Tetrahedron Letters No.49, pp. 4477-4479, 1965. Pergamon Press Ltd.
Printed in Great Britain.

# REACTION OF ENOL LACTONE WITH LITHIUM ALUMINUM HYDRIDE

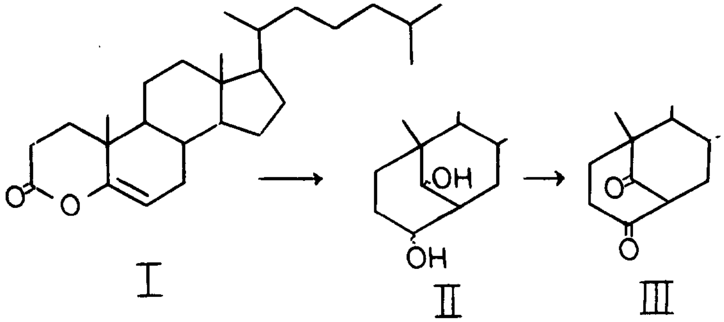
George I. Fujimoto and John Pavlos
Department of Biochemistry
Albert Einstein College of Medicine, Yeshiva University
New York City, N. Y. 10461

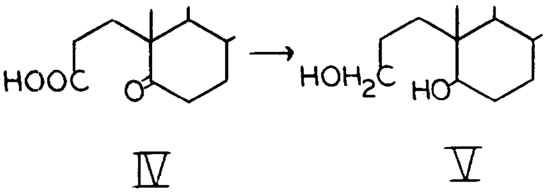
(Received 14 October 1965)

Although carboxyl functions are well known to be reduced by excess lithium aluminum hydride to primary alcohols, we have observed an exception to this reaction with the enol lactone, 4-oxa-$\Delta^5$-cholesten-3-one (I).[1,2] In the reaction of I with LAH there is a 4,6 migration of the C-3 function to yield the bridged ring structure II.

In the course of our investigation of the enol lactone and enol ester rearrangement reactions[3] we treated the enol lactone I with excess LAH in ethylene glycol dimethyl ether. After standing 4 hr, the reaction mixture was treated with wet ether, then with dilute $H_2SO_4$ and extracted with methylene chloride. The major product proved to be 3,5-seco-3,6-cyclo-A-norcholestane-$3\xi,5\xi$-diol [II, 47% yield; m.p. 147-148°; $\alpha]_D^{28}$ +9.6° (c .825 $CHCl_3$); $\nu_{max}^{CS_2}$ 931, 946, 962, 982, 1020, 1040, 1056, 1376, 2860, 2960, 3630 $cm^{-1}$. Found: C, 79.94; H, 12.14. Calcd for $C_{26}H_{46}O_2$: C, 79.95; H, 11.87], which differed from the glycol V obtained from LAH reduction of the keto acid IV.[4] The following evidence supported the structure of glycol II. With pyridine and acetic anhydride, glycol II formed a diacetate [m.p. 159.5-160°; $\alpha]_D^{26}$ +6.3° (c .708); $\nu_{max}$ 962, 982, 1023, 1033, 1243, 1365, 1748, 2870, 2960 $cm^{-1}$. Found: C, 75.99; H, 10.82. Calcd for $C_{30}H_{50}O_4$: C, 75.90; H, 10.62]. The diacetate was hydrolyzed to the parent glycol II by refluxing in ethanolic sodium hydroxide. Additional evidence to eliminate a lactol or hemiketal structure for the rearrangement product came from the observation that only starting glycol II was recovered from further LAH treatment. Oxidation of glycol II with chromic acid-pyridine yielded the β-diketone, 3,5-seco-3,6-cyclo-A-norcholestane-3,5-dione [III, m.p. 113-114°; $\alpha]_D^{25}$ +8.1° (c .520); $\nu_{max}$ 1380, 1714, 1744, 2856, 2950 $cm^{-1}$. Found: C, 80.87;

H, 10.39. Calcd for $C_{26}H_{42}O_2$: C, 80.77; H, 10.95]. Dioxime of III melted at 116-119°. Found: N, 6.89. Calcd for $C_{26}H_{44}O_2N_2$: N, 6.72. Refluxing III in aqueous methanolic potassium carbonate resulted in hydrolytic cleavage to the keto acid IV. The structure of diketone III is consistent with its n.m.r. spectrum ($\delta$ = 3.28 p.p.m. for the C-6 proton; this appears to be a pair of doublets and $\delta$ = 1.13 p.p.m. for the C-19 methyl). Further evidence against an acyclic glycol structure for the rearrangement product was obtained by oxidation of glycol V with chromic acid-pyridine. A mixture of products was obtained, none of which had diketone properties and the major fraction of which appeared to be the lactone, 4-oxa-5α-cholestan-3-one[4] on the basis of infrared spectral identity with an authentic sample.





Thus, our evidence for the structure of the major reaction product, glycol II, is based on elimination of the other likely structures, the acyclic glycols, lactol, hemiketal and keto aldehyde, and on reaction and properties consistent with the cyclic glycol structure II. The configuration of the 3 and 5 hydroxyl groups have not yet been established. Glycol II does not appear to form cyclic borate, sulfite or acetonide derivatives under usual conditions, thus ruling out the cis 3β,5α-diol configuration.

Acknowledgments - We are grateful to Dr. A. S. Kende of Lederle Laboratories for the n.m.r. spectral data. This research was supported by Public Health Service Research Grant HE-02818 from the National Heart Institute, U. S. Public Health Service.

## References

1. R. B. Turner, J. Am. Chem. Soc., 72, 579 (1950).

2. J. Martin, W. Parker, and R. A. Raphael, J. Chem. Soc., 289 (1964) have reported a similar type of rearrangement with lithium tri-t-butoxyaluminum hydride; see also A. Yogev and Y. Mazur, J. Am. Chem. Soc., 87, 3520 (1965).

3. K. D. Zwahlen, W. J. Horton, and G. I. Fujimoto, J. Am. Chem. Soc., 79, 3131 (1957); G. I. Fujimoto and K. D. Zwahlen, J. Org. Chem., 25, 445 (1960); J. Pavlos and G. I. Fujimoto, Abstracts of the 140th Meeting of the American Chemical Society, Chicago, Ill., Sept. 1961, p. 61Q.

4. Cf. J. T. Edward and P. F. Morand, Can. J. Chem., 38, 1325 (1960).