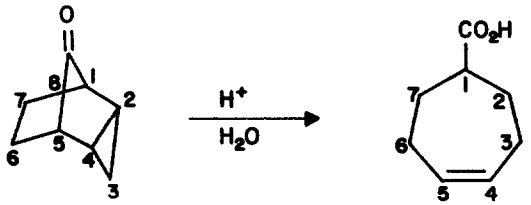
Tetrahedron Letters No. 40, pp 4095 - 4097, 1972. Pergamon Press. Printed in Great Britain.

STEREOCHEMISTRY OF CYCLOPROPANE RING OPENING IN THE ACID-CATALYZED FRAGMENTATION OF endo-8-TRICYCLO[3.2.1.$0^{2,4}$]OCTANONE[1a]

Merle A. Battiste* and Judith Mackiernan[1b]
Department of Chemistry
University of Florida
Gainesville, Florida 32601

(Received in USA 24 July 1972; received in UK for publication 1 September 1972)

The reported instances of inversion of configuration in the acid-catalyzed opening of cyclopropane rings are rare.[2] The recent report[3] of exclusive inversion in the hydrogen chloride promoted opening of a fused cyclopropane ring prompts us to amplify our previous observations[4] of a similarly striking stereochemical result in the acid-catalyzed fragmentation of endo-8-tricyclo[3.2.1.$0^{2,4}$]octanone (1).



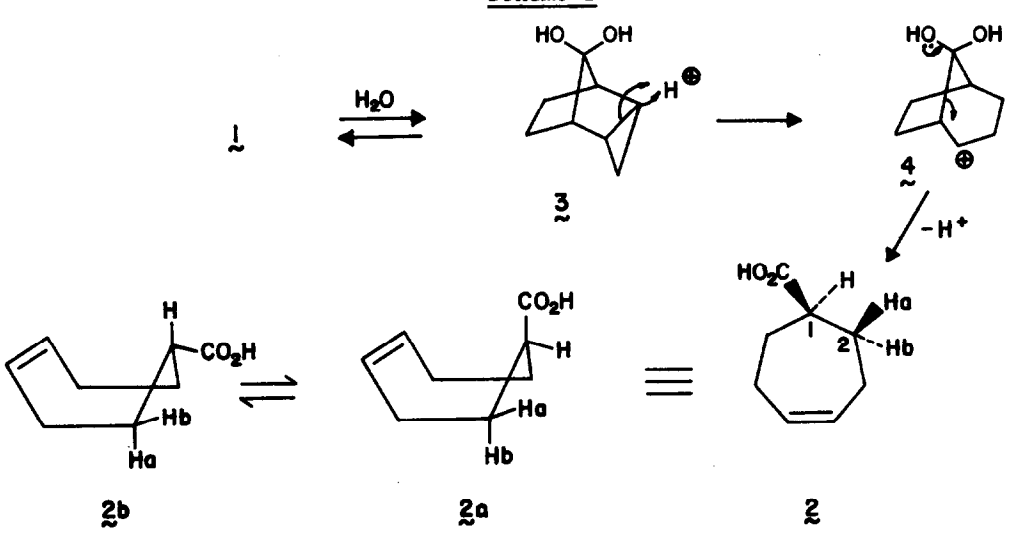
1 2

In our original synthesis of ketone 1[5] it was observed that whereas wet acetic acid or dilute (pH 4) aqueous acids hydrolyzed the corresponding dimethyl ketal of 1 without difficulty treatment of 1 with 46.6% aqueous sulfuric acid (w/w) for 30 minutes resulted in facile bridge cleavage to 4-cycloheptenecarboxylic acid (2); isolated yield ca. 80%. Under the same strong acid conditions ketone 1 gave the identical result.

