One pot oxidative cleavage of 1,2-arylalkenes into arylketones under microwave in aqueous conditions

1.1 Introduction
The oxidative functionalization and cleavage of alkenes represents a fundamental transformation [Lee and Chen (1991); Kuhn et al. (2004)] in organic synthesis [Thottumkara and Vinod (2010)]. Depending upon the substitution pattern around the double bond i.e. 1,2 or 1,1-disubstituted alkenes, the oxidative cleavage of respective alkenes can lead to the formation of either aldehydes or ketones respectively (Scheme 1).

1.2 Significance of oxidative cleavage
Oxidative cleavage has wide spread applications in synthesis of biologically important compounds besides total synthesis of natural products [Green et al. (2008); Hirashima et al. (2009)]. The major utility of such cleavage reactions is due to their unique ability to truncate readily available hydrocarbon feedstocks with simultaneous introduction of carbonyl functionality.

1.3 Reported methods for oxidative cleavage of alkenes
The oxidative cleavage of alkenes has been conventionally achieved mainly through two principal approaches i.e. Ozonolysis [Bailey (1978); Larock (1999)] and Lemieux-Johnson reaction [Shing et al. (1991)].

1.3.1 Conventional approaches

1.3.1.1 Ozonolysis
Ozonolysis has been used extensively in academic, research and industrial domains and it involves the cleavage of an alkene or alkyne with O₃ (ozone) to form organic compounds
with carbonyl [Bailey and Erickson (1973); Claus and Schreiber (1990); Tietze and Bratz (1998)] via the formation of ozonide intermediate through Criegee mechanism (Scheme 2). The outcome of the reaction depends on the type of multiple bonds being oxidized and the work up conditions. Oxidative workup results in the formation of acid along with ketone while, reductive work up gives rise to aldehyde and ketone. Synthesis of (+) artemisinin via Avery’s approach using ozone in the final step [Avery et al. (1992)] is a well known example of ozonolysis. Inspite of immense applications, ozonolysis has generated grave concerns due to the handling and health hazards related to ozone.

**Scheme 2**

### 1.3.1.2 Lemieux-Johnson reaction

In comparison to ozonolysis reaction, the Lemieux-Johnson reaction involves two step methodology (Scheme 3), i.e. dihydroxylation of the carbon-carbon double bond by the **Lemieux-Johnson reagent** (sodium periodate-osmium tetroxide) followed by cleavage into
carbonyl compounds. However the strong oxidizing conditions associated with the above protocol also enhances the probability of over oxidation into acids. Lemieux-Johnson reaction has also been used in total synthesis of natural products like isosteviol (Scheme 4) [Snider et al. (1998)] using sodium periodate-osmium tetraoxide.

![Scheme 4](image)

**Scheme 4**

In spite of their immense utility, the ozonolysis and Lemieux-Johnson reaction are considerable challenges in view of safety and over oxidation concerns. In particular, ozone gas is highly toxic and its generation requires specialized equipment. Consequently, the development of safer alternatives as well as conceptually newer olefinic cleavage approaches has attracted increased attention.

### 1.3.2 Contemporary approaches for oxidative cleavage of alkenes

Travis et al. explored a mild, organometallic alternative to ozonolysis using OsO₄ with oxone as the co-oxidant in DMF, for oxidative cleavage of olefins to provide carboxylic acids. Plausible mechanism involves the intermediacy of an osmate ester which undergoes cleavage to provide the final oxidized product (Scheme 5) [Travis et al. (2002)].

![Scheme 5](image)

**Scheme 5**

On the other hand, Yang et al. have successfully cleaved aryl olefins into aromatic
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aldehydes rather than carboxylic acids, in excellent yields by using the system of RuCl$_3$-Oxone-NaHCO$_3$ in CH$_3$CN-H$_2$O (1.5: 1) (Scheme 6) [Yang and Zhang (2001)].

\[
\begin{align*}
\text{Ph} & \quad \text{Ph} \\
& \quad \quad \text{1.5 eq. oxone, 4.7 eq. NaHCO$_3$} \\
& \quad \quad \text{rt, pH 7-7.5, 0.5 h} \\
& \quad \quad \text{85%}
\end{align*}
\]

Scheme 6

The current trend toward “clean and rapid” synthesis has lead to reagent immobilization to enable easy recovery, reuse and disposal at an acceptable economic cost. In this context, osmium tetraoxide microencapsulated in a polyurea matrix has been used as recyclable catalyst in the dihydroxylation and the oxidative cleavage of olefins (Scheme 7) [Ley et al. (2003)].

\[
\begin{align*}
\text{Os EnCat = OsO}_4 \text{ microencapsulated in a polyurea matrix}
\end{align*}
\]

Scheme 7

Recently, Nicolaou et al. reported a one-pot combination of hydroxylation followed by the addition of stoichiometric Ph(IOAc)$_2$ to effect alkene cleavage in the presence of OsO$_4$ (cat.) and 2,6-lutidine to yield the corresponding carbonyl compounds (Scheme 8). The described synthetic method offers a convenient and economical alternative to the traditional olefin cleavage methods for laboratory operations [Nicolaou et al. (2010)].

\[
\begin{align*}
\text{R}_1, \text{R}_2, \text{R}_3 & = \text{H, alkyl, aromatic etc.}
\end{align*}
\]

Scheme 8
Wang et al. have reported a palladium catalyzed protocol with O$_2$ as the sole oxidant for efficient oxidation of a wide range of olefins into aldehydes or ketones (Scheme 9) [Wang and Jiang (2010)].

![Scheme 9](image)

In another report, Ho et al. utilized heterogeneous recyclable catalyst comprising ruthenium nanoparticles grafted onto hydroxyapatite for cis-dihydroxylation and oxidative cleavage of alkenes (Scheme 10). The utility of protocol was demonstrated both on small and larger scale [Ho et al. (2004)].

![Scheme 10](image)

Similarly, catalytic amounts of environmentally benign organo iodine reagent 4-IB Acid (4-iodobenzoic acid) in the presence of oxone as a co-oxidant was employed for oxidative cleavage of different alkenes (Scheme 11) [Thottumkara and Vinod (2010)].

![Scheme 11](image)

In the same vein, Xing et al. developed a unique gold catalysed homogeneous oxidation process (Scheme 12) for cleavage of C=C bond to afford ketone or aldehyde products with tertiary butyl hydrogen peroxide (TBHP) as the oxidant in water [Xing et al. (2006)].
In an another strategy, Singh et al. utilized m-chloroperbenzoic acid (Scheme 13) for the oxidative cleavage of 1,1-diarylalkenes into benzophenone via the formation of epoxide intermediate [Singh et al. (2009)].

However, only a limited number of papers in the field of microbial alkene cleavage have been published. In one such report, an enzymatic oxidative cleavage of alkene using the cell free extract of Trametes hirsuta has also been reported (Scheme 14) [Lara et al. (2009)] in the presence of O₂.

Recently, Sharma et al. have used newly isolated Pseudomonas mandelii KJLPB5 and [hmim]Br for direct conversion of aryl alkene into corresponding one or two carbon shorter aryl aldehydes in H₂O₂ through oxidative cleavage pathway (Scheme 15). The ionic liquid was proposed to either act as activator or help in stabilization of enzymes [Sharma et al. (2011)].
On the other hand, Schiaffo et al. developed a method for ozonolysis of alkenes in a mixture of water and a miscible organic solvent for a fast, convenient and efficient one-pot synthesis of aldehydes and ketones without the need for a separate reductive step and further avoiding the need to isolate or decompose ozonides (Scheme 16) [Schiaffo and Dussault (2008)].

