CHEMISTRY LETTERS, pp. 1151-1152, 1993.

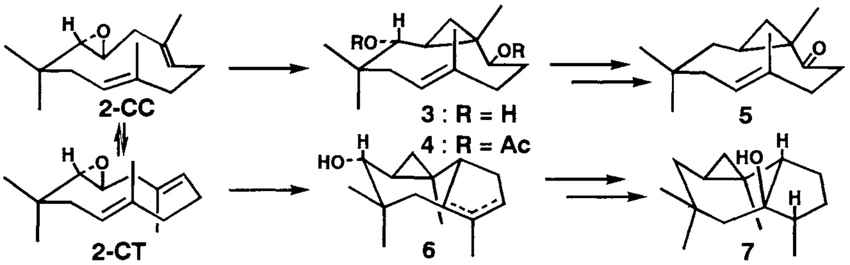
Stereochemistry of Bicyclohumulenediol and Equilibrium between Two Humulene Epoxides II and III. Novel Interconversion of Two Cycloundecatriene Epoxides through Transannular Bond Formation

Kiyoharu HAYANO and Haruhisa SHIRAHAMA*†
Chemistry Laboratory, Hokkaido University of Education, Ainosato, Sapporo 002
† Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060

The structure of bicyclohumulenediol, which was obtained from humulene epoxide II (**1**) and/or III (**2**) by treatment with aqueous solution at pH 4 by Yang and Deinzer, was revised and a new scheme for the equilibrium process among **1**, **2** and tricyclohumulenediol was presented.

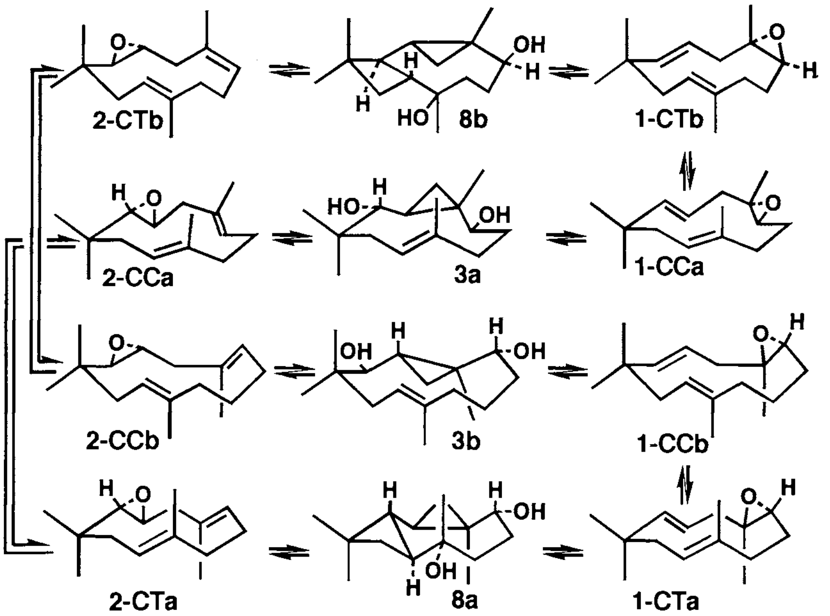
A new synthetic strategy for the syntheses of medium, macro, and polycyclic compounds was recently developed, which consists of the stereoselective functionalization and/or transannular C-C bond formation of macro or medium size cyclic compounds in their stable conformers.[1] Consequently, to find a stable conformer or conformers is essential to achieve the syntheses. The method was widely applied to the syntheses of terpenes, steroids, and macrolides.[1] We derived bicyclohumulenone (**5**) and africanol (**7**) from humulene epoxide III (**2**), a cycloundecatriene epoxide, using Ac_2O and $BF_3 \cdot OEt_2$ through the conformationally selective transannular cyclization of each of its stable conformers, CC and CT, respectively (Scheme 1).[2] Bicyclohumulenediol diacetate (**4**) was a key intermediate of this synthesis and its configuration was unambiguously determined by X-ray analysis. We rationalized the stereochemistry of this unique reaction by taking into account the strain energies of the products, which were obtained by molecular mechanics calculations.[3]

Yang and Deinzer recently described the analysis of an equilibrium among humulene epoxides II (**1**), III (**2**) and tricyclohumulenediol (**8**) in aqueous solution at pH 4.0.[4] They deduced that bicyclohumulenediol (**9**) should be an essential intermediate to establish the equilibrium, and **9** should be produced from the CT form (Scheme 3). We had doubts about the structure of the diol **9** and compared their diol with our diol **3** which was derived from our previously described diacetate **4** by hydrolysis. The two diols were thus found to be

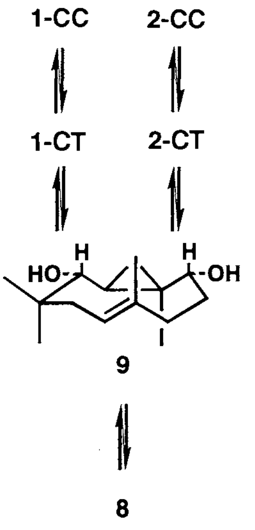


Scheme 1.

identical.5) The structure of **9** should be revised to **3**. The configuration of the bicyclohumulenediol intermediating the equilibrium was revealed to be produced from the CC-form of **1** and/or **2**, as a consequence. These facts showed that our previous explanation for the transannular reaction of **2** using the strain energy3) was really reasonable. Therefore, the itinerary of interconversion between epoxides **1** and **2** in the aqueous solution should not be depicted as Yang and Deinzer's scheme (Scheme 3) but as Scheme 2.



Scheme 2. The symbols, **CC** and **CT**, indicate conformations of the corresponding compounds and **a** and **b** show an enantiomeric pair.



Scheme 3.

References

1) F. Matsuda and H. Shirahama, "A New Look at Natural Products Chemistry in Three Dimensions," in "Carbocyclic Cage Compounds: Chemistry and Applications," ed by E. Osawa and O. Yonemitsu, VCH Publishers, New York (1992), Chap. 4, pp 101-123.

2) H. Shirahama, K. Hayano, Y. Kanemoto, S. Misumi, T. Ohtsuka, N. Hashiba, A. Furusaki, S. Murata, R. Noyori, and T. Matsumoto, *Tetrahedron Lett.*, **21**, 4835 (1980).

3) H. Shirahama, K. Hayano, Y. Kanemoto, T. Ohtsuka, E. Osawa, and T. Matsumoto, *Chem. Lett.*, **1981**, 351.

4) X. Yang and M. L. Deinzer, *J. Org. Chem.*, **57**, 4717 (1992).

5) Deinzer's bicyclohumulenediol was prepared from humulene epoxide III (**2**) according to his procedure.4) On the other hand, bicyclohumulenediol (**3**) was obtained from its diacetate **4**2) by refluxing in aqueous MeOH with NaOH for 12 h. The obtained diol **3** was reconverted to the original diacetate **4** by treatment with Ac_2O in pyridine to prove that this hydrolysis proceeded without a change in stereochemistry. The spectral data and chromatographic behaviors of the two diols were found to be perfectly identical. **3**: ^{13}C-NMR ($CDCl_3$, 400MHz, JEOL JNM-EX400N) 13.64, 16.35, 17.63, 18.36, 28.29, 30.05, 31.09, 31.75, 38.22, 39.67, 40.07, 74.69, 82.41, 124.67, and 132.53 ppm.

(Received April 27, 1993)