Since 1 is unusually hygroscopic the initial mechanistic arguments pointed

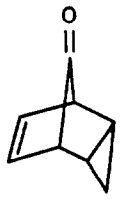
to edge or corner attack by proton on hydrate 3 to give carbonium ion 4 as shown in Scheme I. Subsequent bridge cleavage in 4 leads to the observed acid 2. In order to probe the stereochemistry of electrophilic attack on the C_2-C_4 bond of the endo cyclopropane ring, ketone 1 was treated with 45% deuteriosulfuric acid in deuterium oxide. The resulting acidic product was freed of its carboxylic deuterium by the usual procedures to give 2-d_1 containing 93% d_1: 6% d_0:1.0% d_2 by mass spectral analysis.

Scheme 1

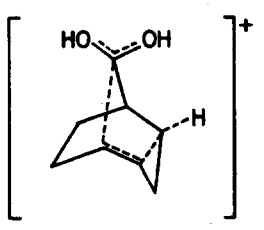


Nmr analysis of 2-d_1 at 100 MHz (CCl_4) revealed a symmetrical six line multiplet at 257 Hz for the carboxyl methine proton H_1. In the undeuterated acid this same proton appeared as a symmetrical seven line multiplet which by first order analysis is consistent with an overlapping series of triplet of triplets. Whichever conformation of 2 (2a or 2b) prevails is immaterial since of the flanking pairs of methylene protons, H_{2a}, H_{7a} should exhibit the larger coupling with the methinyl proton ($J_{1,2a}=J_{1,7a}=9.0$ Hz; $J_{1,2b}=J_{1,7b}=4.0$ Hz). Therefore appearance of a six-line multiplet rather than a five-line multiplet for H_1 on replacement of one of these four methylene protons by deuterium is consistent only with deuteron attack trans to the developing carboxyl function. Hence corner attack by the approaching electrophile with resultant inversion of configuration at C_2 (C_4) is established.

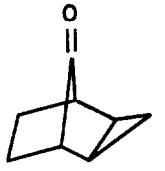
Unlike the case of Hogeveen and coworkers[3] edge attack by proton is not preempted by steric considerations in 1 (or 3). The explanation for corner attack more likely resides with electronic considerations. In view of the large accerleration (ca. 10^5) provided by the C_2-C_4 bent bond for concerted two-bond bridge cleavage (decarbonylation) of unsaturated ketone 5,[6] it is reasonable to expect similar stereoelectronic orbital control of both cyclopropane (C_2-C_4) and bridge (C_5-C_8) bond cleavage prompted by electrophilic attack on the cyclopropane ring of 3.



5



6



7

Thus an acid-promoted concerted fragmentation via transition state 6 would appear to be reasonable mechanistic alternative to Scheme I. In support of this suggestion exo ketone 7 was found to be stable to 46.6% sulfuric acid.[7] Further, the cycloheptene acid 2 was not observed as one of the cleavage products from 7 under more forcing conditions.

REFERENCES

1. (a) Support of this work by the National Science Foundation (Grants GP-9412 and GP-27411) is gratefully acknowledged.
(b) National Science Foundation Undergraduate Research Participant, summer 1969.

2. R.J. Warnett and D.M.S. Wheeler, Chem. Commun., 547 (1971) and references cited therein.

3. H. Hogeveen, C.F. Roobeek and H.C. Volger, Tetrahedron Lett., 221 (1972).

4. J. Mackiernan and M.A. Battiste, Abstracts of the 21st Southeastern Regional Meeting of the American Chemical Society, Richmond, Virginia, November 5-8, 1969, no. 202.

5. M.A. Battiste, C.L. Deyrup, R.E. Pincock, and J. Haywood-Farmer, J. Amer. Chem. Soc., 89, 1954 (1967); C.L. Deyrup, Ph.D. Dissertation, Boston University (1970).

6. B. Halton, M.A. Battiste, R. Rehberg, C.L. Deyrup, and M.E. Brennan, J. Amer. Chem. Soc., 89, 5964 (1967).

7. Unpublished results of Dr. C.C. Ong in these laboratories.