of reactants and products

17 produced the target compounds in better yield (71%), while poor yield was given by substrate 15 (41%). The possible reason of greater reactivity of substrate 21 may be the combined effect of resonance due to benzene ring and hyperconjugation due to methyl group present in the compound which gives stability to the ionized form of the molecule and increases the reactivity of molecule while the decreased reactivity of substrate 21 may be due to the bulkiness created in the molecule by the two benzene rings that hinders the approach of HMTA to the molecule.

Investigating Krohnke oxidation for aldehydes and ketones synthesis from iodomethyls

The second approach applied for the production of aldehydes and ketones from all the substituted/non-substituted benzyl and alicyclic iodides was Krohnke oxidation (Table 2) (Krohnke 1963). In this approach, the substrates were first vigorously stirred with excess pyridine at 100 °C to furnish pyridinium salts. The salts were then converted into nitrones by treatment with *p*-nitrosodimethylaniline in



Table 1	Synthesis of librar	y of carbonyl con	mpounds by iodometh	yl oxidation through	Sommelet reaction
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R R'	HTMA, 50% ii) con	AcOH, 100°C, 2.5 lc. HCl, 100°C	5-4.5 h ► R´ Yield	O R=a R' R'=H, al = 41-71 %	aryls Ikyls, aryls	
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	3	2.5	3.2	3.5	3	3
Yield (%) ^c	62 ^a	64 ^a	52 ^a	63 ^a	52 ^a	54 ^a
Acidic product yield (%)	11	23	< 10	12	< 10	11
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	3	3.5	4.5	3	4	
Yield (%) ^c	69 ^a	41 ^a	71 ^b	44 ^a	71 ^a	
Acidic product yield (%)	23	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (0.05 mol), hexamethylene tetramine (0.09 mol), 25 mL of 50% acetic acid

^bReaction conditions: iodomethyl compound (0.04 mol), hexamethylene tetramine (0.09 mol), 25 mL of 50% acetic acid

^cYield of product after column chromatography; NOB not observed (no over-oxidation towards acidic product was observed)

Table 2 Synthesis of series of carbonyl compounds by iodomethyl oxidation through Krohnke reaction

R R' ii)	i) Excess p <i>p</i> -Nitrosodimethyla	oyridine, 3 h, 10 aniline, NaNH ₂ , iii) H ₃ O⁺	0ºC H₂O, 2.5-4.5 h	O R R' R'= Yield = 67-82 G	R=aryls H, alkyls, aryls %	
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	10	12	11	12	12	10
Yield (%) ^c	82 ^a	81 ^a	78 ^b	67 ^a	75 ^a	74 ^a
Acidic product yield (%)	11	12	> 10	34	5	11
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	11	12	12	10	12	
Yield (%) ^c	79 ^a	81 ^a	81 ^a	78 ^a	80 ^a	
Acidic product yield (%)	> 12	NOB	NOB	NOB	NOB	

^aReaction conditions: pyridinium salt (0.03 mol), *p*-nitrosodimethylaniline (0.06 mol)

^bReaction conditions: pyridinium salt (0.08 mol), *p*-nitrosodimethylaniline (0.06 mol)

^cYield of product after column chromatography; NOB = not observed (no over-oxidation towards acidic product was observed)

the presence of NaNH₂ in water for 2.5-4.5 h at 20-30 °C and then acid hydrolysis of nitrones afforded aldehydes or ketones in 67-82% overall yield. This reaction produced aldehydes and ketones in better yields as compared to Sommelet oxidation. Benzyl iodides produced benzaldehydes in excellent yield, i.e., 82% while benzyl iodides methylated at meta-positions yielded methylated benzaldehydes in moderate yield of 67%. Substrates 1, 3, 5, 7, 9, 11, 13, 15 and 20 produced aldehydes and ketones in yield of 81, 78, 81, 67, 78, 74, 79, 81 and 79%, respectively, that are also excellent from applications point of view.

 Table 3
 Synthesis of series of carbonyl compounds via sodium metaperiodate-based protocol

$$R \xrightarrow{\text{NalO}_4 \text{ in DMF}} R \xrightarrow{\text{O}} R = \text{aryls}$$

$$R \xrightarrow{\text{O}} R \xrightarrow{\text{R}'} R' = \text{H, alkyls, aryls}$$

$$R \xrightarrow{\text{O}} R = \text{aryls}$$

$$R \xrightarrow{\text{O}} R' = \text{H, alkyls, aryls}$$

$$R \xrightarrow{\text{O}} R' = \text{H, alkyls, aryls}$$

Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (min)	60	60	120	120	60	60
Yield (%) ^d	51 ^a	43 ^a	25 ^a	41 ^a	41 ^a	51 ^a
Acidic product yield (%)	32	22	11	21	> 20	44
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	60	100	180	120	120	
Yield (%) ^d	43 ^a	35 ^b	26 ^c	43 ^a	49 ^a	
Acidic product yield (%)	33	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (1 mmol), sodium metaperiodate (1 mmol)

^bReaction conditions: iodomethyl compound (0.8 mmol), sodium metaperiodate (1 mmol)

