Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 12763–12768
Tetrahedron

Iodocyclization/base-induced hydrodeiodination reaction of 5-substituted 4-alkenols. The influence of substituent on the stereoselective pathway

Claudio Paolucci* and Paolo Righi

Dipartimento di Chimica Organica 'A. Mangini', Alma Mater Studiroum—Università di Bologna, Viale del Risorgimento n.4, 40136 Bologna, Italy

Received 6 July 2007; revised 10 September 2007; accepted 27 September 2007
Available online 29 September 2007

Abstract—The electrophilic iodocyclization reaction of (*Z*)- and (*E*)-5-*n*-alkylsubstituted 4-alken-1-ols followed by base-induced hydrodeiodination reaction stereoselectively gave, respectively, (*Z*)- and (*E*)-alkylidentetrahydrofurans in high yield. Completely different outcomes were observed with (*Z*)- and (*E*)-6,6-dimethylhept-4-en-1-ol: their iodocyclization furnished, respectively, *threo*- and *erythro*-2-(1-iodo-2,2-dimetylpropyl)tetrahydrofuran with high stereoselectivity. The *threo* isomer gave clean formation of 6-*tert*-butyl-3,4-dihydro-2*H*-pyran by base-induced ring expansion, while *erythro* isomer underwent a base-induced ring contraction to 1-cyclopropyl-3,3-dimethylbutan-1-one. Moreover, (*Z*)- and (*E*)-5-cyclopropylpent-4-en-1-ol underwent a 6-*endo*-iodocyclization to *threo*- and *erythro*-2-cyclopropyl-3-iodotetrahydro-2*H*-pyran, respectively, that under the same basic treatment, gave two isomeric 6-cyclopropyldihydro-2*H*-pyrans in a stereoselective fashion.

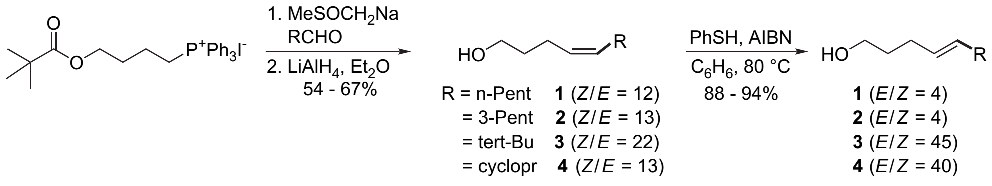
1. Introduction

Cyclic enolethers are of great interest because of their importance in organic chemistry and their role as versatile compounds in synthesis. Recently, they have been utilized for the preparation of 1,2,3,4-tetrahydroquinoline derivatives,[1] substituted indoles,[2] arylated oxacycles[3] and have been used as dienophiles in asymmetric hetero Diels–Alder[4] reactions catalyzed by Cu(II) chiral complexes. The synthesis of cyclic enolethers has attracted the interest of several research groups.[5] Herein, we present some results focused on stereochemical aspects of the preparation of cyclic enolethers by the iodocyclization reaction of 5-substituted 4-alken-1-ols followed by *t*-BuOK induced elimination of hydrogen iodide.

2. Results and discussion

The unsaturated alcohols **1**–**4** were obtained by Wittig olefination with methylsulfynyl carbanion–dimethyl sulfoxide as base-solvent[6a] and successive $LiAlH_4$ reduction of the unsaturated ester intermediates (Scheme 1). This methodology gave *Z*-alkenols with high selectivity (*Z*/*E*=12–22). The treatment with azobisisobutyronitrile–PhSH[6b] allowed their conversion into mixtures in which the (*E*) isomers are greatly predominant (Scheme 1).

Alcohols **1**–**3**, when treated with iodine, underwent a very efficient and clean 5-*exo* cyclization[7] (Scheme 2) that stereoselectively afforded *threo*- (**5t**, **6t**, **7t**) and *erythro*-2-(1-

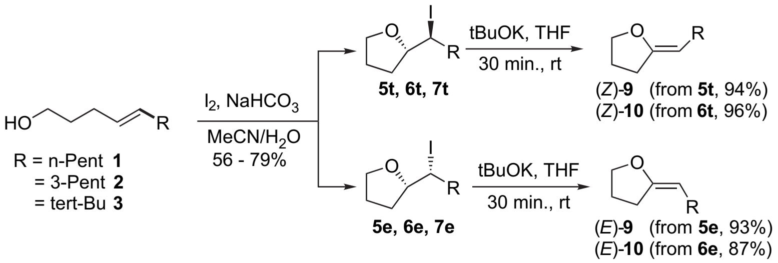


Scheme 1.

Keywords: β-Iodoethers; Enolethers; 2-Alkylidentetrahydrofurans; Ring expansion.

