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An Expedient Procedure for the Oxidative Cleavage of Olefinic Bonds with $\text{PhI}(\text{OAc})_2$, NMO, and Catalytic OsO_4

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Abstract

$\text{PhI}(\text{OAc})_2$ in the presence of OsO_4 (cat.) and 2,6-lutidine cleaves olefinic bonds to yield the corresponding carbonyl compounds, albeit, in some cases, with α -hydroxy ketones as by-products. A more practical and clean protocol to effect oxidative cleavage of olefinic bonds involves NMO, OsO_4 (cat.), 2,6-lutidine, and $\text{PhI}(\text{OAc})_2$.

The oxidative cleavage of olefinic bonds, either through their ozonides or diols, is used widely in organic synthesis as a useful method to truncate carbon chains or, more usefully, to prepare carbonyl compounds. The most common methods employed to carry out these operations involve ozonolysis (Scheme 1a) or Johnson–Lemieux oxidation¹ [NaIO_4 , OsO_4 (cat.)], and its variants² (Scheme 1b), including the recent improvement (addition of 2,6 lut.) introduced by Jin et al.,³ all of which are onestep procedures. The disadvantages involved with these methods (e.g. safety,⁴ drastic or inconvenient conditions) led to the introduction of the two-step procedure employing sequential Upjohn dihydroxylation⁵ [NMO , OsO_4 (cat.)] and periodate cleavage of the resulting 1,2-diol (Scheme 1c), which became as popular, if not more, than the first two methods. More recent attempts to improve upon these protocols led to the procedures of Borhan et al.⁶ [oxone, OsO_4 (cat.)] and Ochiai et al.⁷ [$m\text{CPBA}$, HBF_4 , $\text{ArI}(\text{cat.})$] that oxidatively cleave olefinic bonds. The use of strong conditions, and the fact that both of these procedures lead to carboxylic acids, also endows them with certain limitations.

As part of a total synthesis program we recently developed practical and convenient protocols for cleaving 1,2-diols and olefinic bonds to aldehydes and ketones employing hypervalent iodine reagents [e.g. $\text{PhI}(\text{OAc})_2$]⁸ as the main oxidant. In this letter we highlight the practicality of using $\text{PhI}(\text{OAc})_2$ to achieve a clean oxidative cleavage of 1,2-diols and demonstrate its compatibility and effectiveness in oxidatively cleaving olefinic bonds into the corresponding carbonyl compounds when coupled with dihydroxylation conditions.

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Supporting Information Available Experimental procedures, characterization and spectroscopic data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

PhI(OAc)₂ is an excellent reagent for the cleavage of 1,2-diols,⁹ and it is rather surprising that it is not commonly employed in that capacity, despite a seven decade old publication by Criegee and Beucker⁸ demonstrating its ability to effect this transformation. More recently, Arseniyadis et al. elegantly employed this reagent to initiate cascade sequences that lead to novel heterocyclic systems through transient dialdehydes.^{9a} A polymer-supported version of this reagent has also been reported, but its use has been limited.¹⁰

The rarity of reports¹¹ using PhI(OAc)₂ to cleave 1,2 diols can be attributed to the absence of a systematic study demonstrating its capabilities in this regard. Thus, in order to illustrate the generality and scope of PhI(OAc)₂ as an efficient 1,2 diol cleaving reagent, and as a prelude to our subsequent investigations, we employed it to that effect on a variety of diol substrates as shown in Table 1 (entries 1–10). In all the examples studied, a clean conversion of the diol into the corresponding aldehydes/ketones was observed. Experimentally, the procedure involves mixing of the substrate and PhI(OAc)₂ in CH₂Cl₂ at room temperature, and upon completion, the product could conveniently be isolated in pure form by removal of the solvent and chromatography.^{12,13}

Importantly, the PhI(OAc)₂-based diol cleavage strategy offers an opportunity for further reactions of the resulting carbonyl compounds in the same pot. Thus, as shown in Scheme 3a, addition of the stabilized phosphorane **11** to the resulting mixture of the cleavage of diol substrate **1** led to the isolation of conjugated ester **12** in high overall yield (81%). Likewise, Grignard addition to the same aldehyde produced propargylic alcohol **13** in 86% overall yield (Scheme 3b). On the other hand, addition of DIBAL-H to the resulting mixture of the cleavage of diol substrate **2** led to isolation of diol **14** in 60% overall yield for the one-pot sequence (Scheme 3c). Finally, reductive amination¹⁴ (Scheme 3d) and dithiane protection (Scheme 3e) were also achieved in high yields (94% and 85%, respectively) by adding the indicated reagents to the aldehyde generated *in situ* from 1,2-diol **3** according to the conditions of Table 1. Additional such sequential reactions are envisioned, thus making this technology potentially appealing for applications in a variety of situations.

We then proceeded to explore the usefulness of PhI(OAc)₂ in cleaving olefinic bonds in the presence of catalytic amounts of OsO₄ and 2,6-lutidine. As shown in Scheme 4 and Table 2, this reaction works well in most instances (Table 2, entries 1–6) but fails to go to completion or leads to by-products, namely α-hydroxy ketones in certain cases (Table 2, entries 7–10). It should be noted that such by-products are also observed under Johnson Lemieux conditions.³

From a more practical perspective, we discovered that a one-pot combination of dihydroxylation using Upjohn conditions followed by diol cleavage with PhI(OAc)₂ was a superior method to cleave olefins (Scheme 5 and Table 3, entries 1–10). Thus, treating olefins with NMO and 2,6-lutidine in the presence of catalytic OsO₄ in acetone:water (ca. 10:1) followed by the addition of PhI(OAc)₂ effected the cleavage of olefinic bonds in one pot to give the corresponding carbonyl compounds. This process obviously proceeds through the corresponding diol and liberates two molar equivalents of AcOH and one molar equivalent of PhI, both of which can be removed easily on work-up and chromatography, respectively.

