ISOLATION OF NEW TC CONFORMATIONAL HUMULENE 2,3;6,7-DIEPOXIDE

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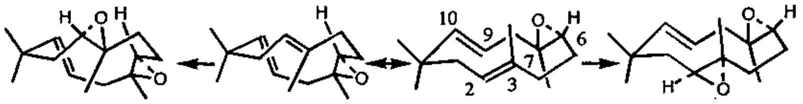
Abstract-The epoxidation of (2*E*, 9*E*)-6,7-epoxy-3,7,11,11-tetramethylcycloundeca-2,9-diene (**1**) with *m*-CPBA gave a new TC and known CT diepoxides, (9*E*)-(2*R**, 3*R**, 6*R**, 7*R**)-2,3;6,7-diepoxy-3,7,11,11-tetramethylcycloundec-9-ene (**3**) and (9*E*)-(2*S**, 3*S**, 6*R**, 7*R**)-2,3;6,7-diepoxy-3,7,11,11-tetramethylcycloundec-9-ene (**2**), respectively, in the ratio of **2**:**3**=91.5:8.5. The conformation of **3** was determined by X-ray crystallography ($C_{15}H_{24}O_2$: monoclinic space group $P2_1/n$ with a=13.735(4) Å, b=15.910(3) Å, c=6.553(2) Å, β=100.90(2)°, Z=4).

Tow compounds, (9*E*)-(2*S**, 3*S**, 6*R**, 7*R**)- and (9*E*)-(2*R**, 3*R**, 6*R**, 7*R**)-humulene 2,3;6,7-diepoxides (**2** and **3**), have been considered for diepoxide derived from humulene 6,7-epoxide (**1**) by epoxidation, since **1** can maintain CT and TC conformations due to the rotaion of the 2,3-double bond plane[1] as shown in Scheme 1. Indeed, one of the conformations, CT, has already been isolated and characterized as the unique product, humulene 2,3;6,7-diepoxide (**2**), that was derived from **1** using perbenzoic acid. The conformation of the CT diepoxide (**2**) was also determined by X-ray crystallography.[2] On the other hand, the other conformation, TC, has so far neither been isolated nor detected experimentally for the mono- and di-epoxides. In the present study, we carefully investigated the epoxidation product of **1** using *m*-chloroperbenzoic acid (*m*-CPBA), and found that the TC diepoxide (**3**) was also formed as a minor product. The new TC diepoxide (**3**) was separated by hplc and isolated as a single crystal, and its conformation was confirmed by X-ray crystallography.



3 (TC diepoxide) **1TC** **1CT** **2 (CT diepoxide)**

Scheme 1. C and T denote crossed and parallel arrangement of 6,7- and 9,10-bonds against 2,3-bond, respectively. For instance, first T and second C of **1TC** represent pararell and crossed arrangement of 2,3- and 9,10-bonds, and 2,3- and 6,7-bonds, respectively.

The epoxidation of humulene 6,7-epoxide (**1**) with *m*-CPBA (1 eq.) in dry CH_2Cl_2 at 0 °C under an argon atmosphere followed by chromatographic separation produced a mixture of humulene 2,3;6,7-diepoxides (**2** and **3**, 97%). Crystallization of the mixture from hexane gave the pure diepoxide (**2**, 83.2% from **1**, mp 102-105 °C), and a mixed oil (13.7% from **1**) in the ratio of **2**:**3**=27.3:72.7 that was calculated from the hplc peak areas. An authentic sample (mp 66-69 °C) of **3** was prepared from the mixture of **2** and **3** by hplc separation using the 7.8 x 300 mm column of µPORASIL (Waters, 10% EtOAc/hexane). Although the HRms of **3** showed the same molecular formula, $C_{15}H_{24}O_2$, as that of **2**,[2] the diepoxide (**3**) differed from **2** in these ^{1}H and ^{13}C nmr spectra.[3] In order to determine the conformation of **3**, a single crystal of **3** was supplied for X-ray crystallography,[4] which revealed its TC conformation as depicted in Figure 1.

