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Graphical Abstract

Tandem Oxidation–Wittig Reaction Using Barium Manganate (BaMnO$_4$); an Improved One-Pot Protocol

Mohammad Gholinejad$^a$*, Habib Firouzabadi$^b$*, Maedeh Bahrami$^a$, Carmen Nájera$^c$

\[
\text{RCH}_2\text{OH} + \text{Br}\overset{\text{CO}_2\text{Et}}{\xrightarrow{\text{BaMnO}_4(1.2 \text{ eq})}} \text{PPh}_3(1.2 \text{ eq}), \text{CH}_3\text{CN}
\]

24 h, 80 °C

Base-free

18 examples
Alcohols are readily available chemicals which are used for the synthesis of important materials through their facile conversion into other classes of compounds such as aldehydes and ketones. The stereoselective conversion of carbonyl compounds into olefins via the Wittig reaction is widely employed. In a traditional Wittig reaction, aldehydes are usually added to a mixture of the phosphonium halide salt in the presence of a base. It is well noted that handling aldehydes may raise problems due to their volatility, toxicity, and their tendency for polymerization. In recent years, particular attention has been paid to one-pot, multi-step reactions which shorten a synthetic pathway, and bring about significant time-cost benefits and enhancement in reaction efficiency. Along this line, one-pot, tandem oxidation-Wittig reactions via the oxidation of primary alcohols to aldehydes, followed by in situ reaction with phosphorus ylides are an effective strategy for the efficient generation of alkenes. Paying attention to this approach, Ireland and Norbeck, reported a procedure in which an aldehyde was generated in situ by the Swern oxidation of an appropriate alcohol, which subsequently underwent reaction with the Wittig reagent to produce an olefin. Using this method, the isolation of the aldehyde was removed from the protocol and as a consequence, the product yield was noticeably improved. After the introduction of this protocol, several oxidation methods such as Dess-Martin periodinane, tetrapropylammonium perruthenate (TPAP), ortho-iodoxybenzoic acid (IBX), BaMnO₄, MnO₂, in situ aerobic oxidation using a ruthenium catalyst, SO₂Py, and a TEMPO-BAIB system were employed for the one-pot Wittig reaction. In all of the reported reactions, stabilized phosphonium ylides were employed and added to the reaction mixture. Using stabilized ylides, which are limited in number, limits the application of the reported methods. Choudary and co-workers also reported the application of nanocrystalline magnesium oxide as a heterogeneous, solid base catalyst for the one-pot Wittig reaction. However, this method was performed under non-oxidative conditions and aldehydes were used as the starting materials.

In order to expand this methodology, we report a one-pot, tandem oxidation-Wittig procedure in which the reacting components are generated in situ from alcohols, triphenyl phosphine and ethyl bromoacetate using barium manganate as a mild oxidizing agent without the addition of an external base.

**Keywords:** Tandem Oxidation Wittig BaMnO₄ Base-free
in 90% yield with an E/Z ratio of 98:2 as determined by \(^1\)H NMR spectroscopy.

Table 1. Optimization of the reaction conditions for the reaction of benzyl alcohol and ethyl bromoacetate

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>H(_2)O</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>CH(_3)CN</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>1,4-Dioxane</td>
<td>54</td>
</tr>
<tr>
<td>6</td>
<td>CH(_3)CN</td>
<td>73c</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: ROH (1 eq.), BaMnO\(_4\) (1.2 eq.), PPh\(_3\) (1.2 eq.), ethyl bromoacetate (1.2 eq.), solvent (5 mL).

\(^b\) GC yields with similar E/Z stereoselectivity.

\(^c\) Reaction performed at 60 \(^\circ\)C

Using the optimized condition, different primary benzyl alcohols as well as 3-phenyl-1-propanol and cinnamyl alcohol were examined (Table 2). Reactions of benzyl alcohols containing electron donating and electron withdrawing groups proceeded efficiently and the desired alkenes were obtained in high to excellent yields (81-93%), with excellent stereoselectivities (Entries 1-10, 13-17). Sterically hindered benzyl alcohols containing \(o\)-substituents reacted well and produced the desired olefins (Entries 7, 10, 13, 16) in high yields (83-86%). 3-Phenyl-1-propanol was reacted under the optimized conditions and afforded a 78% isolated yield with 100% \((E)\)-selectivity (Entry 11). Cinnamyl alcohol also produced the corresponding conjugated diene in 91% yield with absolute \((E)\)-stereoselectivity (Entry 18).

