

A Facile Construction of Eudesmanolide Denebutenolide via SmI₂-catalyzed Rearrangement of an Enol Ester Epoxide

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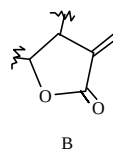
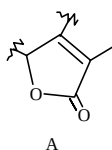
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Abstract: A very convenient construction procedure of the α , β -unsaturated lactone has been carried out in 98% yield. SmI₂ (10%) was used as catalyst for rearrangement of an enol ester epoxide of eudesmanolide sesquiterpene. The possible mechanism was also discussed.

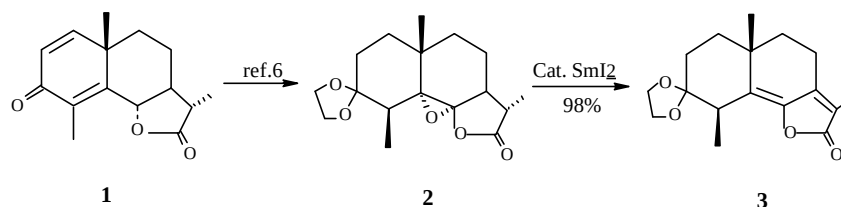
Keywords: Construction, α , β -unsaturated lactone, catalyzed- rearrangement.

Quite a number of naturally occurring sesquiterpenoids possessing α , β -unsaturated lactone moiety **A** have been demonstrated to have many important biological activities¹, such as antitumor, anticancer, antiinflammatories, antipsoriasis properties, and so on. Thus the construction procedures of this key structure has been attracting a great interest of organic chemists, and some procedures toward the double bond introduction to α -methyl- γ -lactone have been developed². However the procedures reported were relatively complicated and the reaction conditions were strict. Besides, in most cases, the by-product with exocyclic double bond like **B** was formed. Herein, we would like to report a facile procedure newly developed for construction of the eudesmanolide denebutenolide based on samarium diiodide catalysis. Although the reagent samarium diiodide has been showing its great utility in organic synthesis since its first application³. The amount of employed catalyst in most cases was equivalent or excessive, and to our knowledge only two examples employing catalytic amount of samarium diiodide have been reported⁴, but neither of them involved the rearrangement-dehydration reaction of epoxide.



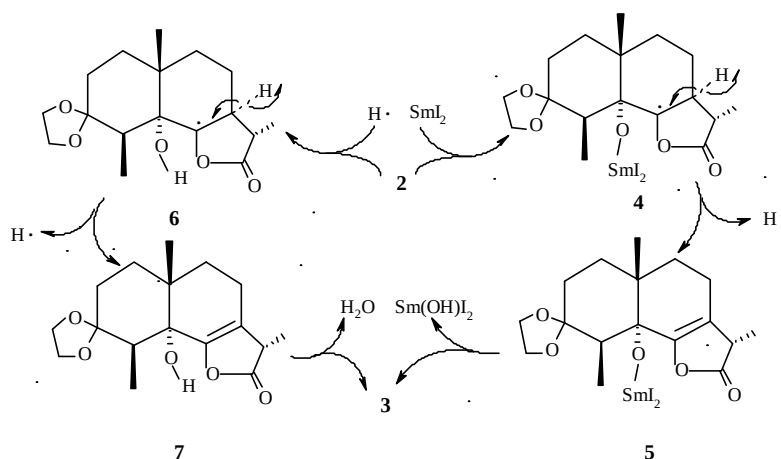
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Scheme 1



Our research started from the naturally abundant and versatile α -santonin **1**, which has always been used for synthesis of natural products⁵. Thus α -santonin **1** was first converted to epoxide **2** by our previous procedure⁶. In the initial studies, we found that treatment of epoxide **2** with 5% or even smaller amount of SmI_2 in dry benzene afforded a mixture mainly contained the rearrangement-dehydration product **3**. Further investigation led to the observation that employment of 10% SmI_2 could promote the complete conversion of **2** to **3** in 98% yield (as shown in **Scheme 1**). Other Lewis acids, such as AlBr_3 , $\text{BF}_3 \cdot \text{OEt}_2$, NiCl_2 , PdCl_2 could not lead to the same product **3**. Consequently we thought that SmI_2 did not work as a Lewis acid in this reaction. We proposed a radical mechanism (as shown in **Scheme 2**) would be incorporated in this reaction process. The initial cooperation between SmI_2 and epoxy led to the ring opening of epoxy and formed the free radical intermediate **4**, which after generation of a proton radical formed the olefin intermediate **5**. The final elimination of $\text{Sm}(\text{OH})\text{I}_2$ gave the α,β -unsaturated lactone product **3**. Subsequently, the generated radical took part in the activation-ring opening of epoxy to form the intermediate **6**, which after generation of a proton radical formed the olefin intermediate **7**. The final elimination of one equivalent of water gave the α,β -unsaturated lactone product **3**. So we could see that catalytic process of this reaction was recycled by the proton radical.

Scheme 2



In conclusion, we have found an interesting SmI_2 -catalyzed epoxide rearrangement, which was a novel and very convenient procedure for construction of the butenolide.

Experimental

^1H NMR and ^{13}C NMR spectrum were recorded in CDCl_3 on a Bruker Am-400 spectrometer with TMS as internal standard (chemical shift in δ ppm). EIMS and FAB-HRMS were determined on an Aufostec-3000 spectrometer (energy of ionizing electrons 70 eV).

Denebutenolide 3: 50 mg of **2** (0.16 mmol) dissolved in 2 mL dry benzene was added into 0.16 mL of 0.1 mol/L SmI_2 solution in THF. The mixture was refluxed for 10 hr., after which, AcOEt (20 mL) was added. The organic layer was then washed with saturated NaHCO_3 and brine, dried over Na_2SO_4 and chromatographed on silicon column (petroleum ether/AcOEt: 2/1) to give 46 mg of **3** (98%).

Spectral data of **3**: ^1H NMR (CDCl_3 , δ ppm): 4.02-3.87 (m, 4H), 3.03 (m, 1H), 2.72-2.64 (m, 2H), 2.13-2.04 (m, 2H), 1.80 (s, 3H), 1.75-1.49 (m, 4H), 1.28 (s, 3H), 1.17 (d, 3H, J 7.3 Hz); ^{13}C NMR (CDCl_3 , δ ppm): 171.3, 148.8, 145.5, 131.1, 119.2, 110.9, 65.0, 64.6, 40.2, 38.6, 38.1, 34.9, 27.1, 25.6, 19.9, 18.2, 8.2; EIMS: m/z 290 (M^+ , 63), 189 (26), 119 (31), 105 (38), 99 (100), 79 (38), 67 (35), 55 (82); HRMS for $\text{C}_{17}\text{H}_{22}\text{O}_4$: Calcd. 290.1518. Found 290.1520.

Acknowledgments

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