* Corresponding author. Tel.: +39 0512093634; fax: +39 0512093630; e-mail: paolucci@ms.fci.unibo.it

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.074

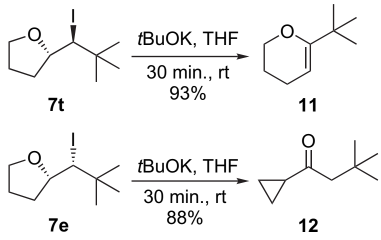


Scheme 2.

iodoalkyl)tetrahydrofurans (**5e**, **6e**, **7e**), respectively, from the *Z*- and *E*-components in the mixture, according to an *anti* addition reaction across the π-bond.[8]

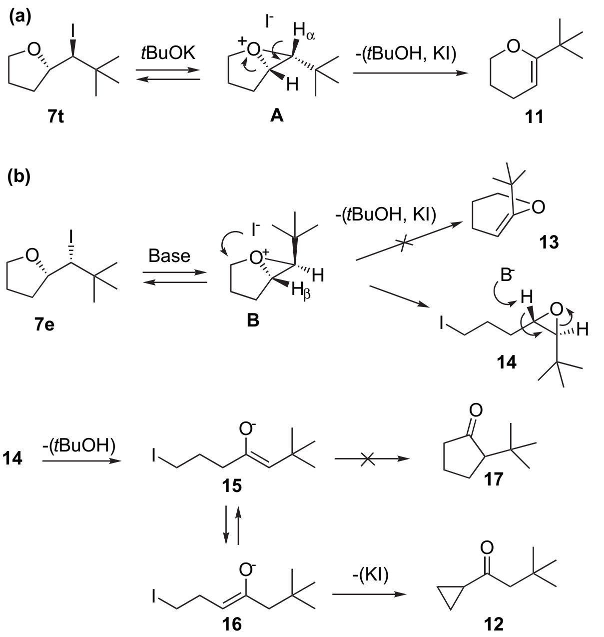
Upon treatment with *t*-BuOK in THF at room temperature, the iodoethers **5t**,**e** and **6t**,**e** underwent a highly and clean stereoselective *anti* hydrogen iodide elimination to give (*Z*)-, (*E*)-**9** and (*Z*)-, (*E*)-**10**, respectively. Therefore, the iodocyclization–hydrodeiodination sequence constitutes a selective and efficient route for the preparation of (*Z*)- and (*E*)-2-alkylidentetrahydrofuran starting from (*Z*)- and (*E*)-alkenols, respectively (Scheme 2). An analogous dehydrohalogenation to enolethers was already observed.[9]

The approach depicted in Scheme 2 resulted as a general route when applied to linear 4-alkenols and also for 4-alkenols with a side chain on C6 but different outcomes were observed with (*Z*)- and (*E*)-6,6-dimethylhept-4-en-1-ol (**3**). Whereas they were efficiently converted into the corresponding *threo*- (**7t**) and *erythro*-2-(1-iodo-2,2-dimethylpropyl)tetrahydrofuran (**7e**) (Scheme 2), the base-induced elimination performed on *threo*- (**7t**) gave 6-*tert*-butyl-3,4-dihydro-2*H*-pyran (**11**) in high yield (93%) by incorporation of the exocyclic halogen-bearing carbon into the ring,[10] while the same reaction performed on the *erythro* isomer (**7e**) furnished the 1-cyclopropyl-3,3-dimetylbutan-1-one (**12**) with similar efficiency (88% yield) (Scheme 3).



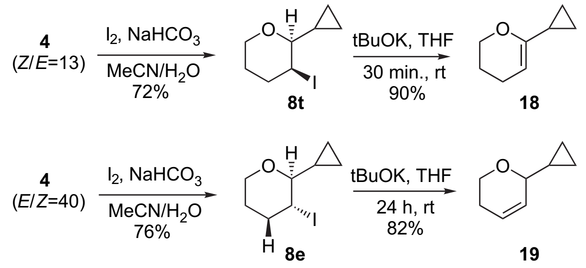
Scheme 3.

The conversion of **7t** into the dihydropyran **11** and **7e** into **12** could occur through the β ethereal-oxygen assisted expulsion of iodide with formation of an oxonium-iodide ion-pair (**7t**→**A** **7e**→**B**, Scheme 4a,b) with concomitant inversion at the carbon. The different evolutions of the two isomeric **A** and **B** forms could be justified by stereoelectronic factors: abstraction of proton H_α or H_β from the oxonium intermediate **A** and **B** (Scheme 4a,b), leads to the enol ether having a *Z* or *E* endocyclic double bond, respectively. Since the incipient six-membered ring cannot accommodate an *E* double bond giving **13** (Scheme 4b), the elimination with ring-contraction process to cyclopropyl ketone takes over. In this case, none of the possible 1,2-elimination products could be detected, and this could be explained by the steric hindrance of the *tert*-butyl group. Scheme 4b depicts the formation of the cyclopropylic ketone **12** from **7e**. In this model, the iodo epoxide **14**,[11] derived from tetrahydrofuran ring-opening by nucleophilic attack of ionic iodide, undergoes a base-induced elimination to enolate **15**.[11a,b] The enolate, due to the steric hindrance of the *tert*-butyl group, isomerizes to enolate **16** that finally cyclizes to give the ketone **12** by intramolecular alkylation.



Scheme 4.

A further different cyclization outcome was observed when (*Z*)- and (*E*)-cyclopropyl alkenols **4** were subjected to the same reaction conditions (Scheme 5). In this case a 6-*endo*



Scheme 5.