^cReaction conditions: iodomethyl compound (0.5 mmol), sodium metaperiodate (1 mmol)

^dYield of product after column chromatography; *NOB* not observed (no over-oxidation towards acidic product was observed)

Table 4 Synthesis of series of carbonyl compounds via manganese dioxide-based protocol

$$R \xrightarrow{HnO_2 \text{ in Refluxing CHCl}_3} R \xrightarrow{O} R=aryls$$

$$R \xrightarrow{R'} R'=H, alkyls, aryls$$
Yield = 11-62 %

Reactant 1 3 5	7	9	11
Product 2 4 6	8	10	12
Time (h) 4 6 7	5	5	6
Yield (%) ^c 62 ^a 53 ^a 22 ^a	43 ^a	42 ^a	43 ^a
Acidic product yield (%) 33 11 11	32	23	29
Reactant 13 15 17	19	21	
Product 14 16 18	20	22	
Time (h) 6 7 7	4	5	
Yield (%) ^c 41 ^a 30 ^a 11 ^b	51 ^a	52 ^a	
Acidic product yield (%) 35 NOB NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (3 mmol), activated manganese dioxide (15 mmol)

^bReaction conditions: iodomethyl compound (2.5 mmol), activated manganese dioxide (15 mmol)

^cYield of product after column chromatography; NOB = not observed (no over-oxidation towards acidic product was observed)

Sodium metaperiodate-based iodomethyls oxidation to aldehydes and ketones

The third procedure applied to the production of target carbonyl compounds was Sasmita reaction. In this protocol, reactants were treated with an oxidizing agent $NaIO_4$ in the presence of DMF under the atmosphere of argon at temperature of 150 °C for 60–180 min to afford aldehydes or ketones in 25–51% (Table 3) (Das et al. 2003). This approach was less effective for the production of target carbonyl compounds in high yields from most of the prepared iodomethyl groups present on different nucleus
 Table 5
 Synthesis of series of carbonyl compounds via Kornblum oxidation

	R R' 150°C	/ISO, NaHCO ₃ C under nitroge 20-50 min	→ R R' Yield = 61-8	R=aryls R'=H, alkyls, aryls 3 3 %		
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	20	30	20	50	50	20
Yield (%) ^c	81 ^a	83 ^a	62 ^b	82 ^a	72 ^a	61 ^a
Acidic product yield (%)	NOB	NOB	Traces	Traces	NOB	Traces
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	30	40	50	20	40	
Yield (%) ^c	79 ^a	63 ^a	83 ^b	78^{a}	71 ^a	
Acidic product yield (%)	NOB	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (16 mmol), dimethyl sulfoxide (50 ml), NaHCO₃ (84 mmol)

^bReaction conditions: iodomethyl compound (16 mmol), dimethyl sulfoxide (70 ml), NaHCO₃ (90 mmol)

^cIsolated yield; NOB not observed (no over-oxidation towards acidic product was observed)

 Table 6
 Oxidation of series of iodomethyls by Hass–Bender reaction

	R R' <u>2-</u>	Nitropropane, NaOl 2-propanol, r.t. 4-5 h	Et → R' R' R' Yield = 49-1	R=aryls R'=H, alkyls, ar 83 %	yls	
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	4	5	4	4	4	4
Yield (%) ^c	78^{a}	72 ^a	52 ^a	82 ^a	69 ^a	61 ^a
Acidic product yield (%)	10	5	20	10	10	20
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	4	5	5	4	4	
Yield (%) ^c	79 ^a	49 ^a	83 ^b	75 ^a	71 ^a	
Acidic product yield (%)	10	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (2.67 mmol), 2-nitropropane (3.72 mmol), sodium methoxide (5.01 mmol)

^bReaction conditions: iodomethyl compound (1 mmol), 2-nitropropane (3.72 mmol), sodium methoxide (5.01 mmol)

^cYield of product after column chromatography; NOB = not observed (no over-oxidation towards acidic product was observed)

except benzyl and methylated benzyl iodide which produced aldehydes in good yield, i.e., 51%. Also, the same reason as mentioned above may be addressed for substrate **1** while methyl group substituted at *para* position to iodomethyl group also enhances the reactivity therefore; these compounds led to better yields. The remaining compounds are not much compatible with this reaction that may be due to the insolubility of these compounds in DMF, poor reaction with $NaIO_4$, unsuitable reaction temperature as well as other unsuitable reaction conditions.