Shaikh et al. have explored inexpensive iron (III) chloride hexahydrate (FeCl₃·6H₂O, 5 mol%) catalyst in combination with commercially available aqueous 70% TBHP as oxidant for the cleavage of olefins into acids. The method was suitable for a wide range of aromatic olefins and alkynes that contain electron-donating and electron withdrawing functional groups (Scheme 17) [Shaikh and Honga (2011)].

Hart et al. described the oxidative cleavage of olefins with osmium tetraoxide using hydrogen peroxide (H₂O₂) as the terminal oxidant. The protocol offered the corresponding aldehyde and ketone products in moderate to excellent yields (Scheme 18) [Hart et al. (2011)].
Similarly, Yu et al. reported an improved procedure for oxidative cleavage of olefins by OsO₄-NaIO₄. The addition of 2,6-lutidine was found to suppress the side reactions and dramatically improved the yield of the reaction (Scheme 19) [Yu et al. (2004)].

**Scheme 18**

Yusubov et al. disclosed the oxidative transformations of alkenes and alkynes under the action of diacetoxyiodobenzene (DIB) and found that non terminal alkenes behave in a different manner. For instance oxidation of E-stilbene with the DIB-H₂SO₄ system (Scheme 20) gave a mixture of different products with little amount of benzophenone [Yusubov et al. (2004)].

**Scheme 19**

Kim et al. elaborated a new chemoentrapment strategy for recycling osmium in the catalytic olefin cleavage reaction. This approach utilizes KOH/i-PrOH to generate water-
soluble Os (VI) species as a recyclable metal catalyst after the oxidative cleavage reaction (Scheme 21) [Kim et al. (2011)].

It is evident from foregoing discussion that the above contemporary approaches for oxidative cleavage have resulted in a significant improvement over classical protocols. It would also be apparent that the substitution pattern around an olefinic bond largely determines the nature of cleavage products. Thus, all of the above approaches cleave 1,2-disubstituted alkenes into aldehydes while ketone cleavage products are usually obtained only from respective 1,1-disubstituted alkenes (Scheme 1). However, a general approach for the counterintuitive one step formal scission of abundantly available 1,2-arylalkene and diarylalkenes into one carbon shorter arylketones instead of arylaldehydes has not yet been disclosed although in few cases such a transformation has been noticed as a side reaction during oxidation of stilbenes [Yusubov et al. (2004)] (Scheme 20). Moreover the 1,1-dialkyketones formed by the oxidative cleavage of C=C bond of 1,2-arylalkenes constitute an important core structure of several biologically active molecules e.g. hydroxyphenstatin (Figure 1), an anticancer benzophenone.

In this context, it would be highly desirable if an approach complementary to classical ozonolysis & Lemieux-Johnson reaction could be devised leading to selective oxidative cleavage of aryl- & 1,2-diarylalkenes into one-carbon shorter arylketones. Such a methodology would provide a useful complementary tool to the prevalent approaches as it considerably enhances the flexibility for cleaving an olefinic bond into either aldehydes or ketones irrespective of the substitution pattern around a double bond.
1.4 Results and Discussion

In the course of our programme towards catalytic synthesis of biologically important phenolics [Kumar et al. (2008); Sharma et al. (2008), (2009), (2010)], we initially desired to achieve a one step conversion of abundantly available aryl alkenes such as anethole, β-asarone etc. into corresponding α-arylpropionic acids, which are constituents of non steroidal anti-inflammatory drugs (NSAID’s) [Marnett and Blobaum (2007)]. In this context, we planned to utilize our recently developed approach [Sharma et al. (2009)] comprising direct oxidation of aryl alkenes into α-aryl aldehydes for an in situ oxidation [Dvorak (1983); Yan and Zhang (2006)] of such aldehydes into respective α- substituted arylalkanoic acids. Consequently, PDC (pyridinium dichromate) was chosen as the in situ oxidizing agent due to its known ability to convert such α-substituted aryl aldehydes into arylalkanoic acids. However, contrary to our expectations, the reaction of 1a (Table 1) with N-iodosuccinimide (NIS, 1.3 eq), CTAB followed by treatment with PDC (6 eq) in same pot under microwave (MW) provided a product whose detailed GC-MS and NMR investigations revealed it to be one carbon shorter acetophenone (1b, C_{6}-C_{2} unit) instead of the expected α-arylpropionic acid (C_{6}-C_{3} unit). So the direct oxyfunctionalization and cleavage of even 1,2-arylalkenes into ketones instead of aldehydes prompted us to further explore its scope.

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<tr>
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<tr>
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</tr>
<tr>
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<td>PCC</td>
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<tr>
<td>6</td>
<td>Oxone</td>
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<td>–</td>
<td>38</td>
</tr>
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<td>6</td>
<td>–</td>
<td>41</td>
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<tr>
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<td>1.5</td>
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<td>18</td>
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<td>Pyridine-2,5-dicarboxylic acid</td>
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<tr>
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<td>0.05/6</td>
<td>CH_{3}COOH</td>
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[a] CEM monomode microwave. General conditions: 1a (1.35 mmol), NIS (1.75 mmol), CTAB (0.08 mmol) in dioxane (11 ml), water (3.7 ml) were irradiated under MW (115°C, 250 W) for 15 min followed by cooling and addition of oxidant, additive (2.0 mmol) and further MW for 15 min. [b] Based on GC-MS analysis. [c] Isolated yield of pure product.

One pot oxidative cleavage

and mechanistic pathway.

Consequently, a detailed optimization study (Table 1) was conducted to evaluate the effect of various oxidizing agents and additives. Interestingly, the use of other well known oxidizing agents like oxone, TBHP, \( \text{H}_2\text{O}_2 \) etc. didn’t proved beneficial for oxidative cleavage of arylalkenes (Table 1, entries 6, 12-13). However, addition of a reduced amount of PDC (1.5 eq) led to a significantly increased yield of \( 1b \) (71%, Table 1, Entry 3). Amongst the various acidic/basic additives, the use of acetic acid led to further improvement in reaction performance besides helping in work up of the reaction mixture (Table 1, Entry 14).

The apparently counterintuitive cleavage of even 1, 2-disubstituted arylalkenes into aryl ketones instead of aryl aldehydes implied a oxygenation-rearrangement-oxidative cleavage pathway. Thus, arylalkene (a) is initially converted to corresponding \( \alpha \)-arylaldehyde in the presence of NIS/\( \text{H}_2\text{O} \) (Figure 2, a’). Subsequently, the oxidation of this \( \alpha \)-arylaldehyde into one carbon shorter ketone can proceed through a number of intermediates [Perlman et al. (1994); Clennan and Pan (2003); Bryant et al. (2004); Velosa et al. (2007)] including \( \alpha \)-arylacid [Rozner et al. (2007); Das et al. (2008)] and enol [Heathcock et al. (1985); Perlman et al. (1994)] etc. Thus, the incipient \( \alpha \)-arylaldehyde (a’) can undergo oxidation into corresponding \( \alpha \)-arylacid which is further converted into respective ketone through oxidative decarboxylation (Figure 2). In order to evaluate the above possibility, the standard acids i.e. Flurbiprofen (2-(2-fluorobiphenyl-4-yl)propanoic acid) or Ibuprofen (2-(4-(2-methyl propyl)phenyl)propionic acid) were treated with PDC under identical conditions, however, the corresponding ketones were not detected. In another alternative pathway, the incipient \( \alpha \)-arylaldehyde undergoes acid catalyzed enolization [Heathcock et al. (1985); Perlman et al. (1994)] followed by PDC assisted oxidative cleavage into corresponding ketone.

