BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 266—268(1972)

The Epoxidation of Homoallylic Alcohols and the Formation of Sesquiterpene Diols

Shosuke YAMAMURA, Masanobu IGUCHI, Masatake NIWA, and Yoshimasa HIRATA*
Faculty of Pharmacy, Meijo University, Showa-ku, Nagoya
**Chemical Institute, Nagoya University, Chikusa-ku, Nagoya*

(Received June 24, 1971)

The epoxidation of homoallylic alcohols was effected with *m*-chloroperbenzoic acid in ether, and the resulting epoxides were reduced with lithium aluminum hydride to the corresponding diols. Particularly in the cases of calameone and isocalamendiol, the exocyclic double bond at the C_3-position was attacked by the peroxy-acid from the side opposite to the axial hydroxyl group at the C_5-position.

In the course of structural studies of calameone (I), a sesquiterpen-diol isolated from *Acorus calamus* L. (Japanese name "Shyobu"), we obtained some interesting results.

In the cases of homoallylic alcohols generally, a peroxy-acid attacks the double bond from the same side as the hydroxyl group.[1] On the other hand, the double bond can be attacked by the same reagent from the opposite side when a methoxyl group is used instead of the hydroxyl group in the same system.[1] In fact, the dehydrated compound (II), which had been obtained from isocalamendiol (III),[2] was treated with *m*-chloroperbenzoic acid and then reduced with lithium aluminum hydride to afford a mixture of calameone (I) and a new isomer (IV), the structure of which was proposed on the basis of a reaction mechanism analogous to that of calameone (I).[1,3] We could further make a configurational isomer (V) at the C_3-position as follows. When treated with *m*-chloroperbenzoic acid in ether, isocalamendiol (III) did not give a β-epoxide (VI), but an α-isomer (VII), in a 98% yield. Furthermore, the dehydration of VII was effected with $POCl_3$-pyridine to give, in a 48% yield, a dehydrated epoxide (VIII). Finally, the reduction of VIII with lithium aluminum hydride afforded the new diol (V), the structure of which was elucidated by a comparison of the NMR spectra of these four sesquiterpen-diols (see Table 1). In the NMR spectra of the compounds

TABLE 1. NMR SIGNALS OF SESQUITERPEN-DIOLS

Compound	*i*-Pr	$-\overset{\vert}{C}Me-OH$	$-\overset{\vert}{C}=CH_2$
Calameone	δ 0.90 (6H, d, $J=6.8$ Hz)	δ 1.13 (3H, s)	δ 4.80 (1H, br.s)
			4.89 (1H, br.s)
Isocalamendiol (III)	0.90 (3H, d, $J=7.0$ Hz)	1.22 (3H, s)	4.80 (1H, br.s)
	0.93 (3H, d, $J=7.0$ Hz)		4.89 (1H, br.s)
Compound (IV)	0.93 (6H, d, $J=6.5$ Hz)	1.12 (3H, s)	4.68—5.00 (2H, br.m)
Compound (V)	0.88 (3H, d, $J=6.9$ Hz)	1.21 (3H, s)	4.77 (1H, br.s)
	0.91 (3H, d, $J=6.9$ Hz)		4.95 (1H, br.s)

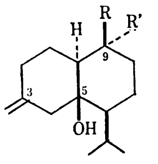
---

[1] H. B. Henbest, *Proc. Chem. Soc.*, **1963**, 159.

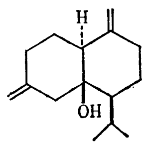
[2] M. Iguchi, A. Nishiyama, H. Koyama, S. Yamamura, and Y. Hirata, *Tetrahedron Lett.*, **1969**, 3729.

[3] M. Iguchi, A. Nishiyama, M. Niwa, S. Yamamura, and Y. Hirata, *Chem. Commun.*, **1970**, 1323.

