

Mechanism of Isomerization of Cyclopropyl Ethers with Zinc Iodide. New Synthetic Route to Optically Active Allyl Alcohols

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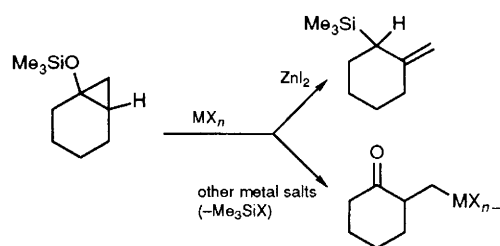
Isomerization of cyclopropyl ethers to allyl ethers in the presence of zinc iodide is confirmed to proceed by a 1,2-hydride shift mechanism by stereochemical and deuterium labelling experiments.

The isomerization of cyclopropyl ethers to allyl ethers with zinc iodide was first found in a study of the Simmons–Smith reaction of trimethylsilyl enol ethers.¹ In this reaction, the cyclopropyl ether initially produced was isomerized by the zinc iodide, which accumulates as the reaction proceeds. In reactions of trimethylsilyl cyclopropyl ether with metal salts other than ZnI₂ [Hg(OAc)₂, AgBF₄, Cu(BF₄)₂ or SnCl₄], desilylation of the substrate exclusively took place affording either stable or intermediary β-metallo ketones (Scheme 1).² The unique isomerization with ZnI₂ suggests that with this reagent the intramolecular 1,2-hydride shift mechanism is favoured over other intermolecular dehydration and hydration mechanisms.

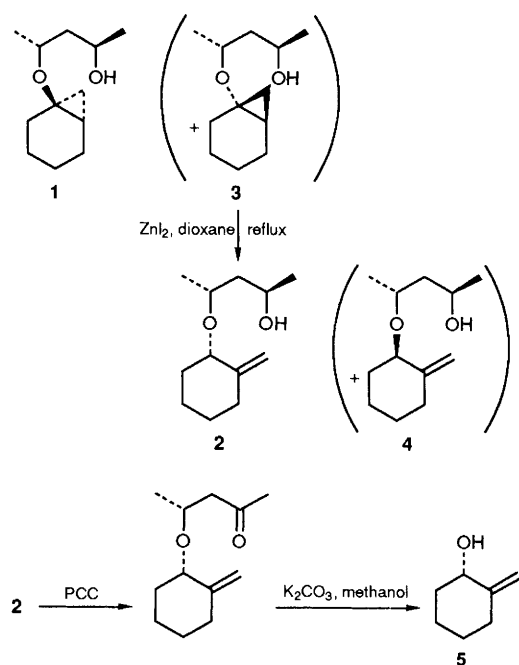
We report herein experimental proof of the involvement of a 1,2-hydride shift in this isomerization, together with a new synthetic route to optically active allyl alcohols.

The optically active cyclopropyl ether **1** (> 99% diastereoisomeric purity) was prepared from cyclohexanone in three steps by the method established by us.³ The reaction of **1** (0.1 mol dm⁻³) with zinc iodide (3 equiv.) in dry dioxane at reflux temperature afforded the allyl ether **2** as a single diastereoisomer in 70% yield (Scheme 2). In this reaction, it was not necessary to prepare zinc iodide *in situ* from zinc–copper and iodine as previously reported.¹ Under the same conditions, a

mixture of the diastereoisomers **1** and **3** (**1**:**3** = 7:3) afforded a mixture of **2** and its diastereoisomer **4** in the same 7:3 ratio. The diastereoisomers **2** and **4** were separable by MPLC on silica gel and their structures were determined by spectroscopy and combustion analysis. The stereochemistry of **2** was assigned by chemical correlation with **5**; pyridinium chlorochromate (PCC) oxidation of **2** followed by treatment with potassium carbonate in methanol gave (+)-(*S*)-**5** {[α]_D 18, lit.⁴ [α]_D 12.7 for 60% enantiomeric excess (e.e.) of (*S*)-**5**}. These results indicated that the chiral 1,3-diol moiety in the substrate did not participate in the mechanism of the stereocontrol of the rearrangement and that the stereochemistry of cyclo-

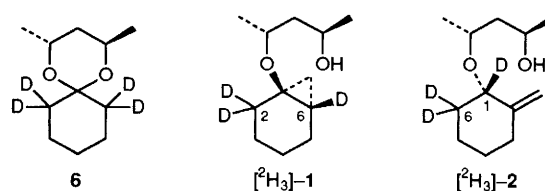


Scheme 1



propyl ether skeleton was fully conserved in the resulting allyl ether. The conservation of the stereochemistry with inversion at the ether chiral centre could be explained only by the 1,2-hydride shift mechanism.

The validity of this mechanism was confirmed by deuterium labelling experiments as follows. The deuteriated ketal $[^2\text{H}_4]$ -**6** (deuterium content 50%) was isomerized with triisobutylaluminium and cyclopropanated with diiodomethane and diethylzinc in tetrahydrofuran (THF) to give $[^2\text{H}_3]$ -**1** (50% $^2\text{H}_3$). As expected, isomerization of $[^2\text{H}_3]$ -**1** with zinc iodide afforded $[^2\text{H}_3]$ -**1**. Deuterium was present only at the 1- and 6-positions of $[^2\text{H}_3]$ -**2**, in the same percentage as in $[^2\text{H}_3]$ -**1**. During this reaction, the deuterium content in **1** and **2** did not vary (monitored by ^1H NMR spectroscopy).



The regioselective deuterium shift with rigorous stereocontrol clearly showed that the isomerization of the cyclopropyl ether proceeded through an intramolecular 1,2-hydride shift. The small difference between the reactivity of $[6\text{-}^2\text{H}]$ -**1** and $[6\text{-}^1\text{H}]$ -**1** also suggested that the rate-determining step of the reaction is not the 1,2-hydride shift but presumably the C-C bond cleavage step.

The present results are also significant from the synthetic point of view. As mentioned before, optically pure cyclopropyl ethers are easily available from prochiral ketones.³ By the present method, these compounds could be converted into allyl alcohols without any loss of optical purity. Thus, the sequence of the above two reactions provides a handy procedure to get optically pure exocyclic methylene allyl alcohols, promising optically pure units for the synthetic chemistry.

We thank Professor Noboru Sonoda of Osaka University and Professor Yoshihisa Inoue of Himeji Institute of Technology for their helpful discussions.

Received, 11th November 1991; Com. 1105714F

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