![Figure 2. Plausible mechanistic pathways for one pot oxidative cleavage of 1, 2-disubstituted arylalkenes into one carbon shorter ketones (Published in Eur. J. Org. Chem. 2010, 6025-6032).](image-url)
ketone (b) (Figure 2) [Rozner et al. (2007); Das et al. (2008)].

In order to further confirm the above mechanistic rationale, arylalkene (1a) was treated with PDC/acetic acid alone in dioxane/water (3:1) under MW. Interestingly, the above reaction afforded only methoxybenzaldehyde, thereby, clearly highlighting the critical role of cascade pathway (Figure 2) in providing an exclusive access to ketone cleavage products. Further, the role of MW [Kappe (2004)] was also evaluated by reaction of 1a under thermal heating at similar temp., however, 1b was obtained in comparatively lower yield (55%) with longer reaction times (6 h). It is pertinent to mention here that such a cleavage of incipient α-arylaldehyde into respective one carbon shorter ketones has earlier been observed using reagents like O₂ (in combination with polyoxometalates/zeolite), ruthenium-oxo complexes, peroxidises and PhI(OAc)₂ etc.

The utility of above optimized protocol for cleavage of C=С double bonds was subsequently ascertained. As would be evident from Table 2, various aromatic and polyaromatic arylalkenes bearing electron donating/withdrawing groups (EDG’s/EWG’s) underwent facile oxidative cleavage into corresponding aryl ketones instead of the aryl aldehydes. Further, the arylalkene with elongated side chain (C₆-C₅ unit) was also found

| Table 2. Oxidative cleavage of 1,2-arylalkenes into arylketones instead of arylaldehydes under focused microwave irradiation[a] |
|---|---|---|
| | Substrate (a) | Product (b) |
| 1 | 1-15a | 1-15b |
| 2 | Same pot ii) PDC, CH₃COOH Dioxane /Water (3:1) MW (115°C, 250W) R = H, OMe, OH, OCH₃, Cl, C₆H₅, OC₆H₄, OC₆H₁₃ etc. R’ = CH₃, CH₂CH₂CH₃ etc. | |
| 3 | R₃CO | H₃COCO |
| 4 | H₃COCO | H₃COCO |
| 5 | H₃COCO | H₃COCO |
| 6 | H₃COCO | H₃COCO |

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (a)</th>
<th>Product (b)</th>
<th>Yield(b) (%)</th>
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<tr>
<td>1</td>
<td>1-15a</td>
<td>1-15b</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>Same pot ii) PDC, CH₃COOH Dioxane /Water (3:1) MW (115°C, 250W) R = H, OMe, OH, OCH₃, Cl, C₆H₅, OC₆H₄, OC₆H₁₃ etc. R’ = CH₃, CH₂CH₂CH₃ etc.</td>
<td>R₃CO</td>
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<td>H₃COCO</td>
<td>H₃COCO</td>
<td>67</td>
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to be compatible (Table 2, Entry 3) with the developed methodology. On the other hand, the olefin possessing free phenolic group (Table 2, Entry 11) provided lower yield of respective aryl ketone owing to probable polymerization besides formation of some side products. Similarly, the relatively unactivated substrates like 1,1-disubstituted (Table 2, Entry 14) and aliphatic alkenes (Table 2, Entry 15) also led to low or no reaction performance presumably due to the reduced formation of corresponding α-substituted aryl aldehydes in the first step as shown in figure 2.

Having successfully realized the oxidative cleavage approach, it was envisaged to further explore the one pot halogenation-oxidative cleavage sequence. However, the *in situ* reaction of 2b (obtained from oxidative cleavage of 2a) with NIS [Yadav *et al.* (2004)]

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[a] CEM monomode microwave. General conditions: Substrate (0.9 mmol), NIS (1.18 mmol), CTAB (0.08 mmol) in dioxane (11 ml), water (3.7 ml) were irradiated under MW (115°C, 250W) for 15 min followed by cooling and addition of PDC (1.36 mmol), CH₃COOH (1.36 mmol) and further MW for 15 min. [b] Yield of pure isolated product (single run). The structure of all products was confirmed by NMR (¹H & ¹³C) and HRMS analysis. [c] Based on GC-MS. [d] Not detected.

didn’t afford the expected 2-iodoacetophenone (2b’) (Scheme 22). Surprisingly, an alternative approach proved fruitful, wherein, initial treatment of 2a with excess NIS [Sharma et al. (2009)] followed by oxidative cleavage with PDC provided the expected iodo derivative 2b’, thereby, demonstrating the successful incorporation of both oxygen and iodo groups in a single operational step (Scheme 22). **Scheme 22.** One-pot halogenation-oxidative cleavage of arylalkene

The success with 1,2-arylalkenes (Table 2) motivated us to explore an analogous oxidative cleavage of 1,2-diaryl alkenes into corresponding diarylketones (benzophenones). However, the developed protocol didn’t provide expected result as stilbenes (16-18a) were selectively cleaved into benzaldehydes (Scheme 23).

**Scheme 23.** Selective oxidative cleavage of symmetrical and unsymmetrical 1,2-diarylalkenes into arylaldehydes

In the view of above result as well as the well known tendency of such diarylalkenes towards cleavage into arylaldehydes, a reduced amount of PDC (0.8 eq.) was also tried but to no avail. On the other hand, the use of other oxidizing agents like H_2O_2, TBHP, K_2Cr_2O_7 etc. did provide desired benzophenone (19b, Table 3) but in low yields. Further, some unreacted starting 1,2-diaryl alkene was also obtained using above reaction conditions. Thereafter, detailed studies were conducted for identifying an oxidation system compatible with such 1,2-diaryl alkenes. Interestingly, a combination of catalytic PDC (0.05 eq.),
TBHP (6 eq.) along with an increased amount of NIS (2 eq. in place of 1.3 eq., Table 2) and acetic acid (at the start) was required to overcome the initial sluggish conversion of such diaryl substituted alkenes into corresponding iodoxydrins (Figure 2) which finally afforded the desired 19b (Table 3, Entry 19) in enhanced 49% yield. Subsequently, above optimum reaction conditions were also found to be applicable on various unsubstituted, electron rich and electron deficient 1,2-diaryl alkenes (Table 3, Entries 19-22 & 25-26).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (a)</th>
<th>Product (b)</th>
<th>Yield (b) (%)</th>
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[a] CEM monomode microwave. General conditions: Substrate (0.79 mmol), NIS (1.5 mmol), CH₃COOH (1.16 mmol), CTAB (0.08 mmol) in dioxane (11 ml), water (3.7 ml) were irradiated under MW (115°C, 250W) for 15 min followed by cooling and addition of PDC (0.04 mmol)/TBHP (4.7 mmol), and further MW for 15 min. [b] Yield of pure isolated product (single run). The structure of all products was confirmed by NMR (¹H & ¹³C) and HRMS analysis. [c] Based on GC-MS. (Published in Eur. J. Org. Chem. 2010, 6025-6032).
along with the substrates having aromatic or polyaromatic cores (Table 3, Entry 23 & 24). It is pertinent to mention that the oxidative cleavage of olefins into benzophenones has been earlier reported using only 1,1-diaryl substituted C=C double bonds. In this context, the developed methodology affords the first direct scission of even 1,2-diaryl olefins into corresponding benzophenones.