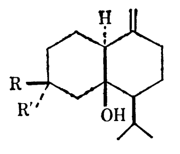
(III and V) with an axial methyl group, the methyl singlets were observed at δ 1.21—1.22 in a magnetic field lower than those of the other two compounds (I and IV) by *ca.* 0.1 ppm. Accordingly, it is clear that the peroxy-acid attacked the double bond in III from the side opposite to the hydroxyl group at the C_5-position. This result does not agree with that of the usual epoxidation in homoallylic alcohols.



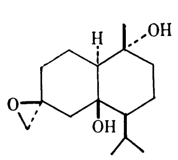
(I) R=OH, R'=Me
(III) R=Me, R'=OH



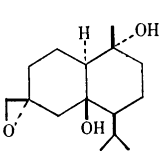
(II)



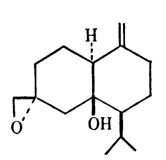
(IV) R=OH, R'=Me
(V) R=Me, R'=OH



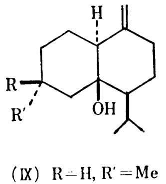
(VI)



(VII)



(VIII)



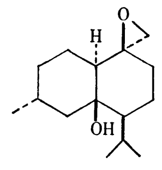
(IX) R=H, R'=Me
(X) R=Me, R'=H

We made further experiments using three different compounds (I, IX, and X), which had already been synthesized from isocalamendiol (III).[2,3] The epoxidation of the (IX) compound, which has an equatorial methyl group at the C_3-position, with *m*-chloroperbenzoic acid gave the expected β-epoxide (XI) in a 76% yield; this substance has then reduced with lithium aluminum hydride to afford a known compound (XII).[3] In the case of the (X) compound, which has an axial methyl group at the C_3-position, we can expect the formation of an α-epoxide analogous to that of isocalamendiol (III). However, the treatment of X with the same peroxy-acid gave a β-isomer (XIII) in an 88% yield; this isomer was also reduced with lithium aluminum hydride to afford a known compound (XIV).[3] On the other hand, in the case of calameone (I), an α-epoxide (XV) was obtained in an almost quantitative yield; its structure was determined by a comparison of the NMR spectra of five epoxides (VII, VIII, XI, XIII, and XV) (see Table 2): the NMR signal of XV, which can be attributed to the methylene protons on the epoxide-ring, is very similar to those of compounds VII and VIII in its chemical shift as well as its coupling constant.

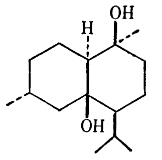
Table 2. NMR signals of several epoxides

Compound	Methylene-protons on the epoxide-ring
VII	δ 2.60 (2H, s)
VIII	2.60 (2H, s)
XI	2.38 (1H, d, J=4.3 Hz), 2.81 (1H, d, J=4.3 Hz)
XIII	2.37 (1H, d, J=4.2 Hz), 2.83 (1H, d, J=4.2 Hz)
XV	2.63 (2H, s)

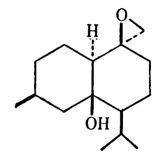
The present studies indicate that such a peroxy-acid as *m*-chloroperbenzoic acid attacks the double bond, as usual, from the same side as the hydroxyl group in homoallylic alcohols which are not sterically hindered (in II and IX), whereas different results have been obtained in the cases of calameone (I) and isocalamendiol (III), as has been described above. Probably, interaction between the peroxy-acid and the homoallylic hydroxyl group at the C_5-position can be prevented by the axial tertiary methyl group at the C_9-position (in III). In the case of I, such an interaction may also be sterically hindered by the 9β-hydroxyl group or prevented by the formation of hydrogen bonding between the two axial hydroxyl groups at the C_5 and C_9-positions. Finally, the epoxidation of the compound (X), which has an axial secondary methyl group at the C_3-position, did not afford the expected α-epoxide, but the β-epoxide (XIII). Probably, the axial secondary methyl group at the C_3-position is easily moved from the normal position so as not to interrupt such an interaction between the peroxy-acid and the hydroxyl group, as compared with the case of the tertiary methyl group in III.