	$R R' \frac{H_5 I}{R}$	D ₆ , [C ₁₂ mim][FeCl ₄] 50°C, 3-5 h	O R R' Yield = 78-9	R=aryls R'=H, alkyls, ary 2 %	ıls	
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	3	4	3	3	4	3
Yield (%)	91 ^{a,b}	92 ^{a,b}	81 ^{a,c}	87 ^{a,b}	78 ^{a,c}	89 ^{a,b}
Acidic product yield (%)	NOB	NOB	Traces	NOB	10	NOB
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	3	3	4	5	5	
Yield (%)	92 ^{a,b}	89 ^{a,b}	82 ^{a,b}	81 ^{a,b}	89 ^{a,b}	
Acidic product yield (%)	NOB	NOB	NOB	NOB	NOB	

 Table 7
 Oxidation of iodomethyls by periodic acid in IL 1-dodecyl-3-methylimidazolium iron chloride

^aReaction conditions: iodomethyl compound (30 mmol), [C₁₂mim][FeCl₄] (1.2 mmol), H₅IO₆ (33 mmol)

^bIsolated yield (no column purification required)

^cIsolated yield after column chromatography; NOB not observed (no over-oxidation towards acidic product was observed)

Table 8 Oxidation of iodomethyls by periodic acid and vanadium pentoxide in 1-butyl-3-methylimidazolium hexafluorophosphate

	H ₅ IO ₆ , V ₂ O ₅ , [bmpy]PF ₆	C)	R=aryls
	70°C, 4-9 h	R	_ R'	R'=H, alkyls, aryls
		Yield :	= 83-	94 %

Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	5	6	7	4	4	4
Yield (%)	92 ^{a,b}	92 ^{a,b}	87 ^{a,c}	91 ^{a,b}	83 ^{a,c}	89 ^{a,b}
Acidic product yield (%)	NOB	NOB	Traces	NOB	5	NOB
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	5	7	9	4	7	
Yield (%)	83 ^{a,b}	84 ^{a,b}	85 ^{a,b}	91 ^{a,b}	94 ^{a,b}	
Acidic product yield (%)	NOB	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (30 mmol), [bmpy]PF₆ (15 mL), H_5IO_6 (36 mmol), V_2O_5 (0.9 mmol)

^bIsolated yield (no column purification required)

^cIsolated yield after column chromatography; NOB = not observed (no over-oxidation towards acidic product was observed)

Transformation of iodomethyls to aldehydes and ketones using manganese dioxide

The fourth approach employed in this research work was Goswami approach (Goswami et al. 2005). In this reaction, all the iodomethyls were reacted with an oxidizing agent MnO_2 in chloroform under reflux for 4–7 h to

deliver carbonyl compounds in 11–62% yield (Table 4). Studies confirmed that this reaction was not effective in case of benzyl iodides as the yields of aldehydes and ketones were very poor by using some substrates such as 5, 7, 9, 13, 15, 11, and 17. However, the remaining

Table 9 Synthesis of series of carbonyl compounds via Chunbao oxidation protocol

	$R \xrightarrow{H} Boiling$	₂ O ₂ , V ₂ O ₅ H ₂ O, Aliquat 3 6-10 h	0 36 R R' Yield = 81-9	R=aryls R'=H, alkyls, ary 2 %	yls	
Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	6	8	8	10	7	6
Yield (%)	86 ^{a,d}	82 ^{a,d}	89 ^{b,e}	81 ^{b,d}	82 ^{a,d}	92 ^{a,d}
Acidic product yield (%)	NOB	NOB	Traces	NOB	NOB	NOB
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	6	6	8	8	6	
Yield (%)	86 ^{a,d}	81 ^{a,d}	90 ^{c,d}	84 ^{a,d}	89 ^{a,d}	
Acidic product yield (%)	NOB	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (3 mmol), H₂O (30 mL), H₂O₂ (30%, 18 mmol), V₂O₅ (0.06 mmol), Aliquat 336 (0.6 mmol)

^bReaction conditions: iodomethyl compound (2.5 mmol), H₂O (30 mL), H₂O₂ (30%, 18 mmol), V₂O₅ (0.06 mmol), Aliquat 336 (0.6 mmol) ^cReaction conditions: iodomethyl compound (2 mmol), H₂O (30 mL), H₂O₂ (30%, 18 mmol), V₂O₅ (0.06 mmol), Aliquat 336 (0.6 mmol) ^dIsolated yield (no column purification required)

elsolated yield after column chromatography; NOB not observed (no over-oxidation towards acidic product was observed)

Table 10 Synthesis of series of carbonyl compounds via Khodaei oxidation method

	Bi(NO ₃) ₃ .5H ₂ O, TBAF	0	R=aryls
R R'	100ºC, 1-2 h	R R'	R'=H, alkyls, aryls
		Yield = 78-	89 %

Reactant	1	3	5	7	9	11
Product	2	4	6	8	10	12
Time (h)	1	2	1	1	1.5	1.5
Yield (%)	89 ^{a,e}	87 ^{a,e}	81 ^{a,e}	81 ^{a,e}	78 ^{a,e}	87 ^{a,e}
Acidic product yield (%)	< 5	< 5	< 10	< 10	Traces	< 5
Reactant	13	15	17	19	21	
Product	14	16	18	20	22	
Time (h)	1	1.6	2	1	1.5	
Yield (%)	89 ^{a,e}	79 ^{b,d}	83 ^{c,d}	81 ^{a,d}	85 ^{a,d}	
Acidic product yield (%)	Traces	NOB	NOB	NOB	NOB	

^aReaction conditions: iodomethyl compound (3 mmol), TBAF (1.5 mmol), Bi(NO₃)₃·5H₂O (3.3 mmol)

^bReaction conditions: iodomethyl compound (2.5 mmol), TBAF (1.5 mmol), Bi(NO₃)₃·5H₂O (3.3 mmol)

^cReaction conditions: iodomethyl compound (2 mmol), TBAF (1.5 mmol), Bi(NO₃)₃·5H₂O (3.3 mmol)

^dIsolated yield (no column purification required)

eIsolated yield after column chromatography; NOB not observed (no over-oxidation towards acidic product was observed)

substrates produced target carbonyl compounds in

moderate yields. The better yields of aldehydes were obtained using simple benzyl iodide under Goswami protocol which was 62%.