Having developed a new approach for oxidative cleavage of diverse arylalkenes, we were intrigued to evaluate further applications of the developed methodology. In this context, we were attracted by several reports of total synthesis of natural products, wherein, a two step sequence of oxidative cleavage followed by condensation [Gwaltney II et al. (1996); Hayes et al. (2006); Somu and Johnson (2006)] has comprised an important strategy. Consequently, the realization of a one pot protocol for tandem oxidative cleavage-condensation would be beneficial as it would eliminate isolation of intermediates [Somu and Johnson (2006)]. As a proof of concept, 1a was subjected to developed oxidation protocol (Table 2) till formation of 1b (Table 2), and thereafter a base such as NaOH (10 \%) and 2,4,5-trimethoxybenzaldehyde

<table>
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<th>Entry</th>
<th>Substrate (a)</th>
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<td>(1a)</td>
<td>HCHO</td>
<td>(4a)</td>
<td>56</td>
</tr>
<tr>
<td>28</td>
<td>1a</td>
<td>Cl</td>
<td>(2a)</td>
<td>60</td>
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<tr>
<td>29</td>
<td>1a</td>
<td>Cl</td>
<td>(2a)</td>
<td>34</td>
</tr>
<tr>
<td>30</td>
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<td>Cl</td>
<td>(2a)</td>
<td>52</td>
</tr>
<tr>
<td>31</td>
<td>(4a)</td>
<td>Cl</td>
<td>(4a)</td>
<td>68</td>
</tr>
</tbody>
</table>
(1.3 eq) was added to the same pot and stirred for 2 h (Table 4). Gratifyingly, this one pot approach proved useful to directly obtain the condensation product (27b) from corresponding arylalkene (1a) in 56% overall yield (Table 4, Entry 27). Later on, the above one pot strategy was also successfully applied for hitherto unknown route to one pot oxidation-condensation of arylalkenes (Table 4). Further various condensation products (Table 4, 28-37) along with some heteroaromatic moieties (Entries 32-37) have also been synthesized.

### 1.5 Conclusion

In conclusion, a new oxidative cleavage approach has been developed which affords for the first time a selective scission of 1,2-disubstituted alkenes into one carbon shorter ketones using NIS and PDC/TBHP as co-oxidants. The methodology considerably enhances the flexibility for cleaving a 1,2-disubstituted olefinic bond into either ketones or aldehydes. Moreover, the reaction showed wide substrate scope as diverse 1,2-arylalkenes as well as...
1,2-diaryl alkenes bearing electron donating or withdrawing groups underwent facile cleavage into corresponding arylketones. Significantly, the protocol also paved way for the synthesis of chalcones and some heteroaromatic chalcones through valuable one pot oxidative cleavage-condensation reaction which has widespread utility in total synthesis of natural products.

1.6 Experimental Section

1.6.1 General

β-asarone was obtained from natural Acorus calamus oil following our earlier reported procedure [Sinha et al. (2002)]. The naphthyl and stilbene derivatives were prepared through a previously reported Grignard–dehydration [Kumar et al. (2008)] or Heck approach [Plevyak and Heck (1978)] respectively. The rest of the arylalkenes and NIS (N-iodosuccinimide) were reagent grade (purchased from Merck and Aldrich). Glacial acetic acid (99-100 % for synthesis), PDC (pyridinium dichromate) and other oxidants were purchased from either Merck or Aldrich and used as supplied. The solvents used for isolation/purification of compounds were obtained from commercial sources (Merck) and used without further purification. Column chromatography was performed using silica gel (Merck, 60-120 mesh size). $^1$H (300 MHz) and $^{13}$C (75.4 MHz) NMR spectra were recorded on a Bruker Avance-300 spectrometer. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet, q = quartet. HRMS-ESI spectra were determined using micromass Q-TOF ultima spectrometer. GC-MS analysis was carried out on Shimadzu MS-QP-2010 system equipped with a stationary phase DB-5MS column (Agilent Technologies, U.S.A.). CEM Discover© focused microwave (2450 MHz, 300W) was used wherever mentioned. The temperature of reactions in microwave heating experiments was measured by an inbuilt infrared temperature probe that determined the temperature on the surface of reaction flask. The sensor is attached in a feedback loop with an on-board microprocessor to control the temperature rise rate. In the case of conventional heating in oil bath, the temperature of reaction mixture was monitored by an inner thermometer.
1.6.2 Optimization of reaction conditions

1.6.2.1 One pot cascade oxidative cleavage of \( p\)-methoxyphenylpropene (1a) into one carbon shorter \( 4'\)-methoxyacetophenone using NIS/PDC as an oxidizing agent (Table 1, Entry 1)

The \( p\)-methoxyphenylpropene (1a, 1.35 mmol) was treated with NIS (1.75 mmol), CTAB (0.08 mmol) in dioxane (11 ml), water (3.7 ml) was conducted under focused microwave system (250 W, 115°C) for 15 min followed by treatment with PDC (6 eq) in same pot under microwave (250 W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na\(_2\)S\(_2\)O\(_3\) solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na\(_2\)SO\(_4\) and vacuum evaporated. The obtained residue was subsequently purified by column chromatography on silica gel (60-120 mesh size) using hexane:ethylacetate (9.3:0.7) to give a product (light yellow solid, 41% yield) whose detailed GC-MS and NMR investigations revealed it to be \( 4'\)-methoxyacetophenone (1b) instead of the expected \( \alpha\)-arylpropionic acid.

\( 4'\)-methoxyacetophenone (1b, Table 1)

![Structure of 4'-methoxyacetophenone](image)

Light yellow solid, m.p. 35-39°C (lit. m.p. 36-38°C) [Ohno et al. (2004)], \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) (ppm) 7.93 (2H, d, \( J = 7.8 \) Hz), 6.93 (2H, d, \( J = 8.2 \) Hz), 3.84 (3H, s), 2.53 (3H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta \) (ppm) 195.6, 162.7, 130.6, 130.3, 113.7, 56.4 and 28.1.

1.6.2.2 One pot cascade oxidative cleavage of \( p\)-methoxyphenylpropene (1a) into one carbon shorter \( 4'\)-methoxyacetophenone using varying amounts of PDC (Table 1, Entries 2-4) as an oxidizing agent

To a stirred mixture of \( p\)-methoxyphenylpropene (1a, 0.2 g, 0.9 mmol) and dioxane (11 ml), water (3.7 ml), CTAB (0.03g, 0.08 mmol) and NIS (0.26 g, 1.18 mmol) were added and the mixture was allowed to stir for 5 min at room temperature. Subsequently, the flask was irradiated under focused microwave system (250 W, 115°C) for 15 min. Thereafter, the above reaction flask was cooled and varying amounts of PDC (3 or 1.5 or 1.2 equiv.
respectively) were added and further irradiated under microwave (250W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na$_2$S$_2$O$_3$ solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na$_2$SO$_4$ and vacuum evaporated and obtained residue subjected to GCMS analysis. The above experiments provided $1b$ in 64, 71 and 61% yields in the case of 3, 1.5 and 1.2 eq of PDC respectively. Thus, 1.5 equiv. of PDC was found to be the appropriate.

