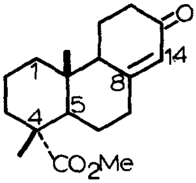
Tetrahedron Letters No. 45, pp. 5483-5487, 1966. Pergamon Press Ltd.
Printed in Great Britain.

THE REARRANGEMENT OF A DITERPENE EPOXY ϵ-LACTONE SYSTEM

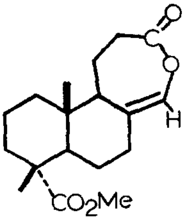
C. W. J. Chang and S. W. Pelletier[1]
Department of Chemistry, The University of Georgia,
Athens, Georgia, U. S. A. 30601

(Received 25 April 1966; in revised form 29 August 1966)

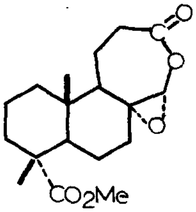
The oxidation of α,β-unsaturated ketones with peracids is known to yield enol and/or epoxy esters or lactones depending on the reaction conditions and on whether the enone is alicyclic or acyclic[2]. For example, we have found that treatment of methyl (+)-13-oxo-deisopropylideneneoabietate I (obtained from methyl (+)-neoabietate) with m-chloroperbenzoic acid in methylene chloride, yields: (A) a crystalline mixture of the enol ϵ-lactone II and the epoxy ϵ-lactone III in a ratio of 35/65 or (B) compound III exclusively, depending upon conditions. Exclusive formation of III resulted from refluxing I with an excess of m-chloroperbenzoic acid for 24 hours.



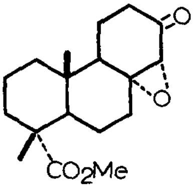
I



II



III



IV

Compound II, $C_{18}H_{26}O_4$*, m.p. 129-130°, ν_{max} (CCl_4) 1770, 1764 (enol lactone), 1739 (ester) cm.$^{-1}$, τ 3.85, 1H singlet (>C=CHOCO-), on further oxidation

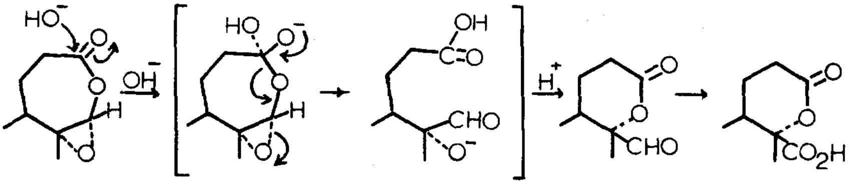
---

*Satisfactory elemental analyses were obtained for all new compounds reported with molecular formulae. Melting points are corrected. Infrared spectra were carried out in Nujol and n.m.r. spectra in carbon tetrachloride unless stated otherwise.

is converted smoothly (88% yield) to III, $C_{18}H_{26}O_5$, m.p. 151-152°, ν_{max} 1754 (epoxylactone), 1709 cm.$^{-1}$, τ 5.28, 1H singlet $(-\underset{O}{C-C}\underline{H}OCO-)^3$. No evidence of the epoxyketone ester IV was present, which suggests that I is converted to III via II, but not via IV[4]. However, oxidation of I with the nucleophilic reagent, hydrogen peroxide in aqueous methanolic sodium hydroxide, afforded in 76% yield, IV, $C_{18}H_{26}O_4$, m.p. 110-111°, ν_{max} 1735 (ester), 1712, 887, 860 (epoxyketone) cm.$^{-1}$, τ 7.20, 1H singlet $(-\underset{O}{C-C}\underline{H}CO-)$. The alpha-configuration of the epoxides is inferred by epoxidation from the less hindered face of compounds I and II.