Effectiveness of Kornblum oxidation to construct carbonyl entities from iodomethyls oxidation

The fifth protocol for the preparation of targeted carbonyl compounds used in this research work was Kornblum oxidation (Kornblum et al. 1959). All the eleven substrates were heated for 20-50 min at temperature of 150°C under nitrogen atmosphere in the presence of DMSO using a base NaHCO₃. This reaction was a best experience for the synthesis of aldehydes and ketones. All the substituted/nonsubstituted benzyl and alicyclic iodides produced the target carbonyl compounds in good to excellent yields (61–83%) and in short reaction time (Table 5). Substrates 3 and 17 were observed to be more efficient substrate in converting into aldehyde and ketone using this procedure with excellent yield of 83%. Only methylated benzyl iodides produced aldehydes in moderate yield, i.e., 61%. All the remaining substrates also produced better to excellent yield of targeted carbonyl compounds. The possible reason of this may be the better solubility of all these compounds in DMSO and favorable reaction conditions for all substituted benzyl and alicyclic iodides.

Hass–Bender reaction for the production of carbonyl units from iodomethyls

Hass-Bender oxidation was the sixth procedure performed for converting iodomethyl groups of different benzyl and alicyclic nucleus into aldehydes and ketones (Hass and Bender 1949). All substrates were treated with 2-nitropropane in the presence of NaOEt in 2-propanol at room temperature for 4-5 h to obtain carbonyl compounds in 49-83% yield (Table 6). The reaction mixture was heated under reflux. Studies showed that this method is convenient and efficient for the oxidation of all nucleus having iodomethyl groups into targeted compounds in better and moderate yield. Excellent yield was obtained from oxidation of benzyl iodide while diphenyl-methyl iodide substrate gave moderate yield (Faisal et al. 2018). The remaining substituted/non-substituted benzyl and alicyclic iodides also gave better results with this reaction by producing these compounds in better vield. The reaction showed that these iodides can act as better substrates under reaction conditions used in Hass-Bender reaction.

Oxidation with periodic acid in IL 1-dodecyl-3-methylimidazolium iron chloride

The next method used in the research work for oxidation of tabulated substrates was reported to be highly effective and environment friendly (Hu et al. 2010a, b). In this method, iodomethyls were treated with periodic acid (H_5IO_6) as an oxidizing agent in the presence of an ionic liquid,

1-dodecyl-3-methylimidazolium iron chloride $[C_{12}mim]$ [FeCl₄] at temperature of 50 °C for 3–5 h. This approach provided 78–92% yield in short reaction time (Table 7). Ionic liquids (ILs) have gradually gained broad appreciation as eco-friendly solvents due to their excellent properties, for example, non-volatility and non-flammability at room temperature, high thermal stability, wide electrochemical window, large liquid range, and strong capability to solubilize a lot of compounds (Rogers and Seddon 2005). Studies demonstrated that IL-based approach is admirable procedure for the oxidation of both substituted/non-substituted benzyl iodides and alicyclic iodides with excellent yields along with good catalytic recyclability. Benzyl iodide, 1-(iodomethyl)naphthalene and 4-methoxybenzyl iodide produced aldehydes and ketones with excellent yields of 91% and 92%, respectively. The remaining substrates were also efficient in transforming to targeted carbonyl compounds with better yields as shown in Table 2.

Recyclability of ionic liquid and the catalyst

The recyclability of the ionic liquid and catalyst was also studied using (iodomethyl)benzene 1 as substrate under identical reaction conditions. Upon reaction completion, the product (benzaldehyde 2) was extracted with dichloromethane from reaction mixture and the rest of the ionic liquid and the catalyst were recovered by decantation of aqueous hydrogen halide produced in the reaction and concentrated under vacuum. (Iodomethyl)benzene 1 was then recharged to the recovered catalyst system and then rerun under identical reaction conditions. The results indicated that the catalyst could be recycled for almost six times with only a small loss of activity. Briefly, the fresh ionic liquid and catalyst afforded compound 2 in 91% yield in reaction time of 3 h. In the first run, the ionic liquid and catalyst provided compound 2 in 86% yield in the same period of reaction time. In the second run, the ionic liquid and catalyst delivered compound 2 in 85% yield in reaction time of 3.5 h. In the third and fourth run, the ionic liquid and catalyst generated compound 2 in 80% yield in reaction time of 4 h. The next run furnished compound 2 in 71% yield in reaction time of 4.3 h. Hence, the approach was highly operative and recyclable catalyst for the preparation of carbonyl compounds.