### 1.6.2.3 One pot cascade oxidative cleavage of 1a into 1b using different oxidizing agent (Table 1, Entries 5-13)

The reactions were performed in the same manner as given in section 1.6.2.2 with PCC, oxone, Ag$_2$O, H$_2$IO$_6$, TBAF, CrO$_3$ and K$_2$Cr$_2$O$_7$ replacing PDC in equal molar amounts in each case, while in case of TBHP and H$_2$O$_2$, 6 equivalents of each were utilized. The above reactions upon completion followed by work up as given in section 1.6.2.2 and followed by GCMS analysis provided $1b$ in 42, 38, 42, 29, traces, 23, 62, 46 and 41% yields in the each case respectively. Thus, PDC (Table 1, Entry 3) was found to be the optimum oxidizing agent and used in all the subsequent experiments.

### 1.6.2.4 One pot cascade oxidative cleavage of 1a to 1b using PDC and different acidic and basic additives (Table 1, Entries 14-18)

The reactions were performed in the same manner as given in section 1.6.2.2 except that (2.0 mmol) of CH$_3$COOH, CF$_3$COOH, NaOH, L-Proline or pyridine-2,5-dicarboxylic acid were added in the second step of each case. The above reactions upon completion followed by work up and GCMS analysis as given in section 1.6.2.2 provided $1b$ in 79 (71% after column purification), 76, 61, 78 and 76% yields in each case respectively. Thus, CH$_3$COOH was found to be the effective additive and used in all the subsequent experiments.

### 1.6.2.5 One pot cascade oxidative cleavage of 1a to 1b using H$_2$O$_2$ and TBHP as co-oxidant with PDC using CH$_3$COOH as additive (Table 1, Entries 19 & 20)

The reactions were performed in the same manner as given in section 1.6.2.2 except that PDC (0.05 equiv.) was used along with H$_2$O$_2$ and TBHP (6 equiv. of each) as co-oxidants.
and acetic acid (2.0 mmol) as additive. The above reactions upon completion followed by work up and GCMS analysis as given in section 1.6.2.2 provided 1b in 30 and 35% yields respectively.

1.6.2.6 Optimized procedure for one pot cascade oxidative cleavage of 1a to 1b using PDC as oxidising agent with CH₃COOH as additive (Table 2)

To a stirred mixture of p-methoxyphenylpropene (Table 2, Entry 1, 0.2 g, 0.9 mmol) and dioxane (11ml), water (3.7 ml), CTAB (0.03g, 0.08 mmol) and NIS (0.26 g, 1.18 mmol) were added and the mixture was allowed to stir for 5 min at room temperature. Subsequently, the flask was irradiated under focused microwave system (250W, 115°C) for 15 min. Thereafter, the above reaction flask was cooled then acetic acid (0.08 ml, 1.36 mmol), PDC (0.51 g, 1.36 mmol) were added and further irradiated under microwave (250W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na₂S₂O₃ solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na₂SO₄ and vacuum evaporated. The obtained residue was subsequently purified by column chromatography on silica gel (60-120 mesh size) using hexane: ethylacetate (9.3:0.7) to give 1-(4-methoxyphenyl)ethanone (1b) as light yellow solid in 71% yield, m. p. 35-39°C.

The above procedure was also followed for oxidative cleavage of all the other arylalkenes (Table 2, 2-14a) into corresponding product (Table 2, 2-14b)

3', 4'- Dimethoxyacetophenone (2b, Table 2)

White solid, m.p. 48-50°C (lit. m.p. 49-51°C) [Jiang and Ragauskas (2007)], ¹H NMR (300 MHz, CDCl₃); δ (ppm) 7.56 (1H, d, J = 8.6 Hz), 7.49 (1H, s), 6.87 (1H, d, J = 8.6 Hz), 3.92 (6H, s), 2.54 (3H, s); ¹³C NMR (75.4 MHz, CDCl₃); δ (ppm) 197.2, 153.8, 149.6, 131.1, 123.7, 110.7, 56.5 and 26.6.
1-(3, 4-Dimethoxyphenyl)-1-butanone (3b, Table 2)

White solid, m.p. 65-68°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.60 (2H, t, $J = 9.2$ Hz), 6.90 (1H, s), 3.94 (6H, s), 2.92 (2H, $t, J = 7.1$ Hz), 1.80-1.72 (2H, m), 1.03 (3H, t, $J = 7.9$ Hz); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 199.4, 153.5, 149.4, 130.8, 123.0, 110.6, 56.4, 40.4, 18.5 and 14.6.

3', 4'- (Dioxymethylene) acetophenone (4b, Table 2)

White solid, m.p. 84-87°C (lit. m.p. 86–89°C) [Giddens et al.(2005)] ; IR (KBr): 1663 cm$^{-1}$ (C=O); $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.57 (1H, d, $J = 8.2$ Hz), 7.43 (1H, s), 6.86 (1H, d, $J = 8.2$ Hz), 6.05 (2H, s), 2.54 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 197.1, 152.7, 149.1, 133.1, 125.7, 108.9, 108.8, 102.8, and 27.4.

1-(6'-Methoxy-2'-naphthyl)ethanone (6b, Table 2)

White solid, m.p. 63-66°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.37 (1H, s), 8.01 (1H, d, $J = 8.4$), 7.84 (1H, d, $J = 8.7$), 7.76 (1H, d, $J = 8.7$), 7.21 (1H, d, $J = 8.7$), 7.14 (1H, s), 3.92 (3H, s), 2.69 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 198.2, 160.2, 137.7, 133.0, 131.5, 130.1, 128.2, 127.5, 125.0, 120.3, 106.5, 55.8 and 26.9. HRMS-ESI: m/z [M+H]$^+$ for C$_{13}$H$_{12}$O$_2$, calculated 201.0894; observed 201.0882.

1-Naphthyl methyl ketone (7b Table 2)
Light yellow liquid, \cite{Yao2003}, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.78 (1H, d, $J = 8.7$), 8.00-7.83 (3H, m), 7.63-7.46 (3H, m), 2.74 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 202.2, 135.8, 134.4, 133.4, 130.6, 129.1, 128.8, 128.4, 126.8, 126.4, 124.7 and 30.3.

**4-Acetylbiphenyl (8b Table 2)**

\[
\begin{align*}
&\text{Creamish solid, m.p. 116-119°C (lit. m.p. 117-120°C), \cite{Balasankar2005},} \\
&^1\text{H NMR (300 MHz, CDCl$_3$); } \delta \text{ (ppm) 8.26 (2H, t, } J = 8.8 \text{ Hz), 7.96-7.92 (4H, m), 7.74 (3H, t, } J = 8.8 \text{ Hz), 2.90 (3H, s); } ^{13}\text{C NMR (75.4 MHz, CDCl$_3$); } \delta \text{ (ppm) 197.8, 145.8, 139.9, 135.9, 129.0, 128.3, 127.3 and 14.2.}
\end{align*}
\]

**Acetophenone (9b, Table 2)**

\[
\begin{align*}
&\text{Colourless liquid, } ^1\text{H NMR (300 MHz, CDCl$_3$); } \delta \text{ (ppm) 8.14 (2H, d, } J = 8.0 \text{ Hz), 7.74 (1H, dd, } J = 6.0, 8.0 \text{), 7.64 (2H, dd, } J = 7.8, 6.7 \text{), 2.75 (3H, s); } ^{13}\text{C NMR (75.4 MHz, CDCl$_3$); } \delta \text{ (ppm) 197.5, 137.1, 132.7, 128.2, 127.9 and 26.1.}
\end{align*}
\]

**4'-Butoxy-3'-methoxyacetophenone (12b, Table 2)**

\[
\begin{align*}
&\text{Creamish solid, m.p. 35-37°C; IR (KBr): 1674 cm}^{-1} \text{ (C=O), } ^1\text{H NMR (300 MHz, CDCl$_3$); } \delta \text{ (ppm) 7.66 (2H, t, } J = 6.5 \text{ Hz), 7.08 (1H, s), 4.30 (2H, t, } J = 7.1 \text{ Hz), 4.07 (3H, s), 2.78 (3H, s), 2.12-2.04 (2H, m), 1.79-1.67 (2H, m), 1.23 (3H, t, } J = 6.7 \text{Hz); } ^{13}\text{C NMR (75.4 MHz, CDCl$_3$); } \delta \text{ (ppm) 197.0, 153.1, 149.4, 130.4, 123.4, 111.2, 110.6, 68.9, 56.2, 31.1, 26.3, 19.3 and 14.0. HRMS-ESI: m/z [M+H]$^+$ for C$_{13}$H$_{18}$O$_3$, calculated 223.1302; observed}
\end{align*}
\]
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223.1315.

