Ring Contraction Reactions Mediated by Hypervalent Iodine(III)

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Introduction

Hypervalent iodine reagents have received a great deal of attention in organic synthesis due to their reactivities similar to that of heavy metals, low toxicity, ready availability and easy handling. Recently we reported ring contraction of 1,2-dihydronaphthalenes mediated by Phl(OH)OTs (HTIB) and their application in diastereoselective total synthesis of (-)-indatraline. This prompts us to investigate the ring contraction of chromenes into benzofuranes which is an important class of bioactive natural products. The reactions of chromene 1 and methyl chromene 2 with HTIB under different conditions afforded 4H-chromene 2 and 4 and additions products 3, 6 and 7 respectively (Table 1).

Table 1. Reaction of Chromenes with HTIB

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Condition</th>
<th>Product yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Substrate 1" /></td>
<td>MeOH, 0 °C, 3 h</td>
<td><img src="image2" alt="Product 1" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Substrate 2" /></td>
<td>TEOF, rt, 4 h</td>
<td><img src="image4" alt="Product 2" /></td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Substrate 3" /></td>
<td>MeOH, rt, 1 h</td>
<td><img src="image6" alt="Product 3" /></td>
</tr>
</tbody>
</table>

Herein we report some of our results that describe the ring contraction in seven and six member cyclic alkenes.

Result and Discussion

The reaction of chromene 8 and 11 with HTIB resulted in expected ring contraction product 9 and 12 in low yield (entries 1 and 2, Table 2). As it is known to us that aldehyde is formed during the ring contraction reaction of dihydronaphthalenes which converts into stable acetal of the neuclophillic solvent, an effort was made to convert aldehyde through in situ reduction into structurally important alcohol 10 (entry 3). The low yield in the case discussed above might be the presence of oxygen atom in the proximity of double bond.

In seven membered rings the olefinic carbon is one carbon remote than in six membered ring from the carbinoic carbon, which offers minimal oxygen influence on the course of reaction. Ring contraction in oxepines 13 and 16 with HTIB resulted in corresponding chromans 14 and 19 (entries 4 and 5) Benzoannulene 18 gives products 19 and 20 (entry 4).

To find out an alternative economical route for the ring contraction, we generated HTIB in situ from iodobenzene, which resulted in the desired alcohols 14 and 19 in good yield (Scheme 1). We are also planning to develop a clean and catalytic method that has low E factor and high atom economy for ring contraction. Studies towards the replacement of mCPBA by environmentally friendly oxidants are in progress (Scheme 2).

Conclusions

Additional results for the iodine(III)-mediated ring contraction of cyclic alkenes are presented, opening a new route for the synthesis of chromans and tetrahydronaphthalenes.

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References