Oxidation of Chromenes with Iodine(III)

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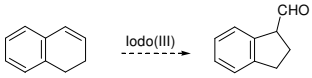
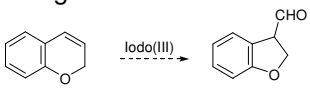
INTRODUCTION

Hypervalent iodine reagents play a key role for a variety of synthetic transformations.[1] The successful ring contraction of 1,2-dihydronaphthalenes mediated by PhI(OH)OTs (HTIB) in different organic solvents (Scheme 1), was a valuable discovery during the course of our synthetic studies aiming the diastereoselective total synthesis of (±)-indatraline.[2]



Scheme 1. Iodine(III) mediated ring contraction.

Based on these results, we decided to expand our area of focus towards ring contraction of chromenes into benzofuranes (Scheme 2), which is an important class of bioactive natural products.[3] Herein, we present a series of reactions with 2*H*-chromenes and 4-methyl-2*H*-chromene using HTIB under different conditions

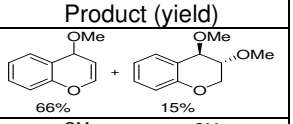
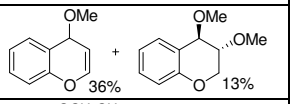
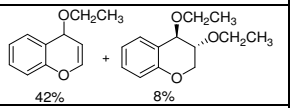
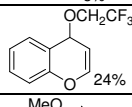
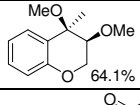
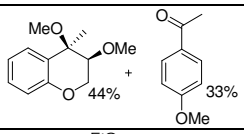
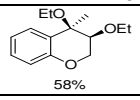


Scheme 2. Iodine(III) mediated ring contraction.

RESULTS AND DISCUSSION

The reactions of 2*H*-chromene with HTIB in MeOH, $HC(OMe)_3$ (TMOF) and $HC(OEt)_3$ (TEOF) as solvents, afforded 4*H*-chromenes (isomerized product) in appreciable yields, whereas addition products possessing *trans*-stereochemistry were obtained in lower yields (entries 1-3, Table 1). The reaction with CF_3CH_2OH (TFE) led to the isomerized product in 24% yield and the addition product was not isolated (entry 4, Table 1). We did not isolate any of our desired ring contraction product under these conditions. At the same time, 4-methyl-2*H*-chromene was subjected to same reaction condition, and we met up with only addition products in good to moderate yields (entries 5, 6 and 7, Table 1). In this case all the products owned *cis*-stereochemistry, confirmed from NOESY analysis. In comparison to 1,2-dihydronaphthalenes structures, which permit oxidative rearrangement,[2] the oxygen lone pair in chromene substrate might allow multiple mechanistic possibilities that lead to different products. Hence we are modifying our approach to mask this effect. In parallel we turned on our focus towards thiochromens. Thiochromene **8**, the parent member of this class was selected as the first substrate for screening. NMR analysis of the crude product showed aldehyde peak and we are expecting a ring contraction. Thus, we are trying to reduce it *in situ* for further analysis. Further studies are in progress towards our goal.

Table 1. Reaction of Chromene and Thiochromene with HTIB.

Entry	Substrate	Conditions	Product (yield)
1		MeOH, 0 °C, 3h	
2		TMOF, 0 °C, 2h	
3		TEOF, rt, 4h	
4		TFE, 0 °C, 2h	
5		MeOH, 0 °C, 1h	
6		TMOF, 0 °C, 2h	
7		TEOF, rt, 4h	
8		TFE, 0 °C, 2h	Complex mixture, crude NMR shows the presence of aldehyde signal

CONCLUSION

In the present study we investigated the reactivity of 2*H*-chromenes in different solvents with HTIB. Our future aim is to find out best conditions for our desired ring contraction.

ACKNOWLEDGEMENTS

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