Tetrahedron Letters No. 2, pp. 111 - 113, 1972. Pergamon Press. Printed in Great Britain.

# A DRAMATIC CHANGE IN THE BALANCE BETWEEN $S_N2$ AND E2 PATHWAYS WITH FORMATE AND OXALATE AS NUCLEOPHILE

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(Received in USA 2 November 1971; received in UK for publication 7 December 1971)

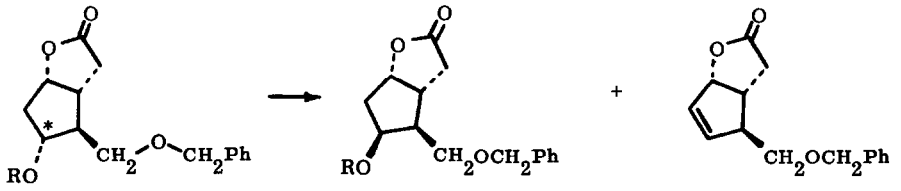
In connection with a plan for the synthesis of 11-epi prostaglandins from the readily available intermediate I (1,2), we have investigated the inversion of configuration at C* in I by reaction of the corresponding p-toluenesulfonate ester with carboxylate nucleophiles. A very large dependence of product composition on structure of the carboxylate nucleophile has been observed with acetone as solvent and tetrabutylammonium ion as the positive counterion. These observations would seem to provide a useful guide for the selection of the nucleophilic reagent for E2 or $S_N2$ processes.

The reaction of the (±)-hydroxy lactone I with 3 equiv. of p-toluenesulfonyl chloride in pyridine at 25° for 20 hr. afforded the tosylate II (3), m.p. 123.5-125°, in 95% yield. Treatment of II with 5.0 equiv. of tetra-n-butylammonium acetate in acetone at 25° for 2 hr. produced in 98% yield a mixture of the inverted acetate IIIb (3b) and the cyclopentene IV resulting from elimination in a ratio of 1.2 to 1. A parallel experiment at 0° gave the same result. Selective cleavage of the acetate IIIb by means of potassium carbonate in methanol at 25° for ca. 1 hr. gave the hydroxy lactone IIIa (3), distinguished from its epimer I by its spectral properties and thin layer chromatographic (t.l.c.) behavior. The unsaturated lactone IV was identical with samples prepared either by iodohydrin elimination as described in the accompanying paper (4) or by cyclization of the hydroxy acid V by means of p-toluenesulfonic acid in tetrahydrofuran at 25° for several hr. (5).

In experiments analogous to that described above for the tosylate II except for the replacement of acetate as reagent by tetra-n-butylammonium oxalate (disalt), the sole product was the unsaturated lactone IV resulting from elimination (82% isolated yield); no oxalate mono ester could be detected.

In contrast, tetra-n-butylammonium formate (6.7 equiv.) in acetone at 25°, the standard conditions, converted the tosylate II mainly to the inverted formate IIIc (3b) (total yield of IIIc and IV, 97% in a ratio of 75:25).

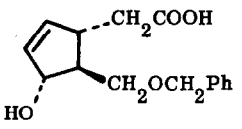
It is clear from these results that tetra-n-butylammonium oxalate is an excellent nucleophile for effecting elimination under very mild conditions with substrates such as II. The preference for elimination



I, R = H
II, R = Tos

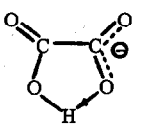
IIIa, R = H
IIIb, R = $CH_3CO$
IIIc, R = HCO

IV



V

over substitution in this case may be the result of a possible "bidentate" attack on hydrogen which should be especially favorable, since it leads to the stabilized (by hydrogen bonding) oxalate mono acid ion (A);



A

The stability of A, which can be reflected in the transition state for elimination, provides no driving force for nucleophilic substitution at carbon.

The greater tendency for substitution at carbon by formate ion relative to acetate ion may be a result of the smaller size of the former or its smaller basicity (at hydrogen) or both (6).

## References

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2. E. J. Corey, T. Ravindranathan, and S. Terashima, ibid. 93, 4326 (1971).
3. Satisfactory (a) analytical and (b) infrared and nuclear magnetic resonance data have been obtained for this compound.
4. E. J. Corey and P. A. Grieco, Tetrahedron Letters, preceding paper.
5. Experiment by Dr. M. Kato of this laboratory.
6. This research was assisted by grants from the Agency for International Development and the National Institutes of Health.