We have observed that the epoxy ϵ-lactone system of III, under a variety of conditions, undergoes a facile rearrangement to the isomeric aldehyde δ-lactone V, $C_{18}H_{26}O_5$, m.p. 175-177°. The rearranged product showed only two bands of equal intensity in the carbonyl region at 1760 and 1726 cm.$^{-1}$. The presence of the aldehyde group was suggested by the small band at 2720 cm.$^{-1}$ and was confirmed by its p.m.r. spectrum which showed a sharp singlet at τ 0.17, integrating for 1 proton. Other signals appeared at τ 9.17, 3H singlet (C(10)-C$\underline{H}_3$); 8.80, 3H singlet (C(4)-C$\underline{H}_3$); 7.20, 2H unresolved multiplet (-C$\underline{H}_2$COO-); 6.30, 3H singlet (COOC$\underline{H}_3$).

This rearrangement may be effected in 86% yield by the action of aqueous methanolic sodium hydroxide at room temperature over a period of fifteen minutes. It is apparently facilitated by the participation of the epoxy moiety in the relactonization of ring C (Fig. 1). The aldehyde was oxidized with Jones' reagent to the



III FIG. I V VI

corresponding acid[5], VI, $C_{18}H_{26}O_6$, m.p. 235-237°, in 93% yield. The acid possessed the requisite spectral characteristics.

Treatment of III with ethanolic hydrochloric acid under reflux for two hours also yielded V (78%), identical to the compound obtained by base catalysis[6]. Since the melting point of III was raised by melting and subsequent solidification, we considered the possibility of the thermal isomerization[7] of III to V (Fig. 2). This was indeed shown to take place (85%) when III was heated under nitrogen for 10 minutes at 160^0. The disappearance of the characteristic singlet attributed to the proton adjoining the epoxy and lactone groups at τ 5.28[3] and the emergence of the sharp singlet of the aldehyde proton downfield at 0.17 was clearly indicated by n.m.r. spectroscopy.

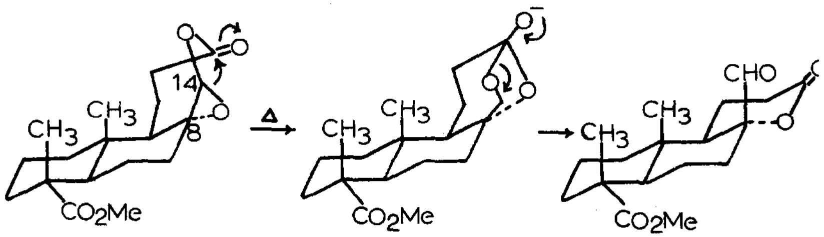


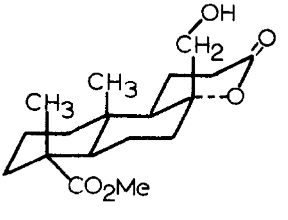
FIG. 2

In Figs. 1 and 2 we have shown the C(8)-CHO group in the beta-configuration for reasons which we now elaborate. In the epoxylactone system, the lactone is conformationally fixed so that the lactone carbonyl is directed away from the backside of the oxiran ring and therefore cannot lead to an alpha-oriented aldehyde. An inspection of Dreiding models makes this clear. It is important to note that the C(8)-O bond and the C(8)-C(14) bonds are not ruptured in the reaction so the aldehyde group must be beta-oriented.

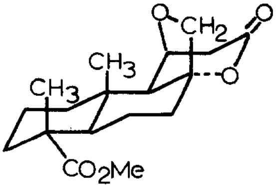
Evidence for the C(8)-beta-CHO grouping was obtained indirectly by action of lead tetraacetate on the alcohol VII, m.p. 198.5-200^0, νmax 3534 (OH), 1734, 1712 (ester, lactone carbonyls) cm.$^{-1}$; τ (CHCl$_3$)9.07, 3H singlet [C(10)-C$\underline{H}_3$]; 6.22, 2H broad AB quartet which sharpens on addition of D$_2$O, [C(8)-C$\underline{H}_2$OH], derived from the controlled sodium borohydride reduction of V.