4’-Hexoxy-3’-methoxyacetophenone (13b, Table 2)

\[
\text{O} \quad \begin{array}{c}
\text{CH}_3 \\
\text{CH}_2 \\
\end{array} \quad \begin{array}{c}
\text{O} \\
\text{CH}_3 \\
\end{array} 
\]

Transparent viscous liquid, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 7.62 (2H, d, \(J = 7.6\) Hz), 6.98 (1H, t, \(J = 9.5\) Hz), 4.17 (2H, d, \(J = 6.9\) Hz), 4.01 (3H, s), 2.65 (3H, s), 1.94 (2H, s), 1.54-1.35 (6H, m), 0.97 (3H, s); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 197.5, 153.7, 150.0, 130.9, 123.9, 111.8, 111.2, 69.8, 56.7, 32.2, 29.6, 26.0, 25.4, 23.2 and 14.7. HRMS-ESI: m/z [M+H]\(^+\) for C\(_{15}\)H\(_{22}\)O\(_3\), calculated 251.1614; observed 251.1628.

1.6.2.7 Representative procedure for one pot halogenation-oxidative cleavage of 3,4-dimethoxyphenylpropene into 1-(2-Iodo-4,5-dimethoxyphenyl) ethanone (2b’, Scheme 22):

To a stirred mixture of 3,4-dimethoxyphenylpropene (2a, 0.2 g, 1.1 mmol) in dioxane (11 ml), water (3.7 ml) added CTAB (0.03 g, 0.08 mmol) and NIS (1.0 g, 4.44 mmol) and the reaction mixture was allowed to stir for 5 min at room temperature. Subsequently the flask was irradiated under focused microwave system (250W, 115°C) for 15 min. Thereafter, reaction flask was cooled, acetic acid (0.096 ml, 1.66 mmol), PDC (1.05g, 2.79 mmol) were added and further irradiated under microwave (250W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na\(_2\)S\(_2\)O\(_3\) solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na\(_2\)SO\(_4\) and vacuum evaporated. The residue was purified by column chromatography on silica gel (60-120 mesh size) using hexane: ethylacetate (9.3:0.7) to give 1-(2-Iodo-4, 5-dimethoxyphenyl) ethanone (2b’, 0.082 g, 24 % yield).

1-(2-Iodo-4, 5-dimethoxyphenyl) ethanone (2b’, Scheme 22)
Yellow viscous liquid, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.34 (1H, s), 7.12 (1H, s), 3.93 (6H, s), 2.57 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 200.0, 151.8, 149.3, 135.9, 123.9, 112.9, 81.9, 56.7 and 55.8. HRMS-ESI: m/z [M+H]$^+$ for C$_{10}$H$_{11}$O$_3$I, calculated 306.9879; observed 306.9826.

1.6.2.8 Representative procedure for selective oxidative cleavage of 1,2-diaryl alkenes (16a, Scheme 23) into corresponding benzaldehydes

To a stirred mixture of trans-stilbene (16a, 0.2 g, 1.1 mmol) and dioxane (11 ml), water (3.7 ml), CTAB (0.03 g, 0.08 mmol), NIS (0.5 g, 2.2 mmol) and acetic acid (0.095 ml, 1.66 mmol) were added and the reaction mixture was allowed to stir for 3-4 hr at room temperature. Subsequently the flask was irradiated under focused microwave system (250W, 115°C) for 15 min. Thereafter, reaction flask was cooled, PDC (0.63 g, 1.67 mmol) was added and further irradiated under microwave (250W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na$_2$S$_2$O$_3$ solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na$_2$SO$_4$ and vacuum evaporated. The GCMS analysis of residue revealed in it 69% benzaldehyde (16c, Scheme 23).

The above procedure was also applied on other symmetrical and unsymmetrical 1,2 diaryl alkenes (Scheme 23, 17a –18a) and products (17c-18c) confirmed through GCMS analysis.

1.6.2.9 Representative procedure for cascade oxidative cleavage of trans-stilbene into corresponding benzophenones

To a stirred mixture of trans-stilbene (19a, 0.2 g, 0.79 mmol) and dioxane (11 ml), water (3.7 ml), CTAB (0.03 g, 0.08 mmol), NIS (0.35 g, 1.5 mmol) and acetic acid (0.07 ml, 1.16 mmol) were added and the reaction mixture was allowed to stir for 3-4 hr at room temperature. Subsequently, the flask was irradiated under focused microwave system (250W, 115°C) for 15 min. Thereafter, the reaction flask was cooled, PDC (0.015 g, 0.04 mmol), TBHP (0.45 ml, 4.7 mmol) were added and further irradiated under microwave (250W, 115°C) for 15 min. The above mixture was cooled, washed with saturated aq. Na$_2$S$_2$O$_3$ solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined
organic layer was washed with brine (1x10 ml), dried over Na$_2$SO$_4$ and vacuum evaporated. The obtained residue was subsequently purified by column chromatography on silica gel (60-120 mesh size) using hexane: ethylacetate (9.3:0.7) to give benzophenone (19b, Table 3) (49% yield).

**Benzophenone (19b, Table 3)**

![Benzophenone](image)

White solid, m.p. 46-48°C (lit. m.p. 47-48°C) [Rao et al. (2009)]; IR (KBr): 1651 cm$^{-1}$ (C=O), $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.02 (4H, d, $J = 6.2$ Hz), 7.80-7.68 (6H, m); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 197.5, 138.4, 133.2, 130.8 and 129.0.

The above procedure was also used for oxidative cleavage of all the other 1,2-diaryl alkenes (Table 3, Entries 20-26)

4, 4'-Dimethoxybenzophenone (20b, Table 3)

![4, 4'-Dimethoxybenzophenone](image)

White solid, m.p. 135-137°C, [Rao et al. (2009)], IR (KBr): 1636 cm$^{-1}$ (C=O); $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.80 (4H, d, $J = 9.5$ Hz), 6.98 (4H, d, $J = 7.5$ Hz), 3.89 (6H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 194.8, 163.2, 132.6, 131.3, 113.9 and 55.8. HRMS-ESI: m/z [M+H]$^+$ for C$_{15}$H$_{14}$O$_3$, calculated 243.1016; observed 243.1026.