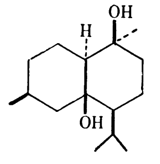
(XI)



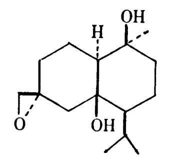
(XII)



(XIII)



(XIV)



(XV)

Experimental

All the melting-points are uncorrected. The IR spectra were recorded on a Hitachi-215 spectrophotometer. The NMR spectra were taken on Varian A-60 and Nihondenshi JNM-60H (60 MHz) spectrometers, using $CDCl_3$ as the solvent, unless otherwise stated. Only prominent peaks are cited. The chemical shifts are given in ppm relative to the internal TMS. The coupling constants are given in Hz (s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet). The mass spectra were obtained on a Hitachi RMU-6D mass spectrometer operating with an ionization energy of 70 eV. Column chromatography was carried out on neutral alumina

(Katayama Co. Ltd., 150—250 mesh).

Epoxidation of Isocalamendiol (III). A solution of isocalamendiol (810 mg) and *m*-chloroperbenzoic acid (705 mg) in abs. ether (30 m*l*) was heated under reflux for 3 hr and then cooled to room temp. After the decomposition of the excess peroxy-acid with 10% aq. Na_2SO_3 (10 m*l*), the ethereal solution was washed with 5% aq. $NaHCO_3$ (5 m*l*×2) and then satu. aq. NaCl, and dried over Na_2SO_4. The subsequent removal of the solvent gave white crystals (835 mg). Recrystallization from *n*-hexane gave white needles; mp 100—101°C; $\nu_{\max}^{\text{KBr}}$ 3520 and 3400 cm^{-1}; δ 0.90 (6H, d, $J=6.3$ Hz), 1.29 (3H, s) and 2.60 ppm (2H, s); *m/e* 236 (M$^+$-18) (Found: C, 70.70; H, 10.31%. $C_{15}H_{26}O_3$ requires: C, 70.83; H, 10.3 %).

Dehydration of Epoxy-isocalamendiol (VII). Into a solution of epoxy-isocalamendiol (296 mg) in abs. pyridine (10 m*l*), we slowly stirred a solution of $POCl_3$ (1 m*l*) in abs. pyridine (3 m*l*) at −16°C. The reaction solution was further stirred for 30 min, and then at 15°C for 2 hr. The reaction solution was then poured into large amounts of ice and extracted with ether. The ether extract was washed well with satu. aq. NaCl and dried over anhydrous Na_2SO_4. The subsequent removal of the solvent gave a pale brown oil, which was chromatographed on alumina (7 g) and eluted with pet. ether-ether (1: 1) to leave a colorless oil (175 mg). This oil was dissolved in *n*-hexane and then allowed to stand at 0°C to give 135 mg of white crystals; mp 61.5—62.5°C (from *n*-hexane); $\nu_{\max}^{\text{KBr}}$ 3560, 3450 br., 1642, 895, and 885 cm^{-1}; δ 0.87 (3H, d, $J=6.8$ Hz), 0.90 (3H, d, $J=6.8$ Hz), 2.60 (2H, s), 4.68 (1H, br. s), and 4.90 ppm (1H, br. s); *m/e* 236 (M$^+$) (Found: C, 76.22; H, 10.56%. $C_{15}H_{24}O_2$ requires: C, 76.22; H, 10.24%).

Reduction of Dehydrated Epoxide (VIII) with Lithium Aluminum Hydride. Lithium aluminum hydride (10 mg) was added to a solution of dehydrated epoxide (130 mg) in abs. ether (20 m*l*), and then the mixture was stirred at room temp. for 2 hr. After the decomposition of the excess lithium aluminum hydride with satu. aq. ether, the reaction solution was washed with 20% aq. potassium sodium tartarate. The ether solution was washed with satu. aq. NaCl and then dried over anhydrous Na_2SO_4. The subsequent removal of the solvent gave 130 mg of white crystals; mp 112.5—114°C (from *n*-hexane); $\nu_{\max}^{\text{KBr}}$ 3450 sh., 3380 br., 3090, 1650, and 895 cm^{-1}; δ 0.88 (3H, d, $J=6.9$ Hz), 0.91 (3H, d, $J=6.9$ Hz), 1.21 (3H, s), 4.77 (1H, br. s), and 4.95 ppm (1H, br. s); *m/e* 238 (M$^+$) (Found: C, 75.90; H, 10.97%. $C_{15}H_{26}O_2$ requires: C, 75.58; H, 11.00%).