Oxidation with periodic acid and vanadium pentoxide in 1-butyl-3-methylimidazolium hexafluorophosphate

The next method used for mild oxidation of alicylic and aromatic methyl iodides was also reported to be highly effective and environment friendly (Hu et al. 2010a, b). In this approach, all the iodomethyls were treated with H_5IO_6 in the presence of V_2O_5 as a catalyst and ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphorate ([bmpy][PF₆]) as a solvent at 70 °C for 4–9 h to deliver carbonyl compounds in excellent yields (83–94%). This method was also very potent and convenient for the production of carbonyl compounds by oxidation of all selected substrates (Table 8). 3,4-Dimethylbenzyl iodide, benzyl iodide and 1-(iodomethyl)-naphthalene were the most reactive for converting into aldehydes and ketones by this procedure with maximum yields of 94% and 92%, respectively, while all the remaining iodides were also very efficient in transforming to carbonyl compounds with excellent yields.

Recyclability of ionic liquid and the catalyst

The recyclability of the ionic liquid and catalyst was also studied using (iodomethyl)benzene 1 as substrate under identical reaction conditions. Upon reaction completion, the product (benzaldehyde 2) was extracted with dichloromethane from reaction mixture and the rest of the ionic liquid and the catalyst were recovered by decantation of aqueous hydrogen halide produced in the reaction and concentrated under vacuum. (Iodomethyl)benzene 1 was then recharged to the recovered catalyst system and then rerun under identical reaction conditions. Results indicated that the catalyst could be recycled for almost six times with only a small loss of activity. Briefly, the fresh ionic liquid and catalyst afforded compound 2 in 92% yield in reaction time of 5 h. In first cycle, the ionic liquid and catalyst provided compound 2 in 82% yield in reaction time of 6 h. In second and third cycle, the ionic liquid and catalyst delivered compound 2 in 81% and 80% yield, respectively, in reaction time of almost 6 h. Fourth and fifth cycle generated compound 2 in yields of 75% and 65%, respectively, in the reaction time of almost 7 h. Hence, the approach was observed to be highly operative and recyclable catalyst for the preparation of carbonyl compounds.

lodomethyl oxidation via hydrogen peroxide catalyzed by V_2O_5 and Aliquat 336

Chunbao protocol was the ninth method which was applied for the oxidation of iodomethyl groups to aldehydes and ketones. In this reaction, all the iodomethyls were treated with H_2O_2/V_2O_5 in boiling water with Aliquat 336 as phase transfer catalyst (Li et al. 2003). This approach provided excellent yields (81–92%) in all cases. The reaction was very efficient in converting all the iodides (in better yield) into aldehydes and ketones (Table 9). The excellent yield was obtained by oxidation of 1-(iodomethyl)-4-methylbenzene **11** (92%) while all the remaining compounds showed better oxidation potential with high yields. It has been experimentally verified by Li et al. that there is no formation of alcoholic product (by solvolysis) during the oxidation of halomethyl group. Under reaction conditions, nucleophile $VO(O_2)_2^-$ is formed. In the next step, halo group is directly attacked by nucleophile $VO(O_2)_2^-$ to furnish an intermediate $ArCH_2OV(O_2)_2$. After losing a proton, intermediate $ArCH_2OV(O_2)_2$ decomposes into carbonyl compound (Li et al. 2003). To investigate the yield sustainability on large-scale reaction, some reactions were performed with 30, 60 and 90 mmol of iodomethyl compounds. The investigation revealed that the yields of Table 9 remained sustainable on a large scale.

Recyclability of the catalyst

The recyclability of this synthetic approach was also studied using (iodomethyl)benzene **1** as substrate under identical reaction conditions. Upon reaction completion, the oily layer was separated from reaction mixture and aqueous phase was reused under identical reaction conditions. The results indicated that the catalyst could be recycled for almost four times with only a small loss of activity. Briefly, the fresh catalyst afforded **2** in 86% yield in reaction time of 6 h. 80, 78, 77 and 65% yields of **2** over the reaction time of 6–8 h for the first, second, third and fourth run, respectively.

Bismuth(III) nitrate pentahydrate in tetrabutylammonium fluoride for in situ oxidation of iodomethyl

The last method that we used for the conversion of alicyclic and aromatic iodides to carbonyl compounds was Khodaei method (Khodaei et al. 2005). This is actually the controlled oxidation of alkyl or aryl halomethyls without further oxidation to carboxylic acid and reaction stops at aldehydes and ketones. All the alicylic and aromatic iodides were treated with bismuth nitrate pentahydrate $Bi(NO_3)_3 \cdot 5H_2O$ in the presence of tetrabutylammonium fluoride (TBAF) as an in situ oxidant at 100°C. In short reaction period of 1-2 h, all the iodomethyls were transformed into the products in yield of 78-89% (Table 10). All the iodomethyls produced the targeted compounds in better yields except benzyl iodide and 4-methoxybenzyl iodide that were oxidized efficiently than other with excellent yield of 89%. One of the merits of bismuth nitrate pentahydrate is that it can be used with large variety of alkyl halomethyls and does not need the isolations of intermediate aldehydes. It has been experimentally verified by Khodaei et al. that there is no formation of alcoholic product (by solvolysis) during the oxidation of halomethyl group (Khodaei et al. 2005). To investigate the yield sustainability on large-scale reaction, some reactions were performed with 30, 60 and 90 mmol of iodomethyl compounds. The investigation revealed that the yields of Table 10 remained sustainable on a large scale.