3, 4, 4'-Trimethoxybenzophenone (21b, Table 3)

![3, 4, 4'-Trimethoxybenzophenone](image)

White solid, m.p. 57-60°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.81 (2H, d, $J = 8.7$ Hz), 7.44 (1H, s), 7.38 (1H, d, $J = 9.1$ Hz), 6.98 (3H, m), 3.96 (3H, s), 3.94 (3H, s), 3.89 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 194.5, 162.9, 152.7, 149.0, 132.3, 130.2, 124.9, 114.3, 112.4, 109.9, 56.1 and 55.4. HRMS-ESI: m/z [M+H]$^+$ for C$_{16}$H$_{16}$O$_4$, calculated 273.1121; observed 273.1132.
3-4-Dioxymethylene-4′-methoxybenzophenone (22b, Table 3)

![Structural formula](image)

White solid, m.p. 96-98°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.80 (2H, d, $J = 9.7$ Hz), 7.33 (2H, d, $J = 9.3$ Hz), 7.00 (2H, d, $J = 9.7$ Hz), 6.95 (1H, d, $J = 8.0$ Hz), 6.07 (2H, s), 3.89 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 194.4, 163.3, 151.5, 148.2, 132.9, 132.6, 131.0, 126.6, 113.9, 110.3, 108.0, 102.1 and 55.9. HRMS-ESI: m/z [M+H]$^+$ for C$_{15}$H$_{12}$O$_4$, calculated 257.0808 observed 257.0816.

(6- Methoxy-2-naphthalen-2yl) (4′-methoxyphenyl) methanone (23b, Table 3)

![Structural formula](image)

White solid, m.p. 128-131°C; IR (KBr): 1645 cm$^{-1}$ (C=O), $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.20 (1H, s), 7.89-7.81 (5H, m), 7.23 (2H, d, $J = 8.4$ Hz), 7.01 (2H, d, $J = 7.6$ Hz), 3.98 (3H, s), 3.97 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 195.8, 163.4, 159.9, 137.1, 133.7, 132.8, 131.6, 131.2, 128.0, 127.3, 127.0, 120.0, 113.9, 106.1, 60.8 and 55.8. HRMS-ESI: m/z [M+H]$^+$ for C$_{19}$H$_{16}$O$_3$, calculated 293.1310; observed 293.1382.

1-(2-Naphthyl )-4′-methoxyphenylmethanone (24b, Table 3)

![Structural formula](image)

Yellow viscous liquid, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.30 (1H, d, $J = 9.7$ Hz), 8.00-7.80 (5H, m), 7.61-7.52 (2H, m), 7.26-7.19 (3H, m), 3.96 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 198.5, 160.3, 139.1, 138.9, 132.8, 131.7, 130.6, 128.9, 127.6, 127.2, 120.4, 106.4 and 56.1. HRMS-ESI: m/z [M+H]$^+$ for C$_{18}$H$_{14}$O$_2$, calculated 263.1066; observed 263.1065.
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4-Chloro-4'-methoxybenzophenone (25b Table 3)

White solid, m.p. 111-115°C, [Rao et al. (2009)], \text{IR (KBr): 1637 cm}^{-1} \text{(C=O), } \text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3); \text{\delta (ppm) } 7.80 \text{(2H, d, } J = 8.9 \text{ Hz), 7.71 \text{(2H, d, } J = 8.6 \text{ Hz), 7.45 \text{(2H, d, } J = 8.9 \text{ Hz), 6.97 \text{(2H, d, } J = 9.1 \text{ Hz), 3.89 \text{(3H, s)}}; \text{\textsuperscript{13}C NMR (75.4 MHz, CDCl}_3); \text{\delta (ppm) 194.2, 163.5, 138.3, 136.7, 132.5, 131.2, 130.0, 128.6, 113.8 and 55.6. HRMS-ESI: m/z \text{[M+H]}^+ \text{ for C}_{14}\text{H}_{11}\text{ClO}_2; \text{calculated 247.0520 observed 247.0519.}

1.6.2.10 Representative procedure for one pot oxidative cleavage-condensation of 4-(methoxyphenyl)propene with 2,4,5-trimethoxybenzaldehyde (Table 4, 27b)

To a stirred mixture of 1a (0.2 g, 1.35 mmol) and dioxane (11ml), water (3.7 ml), CTAB (0.03 g, 0.08 mmol), NIS (0.395 g, 1.75 mmol) were added and the reaction mixture was allowed to stir for 5 min at room temperature. Subsequently, the flask was irradiated under MW (250W, 115°C) for 15 min followed by addition of acetic acid (0.12 ml, 2.0 mmol), PDC (2.0 mmol) and further MW (250W, 115°C) for 15 min. Thereafter, the reaction mixture was filtered and 5-8 ml of 10% sodium hydroxide (till basic conditions) along with a methanolic solution (2-3 ml) of 2,4,5-trimethoxybenzaldehyde (0.29 g, 1.48 mmol) were added. The reaction mixture was allowed to stir for 2 hr after which it was washed with saturated aq. Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} solution (1x10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic layer was washed with brine (1x10 ml), dried over Na\textsubscript{2}SO\textsubscript{4} and vacuum evaporated to obtain a crude mixture which upon addition of methanol, led to precipitation of condensation product (27b, 0.24 g, 56% yield).

1-(4′-Methoxyphenyl)-3-(2,4,5-trimethoxyphenyl)-2-propen-1-ones (Table 4, 27b)
Light yellow solid, m.p. 107-110°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.10-8.00 (3H, m), 7.50 (1H, d, $J = 16.6$ Hz), 7.12 (1H, s), 6.96 (1H, d, $J = 8.0$ Hz), 6.50 (1H, s), 3.87 (3H, s), 3.85 (6H, s), 3.84 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 189.6, 163.5, 154.9, 151.8, 143.1, 139.6, 132.0, 130.8, 120.5, 116.5, 114.1, 112.0, 97.1, 57.3, 57.0, 56.3 and 56.2. HRMS-ESI: m/z [M+H]$^+$ for C$_{19}$H$_{20}$O$_5$, calculated 329.1383; observed 329.1387.

The above procedure was also used for the one pot oxidative cleavage-condensation of all the other arylalkenes (Table 4, 28-31b)

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one, [Dong et al. (2008)] (Table 4, 28b)

Creamish solid, m.p. 128-131°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.97 (2H, d, $J = 9.3$ Hz), 7.69 (1H, d, $J = 16.2$ Hz), 7.50 (2H, d, $J = 8.1$ Hz), 7.46 (1H, d, $J = 16.2$ Hz), 7.31 (2H, d, $J = 8.1$ Hz), 6.92 (2H, d, $J = 8.7$ Hz), 3.81 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.4, 163.5, 142.4, 136.1, 133.6, 130.8, 129.5, 129.2, 122.3, 113.9 and 55.5.

3-(2,4-Dichlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one, [Liu et al. (2001)] (Table 4, 29b)

White solid, m.p. 134-137°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.09-8.00 (3H, m), 7.67 (1H, d, $J = 8.0$ Hz), 7.49 (1H, d, $J = 15.8$ Hz), 7.43 (1H, s), 7.28 (1H, d, $J = 8.4$ Hz), 6.98 (2H, d, $J = 8.2$ Hz), 3.88 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.4, 164.0, 138.6, 136.5, 136.2, 132.4, 131.3, 131.0, 130.4, 128.8, 127.8, 125.2, 114.3 and 55.8.

3-(4-dichlorophenyl)-1-(3, 4-dimethoxyphenyl)prop-2-en-1-one (Table 4, 30b)
White solid, m.p. 104-106°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.79 (1H, d, $J = 15.2$ Hz), 7.71 (1H, d, $J = 8.9$ Hz), 7.64-7.51 (4H, m), 7.42 (1H, d, $J = 8.0$Hz), 6.96 (1H, d, $J = 8.2$ Hz), 3.99 (6H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.6, 153.8, 149.8, 142.8, 136.6, 134.0, 131.6, 129.9, 129.6, 123.4, 122.5, 111.2, 110.4 and 56.5.