Epoxidation of the Equatorial Sec. Methyl Olefin (IX). A solution of IX (102 mg) and *m*-chloroperbenzoic acid (95 mg) in abs. ether (8 m*l*) was heated under reflux for 3 hr; then it was worked up as usual to give a white solid, which was chromatographed on alumina (2.5 g) and eluted with pet. ether-ether (3: 1) to afford 83 mg of white crystals; mp 91.5—92.5°C (from *n*-hexane); $\nu_{\max}^{\text{KBr}}$ 3570 cm^{-1}; δ 0.88 (3H, d, $J=6.0$ Hz), 0.92 (3H, d, $J=6.9$ Hz), 0.93 (3H, d, $J=6.9$ Hz), 2.38 (1H, d, $J=4.3$ Hz), and 2.81 ppm (1H, d, $J=4.3$ Hz); *m/e* 238 (M$^+$) (Found: C, 75.21; H, 11.15%. $C_{15}H_{26}O_2$ requires: C, 75.58; H, 11.00%).

Reduction of the Epoxide (XI) with Lithium Aluminum Hydride. Lithium aluminum hydride (4 mg) was stirred into a solution of the epoxide (49 mg). The reaction solution was stirred at room temp. for 2 hr and then worked up as usual to give 49 mg of white crystals (mp 133—134°C (from *n*-hexane)) which were completely identical with an authentic sample of dihydrocalameone (XII) (mp and IR spectrum).

Epoxidation of the Axial Sec. Methyl Olefin (X). A solution of X (340 mg) and *m*-chloroperbenzoic acid (320 mg) in abs. ether (10 m*l*) was refluxed for 3 hr and then worked up as usual to give a colorless oil, which was chromatographed on alumina (8.5 g) and eluted with pet. ether-ether (2: 1) to give 322 mg of white crystals; mp 61—62.5°C (from *n*-hexane); $\nu_{\max}^{\text{KBr}}$ 3580 and 3450 br. cm^{-1}; δ 0.90 (3H, d, $J=6.9$ Hz), 0.94 (3H, d, $J=6.9$ Hz), 1.13 (3H, d, $J=7.0$ Hz), 2.37 (1H, d, $J=4.2$ Hz), and 2.83 ppm (1H, d, $J=4.2$ Hz); *m/e* 238 (M$^+$) (Found: C, 75.30; H, 11.21%. $C_{15}H_{26}O_2$ requires: C, 75.58; H, 11.00%).

Reduction of the Epoxide (XIII) with Lithium Aluminum Hydride. Lithium aluminium hydride (10 mg) was stirred into a solution of XIII (77 mg) in abs. ehter (10 m*l*). The reaction solution was further stirred at room temp. for 2 hr and then worked up as usual to give 100 mg of white needles, mp 123—124°C (from *n*-hexane), which were completely identical with an authentic sample of the isomer (XIV) of dihydrocalameone (mp and IR spectrum).

Epoxidation of Calameone (I). A solution of calameone (68 mg) and *m*-chloroperbenzoic acid (60 mg) in abs. ether (5 m*l*) was heated under reflux for 3 hr and then worked up as usual to give a crystalline solid; this solid was then chromatographed on neutral alumina (1.5 g) and eluted with chloroform to give 65 mg of white crystals; mp 96—98°C (from *n*-hexane); $\nu_{\max}^{\text{KBr}}$ 3370 br. cm^{-1}; δ 0.91 (6H, d, $J=6.8$ Hz), 1.16 (3H, s), 1.63 (2H, s), 3.12 (1H, s, OH), and 4.44 ppm (1H, s, OH); *m/e* 254 (M$^+$) (Found: C, 70.78; H, 10.45%. $C_{15}H_{26}O_3$ requires: C, 70.83; H, 10.30%).

The authors wish to thank Miss E. Naoi, Meijo University, for the elemental analysis.