Methodology name	Time	Yield (%) ^a	Yield (%) ^b	Yield (%) ^c
Sommelet reaction	3 h for 1	62	NF	NF
Krohnke oxidation	10 h for 1	82	NF	NF
NaIO ₄ -based oxidation	1 h for 1, 40 min for 23	51	80	NF
MnO ₂ -mediated approach	4 h for 1, 2 h for 23, 6 h for 24	62	80	40
Kornblum oxidation	20 h for 1, 10 h for 23	81	80	NF
Hass-Bender reaction	4 h for 1, 3 h for 23, 4 h for 24	78	72	79
H ₅ IO ₆ in IL-based oxidation	3 h for 1, 2 h for 24	91	NF	94
H_5IO_6 and V_2O_5 in IL-based oxidation	5 h for 1, 3 h for 24	92	NF	92
Chunbao oxidation protocol	6 h for 1, 14 h for 23, 6 h for 24	86	84	70
Khodaei oxidation method	1 h for 1, 1 h for 23, 1.5 h for 24	89	91	90

Table 11 Scope of different transformational approaches towards oxidation of 1, 23 and 24

NF not found in literature

^aIsolated yield of product of oxidation of (iodomethyl)benzene **1**

^bIsolated yield of product of oxidation of (bromomethyl)benzene 23

^cIsolated yield of product of oxidation of (chloromethyl)benzene 24

With all these results from experiments in hands, it is clear that diverse kind of both substituted/non-substituted benzylic and alicyclic iodides, both primary and secondary, could be effectively oxidized to the corresponding aldehydes and ketones in poor to excellent yield effectively. Different functional groups, for example, methyl, methoxy and alkene double bonds can stand with reaction conditions used in these reactions. It can also be considered that the presence of these substituents on the aromatic nucleus may have some effect on the rate of oxidation reaction. The position of the substituents on benzene ring may also affect the oxidizing property of these molecules, for instance, substituents present at ortho and *para* positions increase the reactivity of substrates while at meta-positions deactivate the aromatic ring towards further reaction. In some cases, substituents increase the reactivity while in other cases; they decrease the reactivity towards oxidation which may be due to the substituent effect along with replacing the substituents such as chlorine and bromine on the aromatic and alicyclic rings with iodine.

Table 11 is based on the comparison of yields of benzaldehyde 2 obtained from oxidation of (iodomethyl)benzene 1, (bromomethyl)benzene 23 and (chloromethyl)benzene 24 via applying different transformational approaches. The aim of the Table 11 is to disclose the relative capability of different oxidation protocols towards oxidation of organic halides to aldehydes and ketones.

Conclusion

We have investigated various classical and eco-friendly methods reported in the literature for production of aldehydes and ketones by modifying the substrates from chloromethyl and bromomethyl groups to a more reactive iodomethyl group. Research reveals that, overall, oxidation of iodomethyl groups provides comparable yield in less amount of time as compared to oxidation of chloromethyl or bromomethyl groups. The results also show that green approaches are superior over classic approaches. Among all the techniques, periodic acid-based IL protocol, periodic acid in vanadium pentoxide-mediated IL method and hydrogen peroxide in vanadium pentoxide-based approach (aka. Chunbao oxidation protocol) were found to be highly efficient due to the following reasons: these protocols (1) provide excellent yields (> 80%) in most cases, (2) do not lead towards over-oxidation, (3) are highly recyclable without any important loss of catalytic efficiency, (4) have excellent capacity to dissolve many chemicals, (5) show negligible flammability and large thermal stability, (6) are inexpensive, (7) are eco-friendly, and (8) require no special handling (easy work-up). Iodomethyl groups offer a very simple, mild, efficient and inexpensive means to substituted aldehydes and ketones. This work would be applicable for large-scale synthesis of various carbonyl compounds and could be helpful for designing many organic reactions on industrial scale. Moreover, advantages of this research work include such catalytic systems and ionic liquids which are easy to handle and very much recyclable without significant loss of catalytic activity. Most of the catalysts such as V₂O₅ and Aliquat 336 are found to be economical, efficient and stable under different reactions conditions.

Experimental

Materials and general methods

Chemicals, reagents and solvents were obtained from Spectrochem, SRL, Merck, Aldrich and Process Chemicals. The routine reaction monitoring was carried out with pre-coated silica gel-60 TLC plates (Aldrich, Silica gel H TLC Grade). Chromatographic purification was performed with silica gel (70–230 mesh; Wakogel[®] C-100E). The column size was 19×200 mm. Melting points were measured with a capillary apparatus. ¹H NMR was evaluated on a Varian Gem2300 300 MHz spectrometer (chemical shifts are w.r.t residual solvent peaks; tetramethylsilane = δ 0 ppm). All coupling constants are expressed in Hz and are absolute values.