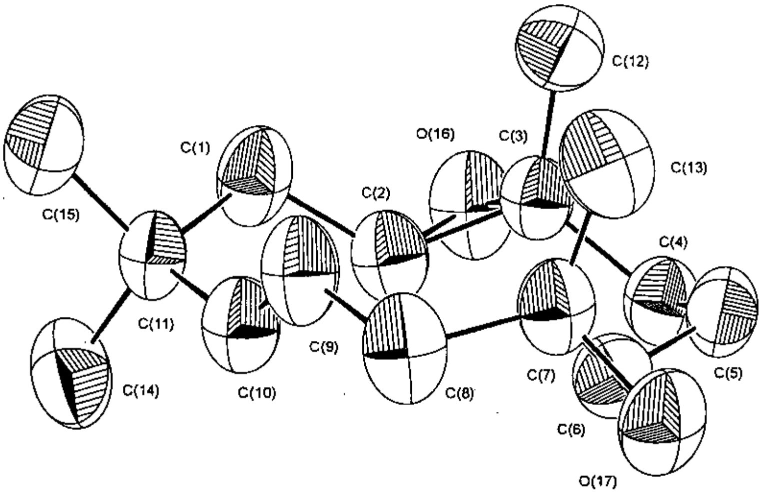


Figure 1. Perspective view of TC conformational humulene 2,3;6,7-diepoxide (**3**). Hydrogen atoms were omitted.

Thus, it was found that the epoxidation of **1** gave a mixture of the known CT and the new TC diepoxides (**2** and **3**) in the ratio of **2**:**3**=91.5:8.5. These results suggest that the TC conformation should exist in the original epoxide (**1**), because the interconversion between **2** and **3** is impossible.

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REFERENCES AND NOTES

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2. M. E. Cradwick, P. D. Cradwick, and G. A. Sim, *J. Chem. Soc., Perkin II*, 1973, 404.
3. **3**: ^{1}H Nmr ($CDCl_3$, 270 MHz), δ 1.10, 1.18, 1.20, 1.39 (each 3H, s), 1.30 (1H, dd, J=3.6, 13.9 Hz), 1.40-1.54 (2H, m), 1.72 (1H, d, J=13.9 Hz), 1.81 (1H, m), 2.00 (1H, dt, J=3.9, 14.9 Hz), 2.24 (1H, dt, J=3.6, 13.9 Hz), 2.58-2.71 (3H, m), 5.51-5.55 (2H, m) ppm; ^{13}C nmr ($CDCl_3$, 270 MHz) δ 16.30 (q), 18.98 (q), 23.51 (t, 5-C), 26.78 (q), 30.01 (q), 34.50 (s, 11-C), 36.77 (t, 4-C), 40.65 (t, 8-C), 42.32 (d, 1-C), 60.56 (d, 3 or 7-C), 62.97 (d, 2 and 6-C), 63.95 (s, 7 or 3-C), 123.76 (d, 9-C), 142.39 (d, 10-C) ppm; HRms (EI) Calcd for $C_{15}H_{24}O_2$: M^+, 236.1777 Found: m/z 236.1780.

   2: ^{1}H Nmr ($CDCl_3$, 270 MHz), δ 1.10, 1.20 (each 3H, s), 1.31 (6H, s), 1.34-1.43 (2H, m), 1.59-1.69 (3H, m), 2.09-2.26 (2H, m), 2.48 (1H, d, J=9.6 Hz), 2.64 (1H, dd, J=4.9, 12.2 Hz), 2.73 (1H, dd, J=4.9, 10.2 Hz), 5.31 (1H, d, J=15.8 Hz), 5.50 (1H, ddd, J=5.0, 10.6, 15.8 Hz) ppm; ^{13}C nmr ($CDCl_3$, 270 MHz) δ 16.39, 16.44, 23.33, 25.18, 30.66, 34.83, 35.62, 38.33, 43.29, 60.06, 60.29, 63.33, 64.64, 122.55, 142.84 ppm.
4. The crystal (monoclinic, 0.70 x 0.65 x 0.46 mm) obtained by recrystallization from 20 %(v/v) EtOAc /hexane was used for the X-ray experiment. The determinations of the crystal class, orientation matrix and accurate unit cell parameters were performed using a MAC Science MXC3k four-circle diffractometer (graphite-monochromatized Mo Kα radiation, $\lambda = 0.71073$ Å). The intensity data were collected by the ω-2θ scan technique in the region $3^\circ < 2\theta < 55^\circ$ at 25 °C. An absorption correction was not applied. A total of 3761 reflections were measured, of which 3241 independent significant reflections ($I \geq 3\sigma(I)$) were assumed to be observed. The structure was solved by the direct method (SIR92) and refined by the full-matrix least-squares method. All the non-hydrogen atoms were refined using anisotropic thermal parameters. Hydrogen atoms were placed in the calculated positions with isotropic thermal parameters fixed at 1.1 times those of the carbon atoms to which they are covalently bonded. The final *R* indices were R=0.059 and Rw=0.054 (weighting scheme, $\omega = \exp(10\sin^2\theta/\lambda^2)/\sigma^2(F_o)$). All the

calculations were carried out using a SUN SPARK 10 workstation (Crystan-GM program system provided by MAC Science).

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