The PhI(OAc)₂-NMO-OsO₄ protocol leads to aldehydes and ketones in high yields and admirably avoids the formation of the α-hydroxy ketone side products (compare Table 2, entries 9 and 10 with Table 3, entries 5 and 6). Notably, epoxides (entry 2, Table 3) survive these oxidative cleavage conditions compared with conditions that employ sodium periodate which lead to oxidative cleavage of the epoxide moiety.¹⁵ The reaction accommodates both cyclic and acyclic olefins, as well as mono-, di-, and tri-substituted alkenes.

The described synthetic methods offer a convenient, robust, and economical¹⁶ alternative to the traditional olefin cleavage methods for laboratory operations. In addition to achieving high

yields in most cases, all the protocols described here involve essentially homogeneous media, endowing them with certain advantages over the heterogeneous Johnson–Lemieux-type oxidations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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16. NMO, NaIO₄, and PhI(OAc)₂ are all relatively inexpensive reagents (~\$1–2/gram).

a. Ozonolysis

b. Johnson-Lemieux

c. Upjohn dihydroxylation/diol cleavage

Scheme 1.

Common Methods for Cleaving Olefinic Bonds to Carbonyl Compounds

Scheme 2.
Cleavage of 1,2-Diols to Aldehydes by $\text{PhI}(\text{OAc})_2$

a) Sequential 1,2-diol cleavage followed by Wittig olefination

b) Sequential 1,2-diol cleavage followed by Grignard addition

c) Sequential 1,2-diol cleavage followed by DIBAL-H reduction

d) Sequential 1,2-diol cleavage followed by reductive amination

e) Sequential 1,2-diol cleavage followed by dithiane protection

Scheme 3.

One-pot Applications of $\text{PhI}(\text{OAc})_2$ Cleavage of 1,2-Diols

Scheme 4.

Oxidative Cleavage of Olefins to Aldehydes and/or Ketones with $\text{PhI}(\text{OAc})_2$ and OsO_4 (cat.) in the Presence of 2,6-Lutidine

Scheme 5.

Cleavage of Olefins to Aldehydes and/or Ketones by NMO, OsO₄ (cat.)/PhI(OAc)₂ in the Presence of 2,6-Lutidine

Table 1Cleavage of 1,2-Diols to Aldehydes by $\text{PhI}(\text{OAc})_2^a$

entry	substrate
1	1

entry	substrate
2
3

entry	substrate
4
5	<p data-bbox="849 1276 865 1297">4</p> <p data-bbox="849 1413 865 1434">5</p>

entry	substrate
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6

7

entry	substrate
8

9

9

entry	substrate
10

^aReactions were carried out on 100 mg scale at 0.1 M concentration in CH₂Cl₂ with 1.2 equiv PhI(OAc)₂ at ambient temperature.

^bIsolated yield.

^cCompetitive over-oxidation observed.

Table 2

Oxidative Cleavage of Olefins to Aldehydes and/or Ketones with $\text{PhI}(\text{OAc})_2$ and OsO_4 (cat.) in the Presence of 2,6-Lutidine^a

entry	substrate
1	17
2	18
3	19

entry	substrate
4	 <chem>COc1cc(C(C(C(C)C)OC)CC=CC)c(Br)cc1OC</chem>

20

entry	substrate
5
6	21
7	22
	23

entry	substrate
8	 <chem>CC1(C)C2C(C1)OC2C=C</chem>

entry	substrate
9	25

entry	substrate
10	26

^a Reactions were carried out on 100 mg scale at 0.1 M concentration in THF with 0.1 mL H₂O, 2.3 equiv PhI(OAc)₂, 2.5 equiv 2,6-lutidine, and 0.02 equiv OsO₄ at ambient temperature.

^b Isolated yield.

^c or 67% yield based on 60% conversion.

^d or 49% based on 93% conversion.

^e Inseparable mixture; ratio by ¹H NMR.

Table 3

Cleavage of Olefins to Aldehydes and/or Ketones by NMO, OsO₄ (cat.)/PhI(OAc)₂ in the Presence of 2,6-Lutidine^a

entry	substrate
1	27
2	24

entry	substrate
3 ^c	28
4	23

entry	substrate
5
6	<p data-bbox="868 1339 893 1365">25</p> <p data-bbox="868 1432 893 1453">26</p>

entry	substrate
7	<p>Chemical structure of a branched alkene with a TIPS (triisopropylsilyl) group. The structure shows a central carbon atom bonded to a methyl group, a propyl group, and a TIPS group. The TIPS group is represented by the letters 'TIPS' followed by a vertical line.</p>
8	<p>Chemical structure of a branched alcohol with a hydroxyl group. The structure shows a central carbon atom bonded to a methyl group, a propyl group, and a hydroxyl group (OH). The hydroxyl group is represented by the letters 'OH'.</p>

entry	substrate
9 ^d
10 ^d

^a Reactions were carried out on 100 mg scale at 0.1 M concentration in 10:1 acetone:H₂O with 2.0 equiv 2,6-lutidine, 1.5 equiv NMO, 0.02 equiv OsO₄ 1.5 equiv PhI(OAc)₂ at ambient temperature.

^b Isolated, yield.

^c 2.2 equiv PhI(OAc)₂ were used.

^d Carried out on 1 mmol scale.