General procedure for Sommelet reaction

The mixture of 25 mL of 50% acetic acid, 0.05 mol of iodomethyl substrate and 12.66 g (0.09 mol) of hexamethylenetetramine was taken in round bottom flask. The reaction content was refluxed with continuous stirring for appropriate period of time [TLC control (EtOAc/*n*-hexane 1:9); 2.5–4.5 h] at 100 °C. After that 10 mL of 1 M HCl was poured in reaction mixture and stirring was maintained for additional 15 min at same temperature. Then, the reaction mixture was cooled to r.t. Organic layer was washed with DCM, dried over anhydrous MgSO₄ and concentrated in vacuo to give a crude liquid product. Crude liquid product was purified by column chromatography using hexane–ethyl acetate (20:80) as an eluent to provide carbonyl compound (41–71%).

General procedure for Krohnke oxidation

Preparation of pyridinium salt

Pyridinium salt was obtained in a quantitative yield from iodomethyl substrate (0.02 mol) by stirring with excess pyridine (50 ml) at 100 °C for 3 h.

Preparation of the nitrone

A suspension of 0.03 mol of pyridinium salt and 3 g of sodium amide was prepared in 60 ml pyridine. 9 g (0.06 mol) of highly purified *p*-nitrosodimethylaniline and 15 ml of water were added to the suspension with stirring while maintaining the reaction temperature to about 20–30 °C. The reaction mixture was refluxed for 10–12 h and was cooled in ice bath followed by filtration. Recrystallization was done in DMF to obtain nitrone. In a recrystallization procedure, an impure nitrone was dissolved in a hot DMF. As the solution was cooled, the pure product crystallized out and the impurities stayed dissolved.

Preparation of carbonyl compound

The nitrone (0.07 mol) was decomposed in a separatory funnel with 250–320 ml of 2 M HCI and 200 ml of ether.

Reaction content was shaken for about 15 min and extracted with 50 ml portions of ether for three times. The combined ether extract was washed with water and dried over Na_2SO_4 . Ether was evaporated and the obtained residue was purified by column chromatography using hexane:ethyl acetate (20 mL:80 mL) to provide carbonyl compound (67–82%).

General procedure for sodium metaperiodate-based oxidation

Iodomethyl compound (1 mmol) and sodium metaperiodate (NaIO₄) (0.21 g, 1 mmol) were taken in round bottom vessel. 15 ml of DMF was added to reaction vessel to dissolve the mixture. The reaction content was refluxed and the reaction progress was examined by TLC using 10% ethyl acetate in hexane solvent system. Reaction was completed in 60–180 min. After reaction completion, reaction mixture was cooled and 20 ml of water was added to reaction content. Then, extraction was performed in ether (2×30 ml). The ether layer was isolated and was dried over anhydrous magnesium sulfate and filtered. Solvent was evaporated and crude product was purified by column chromatography on silica gel using 10% ethyl acetate in hexane as mobile phase. The 25–51% of carbonyl compound was obtained.

General procedure for manganese dioxide-mediated approach

A mixture of iodomethyl compound (3 mmol) and activated manganese dioxide (1.44 g, 15 mmol) in chloroform (30 mL) was refluxed for 4–7 h at 60 °C. TLC in petroleum ether–dichloromethane (3:1) was employed to monitor reaction progress. After reaction completion, which was indicated by TLC, the reaction mixture was filtered and washed with CHCl₃. The combined filtrates after evaporation and purification with silica gel (10% ethyl acetate in hexane) afforded carbonyl compound (11–62%).

General procedure for Kornblum oxidation

A mixture of DMSO (50 ml) and NaHCO₃ (7.1 g, 84 mmol) in a round bottom flask was thoroughly de-gassed and then heated to 150 °C under nitrogen atmosphere. Then, one portion of iodomethyl compound (16 mmol) was added and the resulting mixture was allowed to stir at 150 °C for about 20–50 min. TLC was run in petroleum ether–dichloromethane (3:1) to monitor reaction progress. After reaction completion, reaction content was cooled to 20 °C for 10 min. Et₂O (100 ml) was added, followed by the addition of water (100 ml). Two layers were formed which were then separated and the aqueous layer was further extracted with diethyl ether. The combined organic layers were washed with H₂O and dried over MgSO₄. Solvent was removed under reduced pressure to give carbonyl compound (61–83%).

