**Tetrahedron Letters No. 42, pp 3661 - 3664, 1975. Pergamon Press. Printed in Great Britain.**

# ACID-CATALYSED REACTION OF EPOXY-GERMACRONES

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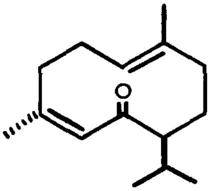
**(Received in Japan 11th August 1975; received in UK for publication 8th September 1975)**

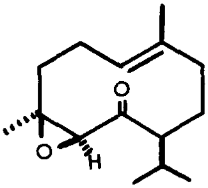
Usually, acid-catalysed cyclization reaction of the (E,E)-germacrene-5,6-oxides has been known to afford the corresponding guaiane-type compounds.[1] In connection with our biogenetic model reactions of ten-membered ring sesquiterpenes and their epoxides,[2] we further examined the acid-catalysed cyclization reaction of (E,E)- or (E,Z)-epoxy-germacrone, in which the keto group is conjugated with the epoxy-ring. In the present paper, we wish to describe the interesting results in the above biogenetic model reactions.

When treated with 30% $H_2O_2$ - 5%aq NaOH in MeOH (room temp., overnight), isoacoragermacrone (I)[3] was readily converted into the corresponding epoxide (II) in 92% yield [m.p. 85.5-86°; $C_{15}H_{24}O_2$ (m/e 236($M^+$)); $\nu_{max}$(KBr) 1720$cm^{-1}$; $\delta$($CDCl_3$) 0.90(3H, d, J= 7Hz), 1.04(3H, d, J= 7Hz), 1.42(3H, s), 1.44(3H, s), 3.43(1H, s) and 5.20ppm(1H, t, J= 7Hz)][4]. This epoxy-isoacoragermacrone was subjected on acid-catalysed reactions using 80%aq AcOH, 80%aq HCOOH and $AlCl_3$ in dry ether, as follows.

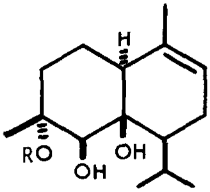
The epoxide (II) is pretty stable for 80%aq AcOH at room temperature. However, when heated at 60° for 3hr, II was converted into a triol (III) in ca.50% yield, whose structure was unambiguously determined on the basis of its spectral data {m.p. 195°; $C_{15}H_{26}O_3$ (m/e 254($M^+$)); $\nu_{max}$(KBr) 3400$cm^{-1}$; $\delta$($CDCl_3$) 0.92(3H, d, J= 7Hz), 0.94(3H, d, J= 7Hz), 1.32 (3H, s), 1.56(1H, s, OH), 1.73(3H, br.s), 2.16(2H, s, OH), 3.90(1H, br.s) and 5.64ppm(1H, m)] coupled with the following chemical evidence. Oxidation of III with $NaIO_4$ in aqMeOH (room temp., overnight) afforded a diketone (IV) as colourless liquid,[5] which was further treated with NaOMe in MeOH to give an $\alpha\beta$-unsaturated ketone (V) in almost quantitative yield [V as colourless liquid; $C_{14}H_{22}O_2$ (m/e 222($M^+$)); $\nu_{max}$(film) 1710 and 1660$cm^{-1}$; $\lambda_{max}$(MeOH) 243nm ($\varepsilon$, 10300); $\delta$($C_6D_6$) 0.86(3H, d, J= 7Hz), 0.91(3H, d, J= 7Hz), 1.56(3H, s), 1.72(3H, s), 2.30(2H, t, J= 7.8Hz) and 2.65ppm(2H, t, J= 7.8Hz)]. In the case of 80%aq HCOOH (room temp., 10min), the triol (III) and the corresponding formate (VI)[6] were obtained in 8 and 15% yields, respectively. On hydrolysis with 10% methanolic KOH, the latter was readily converted into III. Probably, the intramolecular cyclization reaction takes place after cleavage of the epoxy-ring. Particularly, the formation of the tri-substituted olefines (III and VI) is of quite interest.



