

Cyclofunctionalizations using Iodine/Iodine(III)

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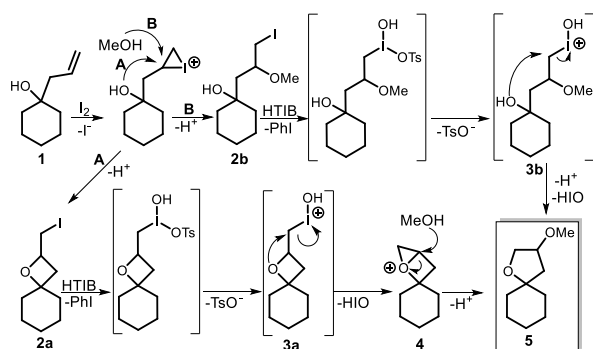
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Abstract

Cyclofunctionalization of homoallylic alcohols with iodine/iodine (III) system to obtain tetrahydrofuran derivatives.

Introduction

There is an interest on synthesis of substituted tetrahydrofuran (THF) moiety because they are present in many biological activity compounds.¹ Our group described a methodology to THF synthesis from tertiary homoallylic alcohols with terminal double bond using iodine/iodine(III). The mechanism using HTIB (PhI(OH)OTs) is described in **Scheme 1**.



Scheme 1 – I₂/I(III) cyclization mechanism

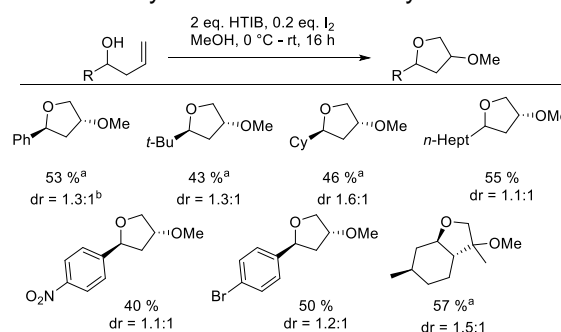
Some experimental evidences suggests two different ways mechanism.² Pathway **A** is derived from the internal hydroxyl group attack to producing oxetane **2a**. The iodine(III) specie **3a** are generated from iodine oxidation followed from a ligand elimination. The hypernucleofuge characteristic of hypervalent specie drives the bicyclic oxonium ion **4** formation.² Finally, MeOH attacks affording THF **5**. Pathway **B** arrives from solvent attack generating **2b** followed by iodine oxidation (**3a**). Cyclization by an intramolecular hydroxyl attack led the cyclic ether formation. We have already shown some examples for secondary alcohols.³ Herein the scope was expanded and is also presented some results from other substrates

Results and discussion

The cyclization of secondary homoallylic alcohols with HTIB and I₂ led to the formation of the desired products (**Table 1**). Applying this methodology to primary homoallylic alcohol, we observed the desired THF product, however, the rearrangement product was the mainly isolated (**Scheme 2A**).

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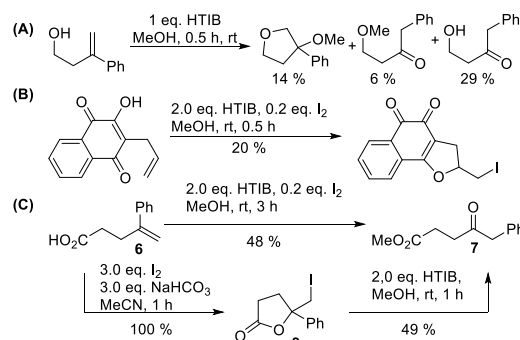
Table 1 – Cyclization of secondary alcohols



^a result previously presented in 15th BMOS

^b cis/trans product determined by NOESY 1D experiment

Using 4-alkenol as substrate, the iodoether product observed (**Scheme 2B**). Performing the reaction with the unsaturated carboxylic acid only the rearrangement product was isolated (**Scheme 2C**). Reacting the carboxylic acid with iodine under basic conditions, β -iodolactone **8** was obtained in quantitative yield. Aiming the ring expansion product, was performed a reaction with HTIB, but only rearrangement product **7** was formed.



Scheme 2 – I₂/I(III) mediated cyclization reactions

Conclusion

Iodine/iodine(III) methodology is useful to obtaining substituted THFs employing secondary homoallylic alcohols. Employing primary alcohols and unsaturated acid, the rearrangement product was observed.

Acknowledgements

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¹Jalce, G.; Franck, X.; Figidère, B. *Tetrahedron: Asymmetry* **2009**, *20*, 2537 ²Vasconcelos, R. S.; Silva, L. F., Jr; Giannis, A. *J. Org. Chem.*, **2011**, *76* 1499 ³Scarassati, P.; Silva, L. F., Jr *15th BMOS*, **2013**, Book of Abstracts, p. 235.