1-(4'-Chlorophenyl)-3-(3,4-dioxymethylenephenyl)-2-propen-1-ones (Table 4, 31b)

White solid, m.p. 149-151°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.68 (1H, d, $J = 15.7$ Hz), 7.57 (1H, d, $J = 8.0$ Hz), 7.49-7.44 (3H, m), 7.40 (1H, d, $J = 15.7$ Hz), 7.31 (2H, d, $J = 8.4$ Hz), 6.82 (1H, d, $J = 8.0$ Hz), 5.98 (2H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 187.9, 151.8, 148.3, 142.7, 136.2, 133.5, 132.8, 129.5, 129.2, 124.7, 122.1, 108.4, 107.9 and 101.9. HRMS-ESI: m/z [M+H]$^+$ for C$_{16}$H$_{11}$ClO$_3$, calculated 287.0469; observed 287.0467.

The above procedure was also successfully followed for the synthesis of heteroaromatic based chalcones (32b-37b) (Table 4).

1-(3,4-dimethoxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (Table 4, 32b)

Light yellow solid, m.p. 97-98 °C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 7.97 (1H, d, $J= 15.3$ Hz), 7.68 (1H, d, $J= 8.4$ Hz), 7.62 (1H, s) 7.41-7.33 (3H, m), 7.01 (1H, t, $J= 4.2$ Hz), 6.94 (1H, d, $J= 8.3$ Hz), 3.97 (6H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.3, 153.7, 149.7, 141.0, 136.7, 132.1, 131.7, 128.8, 128.7, 123.3, 120.9, 111.2, 110.4 and 56.4. HRMS-ESI: m/z [M+H]$^+$ for C$_{15}$H$_{14}$SO$_3$, calculated 275.0736; observed 275.0719.

1-(3,4-dimethoxyphenyl)-3-(1H-indol-3-yl)prop-2-en-1-one (Table 4, 33b)
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Dark orange solid, m.p. 73-75 °C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 8.85 (1H, s), 8.35 (1H, s), 8.16 (1H, d, \(J= 15.5\) Hz), 7.87 (1H, s), 7.78-7.62 (2H, m) 7.36-7.28 (4H, m), 7.00 (1H, d, \(J= 8.3\) Hz), 3.99 (6H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 185.6, 153.3, 149.6, 138.6, 135.9, 132.4, 130.5, 125.8, 124.8, 123.9, 122.1, 121.0, 117.9, 114.9, 112.4, 111.3, 110.5 and 56.5. HRMS-ESI: m/z [M+H]\(^+\) for C\(_{19}\)H\(_{17}\)NO\(_3\), calculated 308.1281; observed 308.1267.

1-(2H-1,3-benzodioxol-5-yl)-3-(furan-3-yl)prop-2-en-1-one (Table 4, 34b)

Brown solid, m.p. 95-97 °C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 7.67 (1H, d, \(J= 8.1\) Hz), 7.60 (1H, d, \(J= 15.3\)Hz), 7.53-7.52 (2H, m), 7.43 (1H, d, \(J= 15.3\) Hz), 6.89 (1H, d, \(J= 8.1\) Hz), 6.70 (1H, s), 6.50 (1H, s), 6.05 (2H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 187.9, 152.2, 152.1, 148.7, 145.2, 133.4, 130.5, 125.0, 119.5, 116.2, 113.0, 108.7, 108.3 and 102.2. HRMS-ESI: m/z [M+H]\(^+\) for C\(_{14}\)H\(_{10}\)O\(_4\), calculated 243.0651; observed 243.0662.

1-(2H-1,3-benzodioxol-5-yl)-3-(6-bromopyridin-3-yl)prop-2-en-1-one (Table 4, 35b)

White solid, m.p. 146-148 °C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 8.56 (1H, s), 7.89 (1H, s), 7.64-7.51 (5H, m), 6.90 (1H, s), 6.07 (2H, s); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)); \(\delta\) (ppm) 180.3, 159.8, 149.7, 148.2, 138.2, 136.7, 133.1, 131.7, 128.8, 124.7, 123.3, 107.9, 107.6 and 101.7. HRMS-ESI: m/z [M+H]\(^+\) for C\(_{15}\)H\(_{10}\)BrNO\(_3\), calculated 331.9916; observed 331.9959.

1-(4-methoxyphenyl)-3-(thiophen-2-yl)prop-2-en-1-one (Table 4, 36b)

Brown solid, m.p. 93-94 °C, \(^1\)H NMR (300 MHz, CDCl\(_3\)); \(\delta\) (ppm) 8.06 (2H, d, \(J= 4.5\) Hz), 7.97 (1H, d, \(J= 15.3\) Hz), 7.42-7.33 (3H, m), 7.10-7.07 (1H, m), 7.01 (2H, d, \(J= 4.5\) Hz),
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3.89 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.4, 163.8, 140.9, 136.8, 132.1, 131.4, 131.1, 128.8, 128.7, 121.1, 114.2 and 55.9. HRMS-ESI: m/z [M+H]$^+$ for C$_{14}$H$_{12}$SO$_2$, calculated 245.0630; observed 245.0611.

3-(Furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (Table 4, 37b)

Brown solid, m.p. 68-70°C, $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.05 (2H, d, $J$= 8.8 Hz), 7.60-7.43 (3H, m), 6.97 (2H, d, $J$= 8.8 Hz), 6.69 (1H, s), 6.50 (1H, s), 3.85 (3H, s); $^{13}$C NMR (75.4 MHz, CDCl$_3$); $\delta$ (ppm) 188.4, 163.8, 152.2, 145.1, 131.4, 131.1, 130.3, 119.6, 116.1, 114.2, 113.0 and 55.8. HRMS-ESI: m/z [M+H]$^+$ for C$_{14}$H$_{12}$O$_3$, calculated 229.0859; observed 229.0831.

1.7 References


Dong, F., Jian, C., Zhenghao, F., Kai, G. and Zuliang, L. (2008). The increased amount of PDC was presumably required due to the comparatively lower reactivity of halogenated α-aryl aldehyde towards oxidative cleavage. *Catalysis communications* **9**: 1924-27.


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Spectral figures of some representative compounds

$^1$H NMR (in CDCl$_3$) spectrum of 3',4'-Dimethoxyacetophenone (2b, Table 2)

$^{13}$C NMR (in CDCl$_3$) spectrum of 3',4'-Dimethoxyacetophenone (2b, Table 2)
$^{1}$H NMR (in CDCl$_3$) spectrum of 4-Chloro-4'-methoxybenzophenone (25b, Table 3)

$^{13}$C NMR (in CDCl$_3$) spectrum of 4-Chloro-4'-methoxybenzophenone (25b, Table 3)
HRMS spectrum of 4-Chloro-4'-methoxybenzophenone (25b, Table 3)

\[
\text{H}_3\text{CO}^+\quad \text{O} \\
\text{H} \quad \text{CO}_3
\]

\(^1\text{H} \text{ NMR (in CDCl}_3\text{) spectrum of (2E)-3-(furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (37b, Table 4)}\]
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$^{13}$C NMR (in CDCl$_3$) spectrum of (2E)-3-(furan-2-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (37b, Table 4)