Synthetic Studies on Bioactive Natural Products Employing Electrochemical Methodology, Synthesis of Heliannuol E

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A considerable amount of synthetic methodologies accumlated during the last decade, have been able to construct a variety of complicated organic molecules. Among such investigations, phenol-derived bioactive substances are of interest, from viewpoints of complicated aryl and alkyl-mixed frameworks, which provide diverse biological activities. In this context, we investigated the anodic oxidation chemistry of halogenated phenols to synthesize isodityrosine-class natural products (ref. 1). As part of our extensive electrochemical investigation, we observed that the mono-brominated spirodienone (type-**A**), electrochemically constructed from the corresponding phenols, was converted into the dihydrobenzopyrans (type-**B**) under Lewis acid conditions. A direction of the rearrangement was conducted by the bromo-substituent: the **B-1**-type products were preferred to the **B-2** (ref. 2). As an application of this conversion into the corresponding benzopyran derivatives, a synthesis of heliannuol E (**1**) will be presented.

Heliannuol E **1** was isolated as a component of *Helianthus annuus* L. cv. SH-222. This sesquiterpene might be related to the allelopathogenic action of cultivar sunflowers (ref. 3). To accomplish the total synthesis of **1**, anodic oxidation of **2** was attempted (CCE, anode: glassy carbon beaker, cathode: platinum wire, $LiClO_4$ as a supporting salt, MeOH, MeCN, acetone or dioxane with/without 60% aq. $HClO_4$ as a solvent). Although **2a** (R_1= R_2= R_3= H) provided only trace amounts of **3a** with considerable amounts of by-products, **2b** (R_1= Br, R_2= R_3= H) produced the desired spiro derivative **3b** in 50% yield. Based on this observation, appropriate substituents were introduced to the side-chain part of **2** to give **2c** (R_1= Br, R_2= H, R_3= CMe_2OH) and **2d** (R_1= Br, R_2= $(CH_2)_2OAc$, R_3= CMe_2OH). Consequently, both of the phenols afforded the spiro derivatives **3c**, **3d**, and their structures were unambiguously confirmed by spectroscopic techniques. The following treatment of **3** with BF_3OEt_2 effected the rearrangement to the dihydrobenzopyrans **4** and **5** in good selectivity. As expected, the desired **4** was preferentially produced (ca. 5:1), probably owing to a combination of the opposite inductive effects of the bromine and methyl substituents.

Details of our research progress to the target molecule will be discussed.

References

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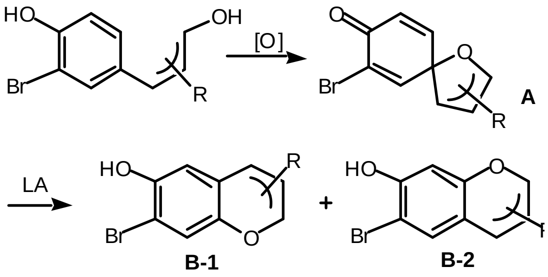
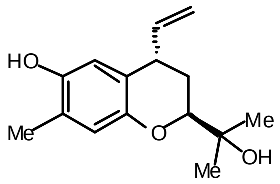
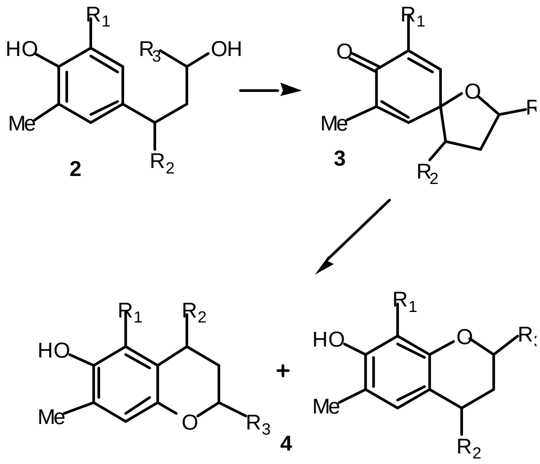




Heliannuol E (1)



a: R_1= H	R_2= H	R_3= H
b: R_1= Br	R_2= H	R_3= H
c: R_1= Br	R_2= H	R_3= CMe_2OH
d: R_1= Br	R_2= $(CH_2)_2OAc$	R_3= CMe_2OH