Table 2. Tandem oxidation-Wittig reaction of different alcohols using BaMnO\(_4\) in the absence of an external base

<table>
<thead>
<tr>
<th>Entry</th>
<th>ROH</th>
<th>Product</th>
<th>Yield (%)</th>
<th>E/Z</th>
<th>Entry</th>
<th>ROH</th>
<th>Product</th>
<th>Yield (%)</th>
<th>E/Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeOH</td>
<td>1a</td>
<td>90</td>
<td>98:2</td>
<td>10</td>
<td>MeOH</td>
<td>1j</td>
<td>83</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>MeOH</td>
<td>1b</td>
<td>88</td>
<td>96:4</td>
<td>11</td>
<td>MeOH</td>
<td>1k</td>
<td>78</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>MeOH</td>
<td>1c</td>
<td>86</td>
<td>93:7</td>
<td>12</td>
<td>MeOH</td>
<td>1l</td>
<td>89</td>
<td>90:10</td>
</tr>
<tr>
<td>4</td>
<td>ClCH(_2)OH</td>
<td>1d</td>
<td>93</td>
<td>99:1</td>
<td>13</td>
<td>ClCH(_2)OH</td>
<td>1m</td>
<td>86</td>
<td>90:10</td>
</tr>
<tr>
<td>5</td>
<td>ClCH(_2)OH</td>
<td>1e</td>
<td>91</td>
<td>99:1</td>
<td>14</td>
<td>ClCH(_2)OH</td>
<td>1n</td>
<td>90</td>
<td>99:1</td>
</tr>
<tr>
<td>6</td>
<td>ClCH(_2)OH</td>
<td>1f</td>
<td>90</td>
<td>99:1</td>
<td>15</td>
<td>ClCH(_2)OH</td>
<td>1o</td>
<td>81</td>
<td>96:4</td>
</tr>
<tr>
<td>7</td>
<td>Chlorinated</td>
<td>1g</td>
<td>85</td>
<td>99:1</td>
<td>16</td>
<td>Chlorinated</td>
<td>1p</td>
<td>84</td>
<td>92:8</td>
</tr>
</tbody>
</table>

Figure 1. TEM images of the nanocrystalline BaMnO\(_4\)

We believe that the nanocrystalline structure of basic BaMnO\(_4\) (see TEM image, average size 30-40 nm with high surface area, Fig. 1) acts as a base in the reaction.\(^{16}\)

In order to further explore the scope and limitations of the method, we performed the reaction of 1-phenylethanol with PPh\(_3\) and ethyl bromoacetate under the optimized reaction conditions. However, the reaction did not proceed cleanly and the obtained ketone was recovered from the reaction mixture. Furthermore, we also studied the reaction of 2-bromopropionate, benzyl alcohol and PPh\(_3\) under the optimized reaction conditions. The reaction proceeded sluggishly and after 24 h only 28% of the product was observed (Scheme 1).

Scheme 1. Reaction of 2-bromopropionate with benzyl alcohol and PPh\(_3\) under the optimized reaction conditions.
It is worth noting that the substitution reaction between ethyl bromoacetate and Ph₂P proceeds much faster than oxidation of the alcohol; therefore, there is no Ph₂P left in the reaction mixture for further oxidation into Ph₃PO. The oxidation of benzyl alcohol in the presence of Ph₂P in CH₃CN at 80 °C for 2 h was studied and it was observed that oxidation of the alcohol proceeded in 98%, whereas, oxidation of Ph₂P proceeded in only 2%.

**Conclusion**

Herein, we present a base-free protocol in which primary alcohols, triphenyl phosphine and ethyl bromoacetate were reacted in a tandem oxidation-Wittig reaction using BaMnO₄. This is an improved one-pot protocol with respect to the previously reported procedures in which the oxidation of the alcohols were performed before using a commercially available phosphonium halide salt. The procedure is highly stereoselective and produces the respected products a (E)-isomers in high yields.

**Acknowledgments**

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**References and notes**

Highlights
A new one-pot tandem oxidation-Wittig procedure has been developed. Reactions were performed in the absence of an external base. High stereoselectivity (E/Z) for Wittig products was obtained.
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\[
\text{RCH}_2\text{OH} + \text{Br}-\text{CO}_2\text{Br} \xrightarrow{\text{BaMnO}_4 (1.2 \text{ eq})} \xrightarrow{\text{PPh}_3 (1.2 \text{ eq}), \text{CH}_3\text{CN}, 24 \text{h, 80}^\circ \text{C}} \text{R}-\text{CO}_2\text{Et}
\]

18 examples Base-free