Heating a mixture of VII, calcium carbonate and lead tetraacetate in cyclohexane with a trace of iodine[8] afforded the furanoether VIII as the major product, m.p. 159-161^0, νmax (CHCl$_3$) 1754, 1737 cm.$^{-1}$; τ (CHCl$_3$) 8.96, 3H singlet [C(10)-C$\underline{H}_3$]; 8.82, 3H singlet [C(4)-C$\underline{H}_3$]; 7.13, 2H complex multiplet [C(12)-C$\underline{H}_2$-]; 6.32, 3H singlet (CO$_2$C$\underline{H}_3$); 6.12, 2H AB quartet [C(8)-C$\underline{H}_2$O-]; 5.63, 1H triplet [C(11)-C$\underline{H}$-].

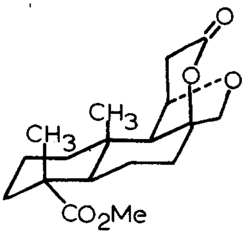
Since the C(10) methyl absorption in VIII is shifted 0.11 ppm downfield from the position in the alcohol VII, it is clear that the $-CH_2OH$ function at C(8) is beta-oriented. An alpha-CH_2OH group reacting to give IX would not account for the deshielding of the C(10) methyl group which is observed.



VII



VIII



IX

Recently, Pinhey and Schaffner found that the reaction of trifluoroperacetic acid with Δ^4 3-keto steroids yielded compounds with the aldehyde δ-lactone system[9]. The intermediate epoxy ε-lactone was suggested, but not isolated. Our observations therefore substantiate the epoxy ε-lactone compound as the precursor of the aldehyde δ-lactone system and illustrate the generality of the reactions which this epoxy ε-lactone system undergoes. This rearrangement is of particular interest since it follows a stereochemical course different from that of the rearrangement of the usual epoxy ester.

Acknowledgment. This work was supported in part through funds provided by the Georgia Forestry Research Council, Macon, Georgia and is a cooperative project of the School of Forestry and the Department of Chemistry.

References

1. To whom inquiries should be addressed.
2. See the excellent review by H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N.Y., 1965, pp. 105-133.
3. The chemical shift for this proton is characteristic of this region in the n.m.r. spectrum. J. J. Riehl, J. M. Lehn, and F. Hemmert, Bull. Soc. Chim. France, 224 (1963).
4. No epoxyketone was detected (by t.l.c. and p.m.r.). In contrast to this observation, Payne and Williams reported the isolation of an epoxyketone on treatment of an enone with a peracid[6].
5. It is interesting to note that through a closely related transformation in the steroid series, the acid δ-lactone system resulted from the reaction of an epoxyketone with hydrogen peroxide in refluxing aqueous methanolic sodium hydroxide. W. Reusch and R. LeMahieu, J. Am. Chem. Soc., **85**, 1669 (1963).
6. G. P. Payne and P. H. Williams, J. Org. Chem., **24**, 284 (1959). Reaction of 3,3-dimethyl-2-acetoxyoxirane with hot acidic ethanol afforded 2-methylpropenal probably by saponification followed by dehydration. In the case of the epoxy ε-lactone ester III, however, opening of the oxiran ring and favorable placement of the carboxy function leads to the six-member lactone ring.
7. A recent example of a thermal rearrangement of an epoxyacetate has been reported. R. W. Hoffmann and H. J. Luthardt, Tetrahedron Letters, 441 (1966). For other examples, see A. L. Draper, W. J. Heilman, W. E. Schaefer, H. J. Shine, and J. N. Shoolery, J. Org. Chem., **24**, 2727 (1962) and references cited therein.
8. von Ch. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner and A. Wettstein, Helv. Chim. Acta, **45**, 1317 (1962).
9. J. T. Pinhey and K. Schaffner, Tetrahedron Letters, 601 (1965).