General procedure for Hass-Bender reaction

2-Nitropropane (0.33 g, 3.72 mmol) and sodium methoxide (0.27 g, 5.01 mmol) were taken in a reaction flask having 30 mL of 2-propanol. The reaction mixture was refluxed for 30 min and then allowed to cool at r.t. Reaction mixture was then charged with iodomethyl compound (2.67 mmol) and was stirred at room temperature for 4–5 h [TLC control (EtOAc/*n*-hexane 1:9)]. Reaction content was concentrated by evaporation of solvent by rotary evaporator and the residue was extracted with water (45 mL) and dichloromethane (315 mL). The organic layer was dehydrated by anhydrous MgSO₄ and concentrated in vacuo. Further purification of residue was performed by column chromatography on silica gel using hexane/ethyl acetate (8:1) as eluent to afford carbonyl compound (49–83%).

General procedure for periodic acid in IL-based oxidation

To a stirred solution of iodomethyl compound (30 mmol) in $[C_{12}mim]$ [FeCl₄] (1.2 mmol), H₅IO₆ (33 mmol) was added and the reaction mixture was left on stirring at the temperature of 50 °C for an appropriate time (3–5 h). The reaction progress was monitored by means of TLC using EtOAc/n-hexane 1:9 solvent system. After reaction completion, the reaction mixture was extracted with dichloromethane $(3 \times 10 \text{ mL})$. The dichloromethane solution was washed with 5% sodiumbicarbonate (NaHCO₃) and dried over anhydrous Na₂SO₄. The carbonyl compound was purified through recrystallization from hexane and ethyl acetate (solid product) or by distillation (liquid product). In some cases, column chromatography was required to purify product. In these cases, the solvent was removed and the residue was purified by column chromatography using hexane/ethyl acetate (8:1) as mobile phase to give carbonyl compound (78-92%). Remaining ionic liquid and the catalyst were recovered by decantation of aqueous hydrogen halide produced in the reaction and concentrated under vacuum. Fresh substrates were then recharged to the recovered catalytic system and then recycled under identical reaction conditions.

General procedure for periodic acid and vanadium pentoxide in IL-based oxidation

A solution of iodomethyl compound (30 mmol) and ionic liquid [bmpy] PF_6 (15 mL) was taken in a round bottom flask, and then H₅IO₆ (36 mmol) and V₂O₅ (0.9 mmol) were added to reaction solution at r.t. Reaction content was heated at 70 °C with continuous stirring for about 4-9 h. Reaction progress was monitored by means of TLC using EtOAc/n-hexane 1:9 as an eluent. After completion of reaction, the product was extracted with DCM (3×10 mL). The organic layer was isolated and washed with 5% NaHCO₃ solution (3×10 mL) and water $(3 \times 10 \text{ mL})$ to make the pH neutral. Then, the organic layer was dried over Na₂SO₄ and filtered. The carbonyl compound was purified through recrystallization from hexane and ethyl acetate (solid product) or by distillation (liquid product). In some cases, column chromatography was required to purify product. In these cases, the solvent was removed followed by column chromatography using hexane/ethyl acetate (8:1) as eluent which afforded carbonyl compound (83-94%). The rest of the ionic liquid and the catalyst were recovered by decantation of aqueous hydrogen halide produced in the reaction and concentrated under vacuum. Fresh substrates were then recharged to the recovered catalytic system and then recycled under specified reaction parameters.

General procedure for Chunbao protocol

A mixture of iodomethyl compound (3 mmol), H_2O (30 mL), H_2O_2 (30%, 18 mmol), V_2O_5 (0.06 mmol) and Aliquat 336 (0.6 mmol) was refluxed for 6–10 h [TLC control (EtOAc/*n*-hexane 1:9)]. After cooling at room temperature, two layers were observed (organic layer and aqueous layer). The organic phase was separated and concentrated to afford pure carbonyl compound. In the case of cinnamaldehyde, the chromatographic purification was also performed. The crude cinnamaldehyde was purified via silica gel-based chromatographic purification technique, in which ethyl acetate in hexanes (1:2) as eluent was employed to afford desired carbonyl compound (81–92%). The aqueous phase was reused under identical reaction conditions.

Note In some cases of Chunbao protocol, after reaction completion, the organic layer was observed to be very thin; in that cases, it is recommended to add Et_2O (10 ml) in order to get assistance for separation from aqueous phase. For the large-scale preparation of carbonyl compounds from the respective iodomethyl compound, the iodomethyl compound must be added in small portions or dropwise.

General procedure for Khodaei method

TBAF (0.474 g, 1.5 mmol) and Bi(NO₃)₃·5H₂O (1.6 g, 3.3 mmol) were taken in a reaction flask. Then, iodomethyl compound (3 mmol) was added to the reaction vessel and reaction mixture was stirred at 100 °C for about 1–2 h. Completion of the reaction was confirmed by TLC in EtOAc/*n*-hexane 1:9 solvent system. Then, the mixture was cooled to r.t and extracted with diethylether (2 × 10 mL). The organic layer was isolated and further extracted with water followed by drying over anhydrous sodium sulfate. Solvent was evaporated in vacuo and crude product was purified by chromatography (column size: 19×200 mm) over silica gel (70–230 mesh; EtOAc–hexane, 1:9) afforded the carbonyl compound in 78–89% yield. In some cases, column chromatography was not required to purify product. In these cases, evaporation of solvent under vacuo afforded pure product.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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