(I)

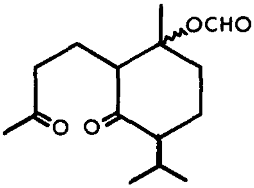


(II)

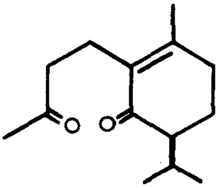


(III) R = H

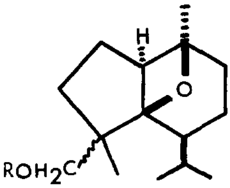
(VI) R = CHO



(IV)

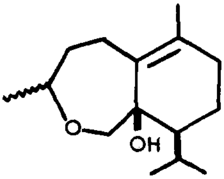


(V)



(IX) R = H

(X) R = Ac



(XI)

When treated with $AlCl_3$ in dry ether at 0° for 10min, II gave a mixture of several compounds, from which an aldehyde (VII) and an alcohol (VIII) both isolated in 27 and 32% yields, respectively. The structures of these two products are based on their spectral and chemical data, as shown below.

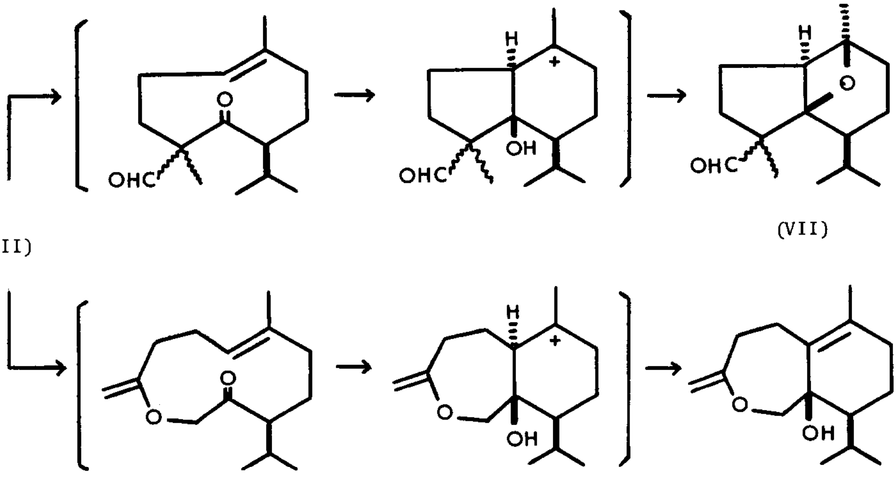
VII as colourless liquid: $C_{15}H_{24}O_2$ (m/e 236(M$^+$)); $\nu_{max}$(film) 2700 and 1720cm$^{-1}$; $\delta$(CDCl$_3$) 0.91(3H, d, J= 7Hz), 0.98(3H, d, J= 7Hz), 1.25(3H,s), 1.52 (3H, s) and 9.75ppm(1H, s).

VIII as colourless liquid: $C_{15}H_{24}O_2$ (m/e 236(M$^+$)); $\nu_{max}$(film) 3560, 3090 and 1650cm$^{-1}$; $\delta$(CDCl$_3$) 0.87(3H, d, J= 7Hz), 0.90(3H, d, J= 7Hz), 1.67(3H, s), 2.90(1H, d, J= 12Hz), 3.31(1H, d, J= 12Hz), 4.66(1H, br.s) and 4.86ppm(1H, br.s).

The aldehyde (VII) was reduced with $LiAlH_4$ in THF (room temp., overnight) to give the corresponding alcohol [IX, $C_{15}H_{26}O_2$ (m/e 238($M^+$)); $\nu_{max}$(film) 3400cm$^{-1}$; $\delta$($CDCl_3$) 0.98(3H, d, J= 6Hz), 1.03(3H, d, J= 6Hz), 1.24(6H, s), 3.56(1H, d, J= 12Hz) and 3.76ppm(1H, d, J= 12Hz)], which was further treated with $Ac_2O$-pyridine to afford the corresponding acetate [X, $C_{17}H_{28}O_3$ (m/e 280($M^+$)); $\nu_{max}$(film) 1740cm$^{-1}$; $\delta$($CDCl_3$) 2.07(3H, s) and 4.10ppm(2H, br.s)]. The alcohol (IX) was easily reconverted into the original aldehyde (VII) in 52% yield, when treated with Jones reagent (room temp., 1.5hr).

