

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.^{1,2} Recently we reported ring contraction of 1,2-dihydronaphthalenes mediated by PhI(OH)OTs (HTIB) and their application in diastereoselective total synthesis of (±)-indatraline.³⁻⁵ This prompts us to investigate the ring contraction of chromenes into benzofuranes which is an important class of bioactive natural products.⁶ The reactions of chromene **1** and methyl chromene **2** with HTIB under different conditions afforded 4*H*-chromene **2** and **4** and additions products **3**, **6** and **7** respectively (Table 1).

Table 1. Reaction of Chromenes with HTIB

| Entry | Substrate | Condition | Product yield |
|-------|-----------|-----------------|---------------|
| 1 | | MeOH, 0 °C, 3 h | 66% + 15% |
| 2 | | TEOF, rt, 4 h | 42% + 8% |
| 3 | | MeOH, rt, 1 h | 64% |

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 nucleophilic solvent⁵, 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.

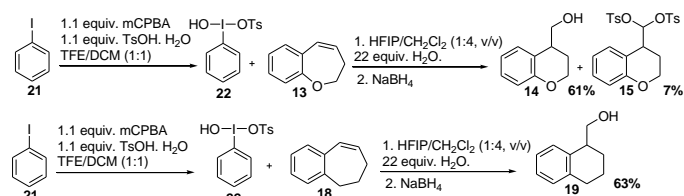
In seven membered rings the olefinic carbon is one carbon remote than in six membered ring from the carbinolic carbon, which offers minimal oxygen influence on the course of reaction. Ring contraction in oxepine **13** and **16** with HTIB results in corresponding chromans **14** and **19** (entries 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).

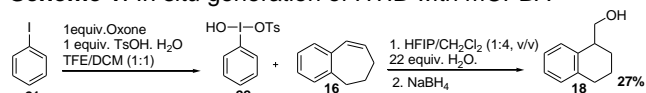
We are also planning to develop a clean and catalytic method that has low E factor and high atom economy for ring contraction. Studies towards the replacement of mCPBA by environmentally friendly oxidants are in progress (Scheme 2).

Table 1. Ring contraction of cyclic alkenes with HTIB

| Entry | Substrate | Condition | Product yield |
|-------|-----------|---|---------------|
| 1 | | MeOH, 0 °C | 30% |
| 2 | | HFIP/CH ₂ Cl ₂ (1:4, v/v), 22 equiv. H ₂ O NaBH ₄ | 31% |
| 3 | | TFE, 0 °C | 24% |
| 4 | | HFIP/CH ₂ Cl ₂ (1:4, v/v), 22 equiv. H ₂ O NaBH ₄ | 87% + 9% |
| 5 | | TFE, 0 °C | 58% |
| 6 | | HFIP/CH ₂ Cl ₂ (1:4, v/v), 22 equiv. H ₂ O NaBH ₄ | 65% + 3% |



Scheme 1. *In situ* generation of HTIB with mCPBA



Scheme 2. *In situ* generation of HTIB with oxone

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.

Acknowledgment

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