The compound (VIII) has no CO group, but instead a hydroxyl group. Furthermore, VII has two tertiary methy groups, whereas VIII has one methyl group and one exocyclic double bond that can be converted into a secondary methyl group on catalytic hydrogenation leading to the formation of the dihydro-compound [XI, $C_{15}H_{26}O_2$ (m/e 238($M^+$)); $\nu_{max}$(film) 3560cm$^{-1}$; $\delta$($CDCl_3$) 1.10(3H, d, J= 8Hz) and 2.85ppm(1H, m)]. Particularly, in the NMR spectra of VIII and XI, both have the two sharp doublets with a geminal coupling constant (J= 12Hz), which can be due to the isolated methylene group ($\delta$2.90 and 3.31ppm in VIII; $\delta$2.86 and 3.18ppm in XI). The tentative stereochemistry of VIII is proposed on the basis of the most stable conformation of the eleven-membered ring intermediate [A].

These two cyclization products (VII and VIII) may be produced according to the following pathways, as shown below.



(II)

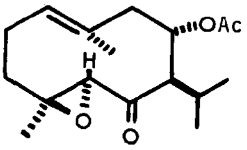
(VII)

[A]

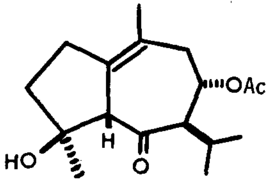
(VIII)

In the next experiment, we used the oxidation product (XII) of shiromodiol-monoacetate[7] as an (E,E)-epoxy-germacrone, as follows.

This epoxy-germacrone (XII) is also stable for 80%aq AcOH at room temperature, as seen in the case of II. However, when heated at 80° for 4hr, XII was converted into a mixture of many products, from which a guaiane-type compound (XIII) was isolated in 15% yield [XIII as colourless liquid, $C_{17}H_{26}O_4$ (m/e 276($M^+$- 18)); $\nu_{max}$(film) 3420, 1735 and 1710cm$^{-1}$; $\delta$($CDCl_3$) 0.98(3H, d, J= 7Hz), 1.05(3H, d, J= 7Hz), 1.36(3H, s), 1.71(3H, br.s), 2.05(3H, s), 3.54(1H, br.s) and 5.30ppm(1H, m)]. XIII was also obtained in 40% yield, on treatment with $AlCl_3$ in dry ether (-5°, 15min). These results are quite similar to that of shiromodiol-monoacetate[7].



(XII)



(XIII)

Further studies on these biogenetic model reactions are in progress, leading to the formation of many sesquiterpenes or their synthetic intermediates.

The authors wish to thank Prof. K. Munakata and Dr. K. Wada (Nagoya University) for the sample and IR spectrum of shiromodiol-diacetate. They are also indebted to Prof. M. Noro (Meijo University) for collection of the plant Parabenzoinn trilobum Nakai.

## REFERENCES AND FOOTNOTES

1. J.K. Sutherland, Tetrahedron, 30, 1651 (1974).
2. M. Iguchi, M. Niwa and S. Yamamura, Chem. Commun., 974 (1971), 689 (1972); Tetrahedron Lett., 1687, 4367 (1973).
3. M. Iguchi, A. Nishiyama, S. Yamamura and Y. Hirata, Tetrahedron Lett., 4295 (1969).
4. The 12% NOE is observed between 5-Me and 6-H.
5. Spectral data of IV: $C_{15}H_{24}O_4$ (m/e 222($M^+$- HCOOH); $\nu_{max}$(film) 1720br.cm$^{-1}$; $\delta$($CDCl_3$) 0.86(3H, d, J= 6.5Hz), 0.93(3H, d, J= 6.5Hz), 1.26(3H, s), 2.12(3H, s), 3.03(1H, dd, J= 10, 2Hz) and 8.00ppm(1H, s).
6. The elemental analysis of this formate (VI) has not been carried out, but its structure can be unambiguously confirmed by its spectral data: m/e 236($M^+$- HCOOH); $\nu_{max}$(film) 3470 and 1720cm$^{-1}$; $\delta$($CDCl_3$) 0.93(3H, d, J= 7Hz), 0.96(3H, d, J= 7Hz), 1.66(3H, s), 1.74(3H, br.s), 2.49(1H, OH), 3.96(1H, d, J= 5.4Hz), 5.65(1H, m) and 8.04ppm(1H, s).
7. K. Wada, Y. Enomoto and K. Munakata, Agr. Biol. Chem.(Japan), 34, 946 (1970) and references cited therein.