Tetrahedron Letters No. 22, pp. 989-992, 1962. Pergamon Press Ltd. Printed in Great Britain.

DISPROPORTIONATION IN ACID-CATALYZED KETONE REARRANGEMENTS[1]

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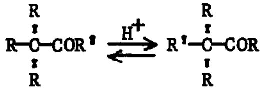
(Received 28 June 1962; in revised form 30 July 1962)

RESULTS of a number of recent studies[2] of acid-catalyzed ketone rearrangements can be rationalized on the basis of an intramolecular mechanism involving alkyl group shifts in the ketone conjugate acid carbonium ions (possibly in combination with oxygen shifts or reversible pinacol formation[3] where oxygen function rearrangement[4] is involved). The net result of these changes is the exchange of a group attached directly to the carbonyl carbon with a group attached to the alpha carbon on the other side of the carbonyl carbon:



$$\mathrm{R{-}\overset{R}{\underset{R}{C}}{-}COR'} \overset{H^+}{\rightleftharpoons} \mathrm{R'{-}\overset{R}{\underset{R}{C}}{-}COR}$$

Such acid-catalyzed rearrangements of ketones are quite general, but in the course of a detailed investigation of the formation of 2-pentanone

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[1] This work was supported by Atomic Energy Commission Contract AT-(40-1)-277.

[2] A. Fry, M. Eberhardt and I. Ookuni, J. Org. Chem. 25, 1252 (1960), and references mentioned there.

[3] T. S. Rothrock and A. Fry, J. Amer. Chem. Soc. 80, 4349 (1958).

[4] A. Fry, W. L. Carrick and C. T. Adams, J. Amer. Chem. Soc. 80, 4743 (1958); C. T. Davis and A. Fry, Chem. & Ind. (London) 277 (1960).

from 3-pentanone[5] and of the reactions of 2-butanone-1-C^{14} and unlabeled butanone, it became evident that an *additional or alternate mechanism* was in operation. Thus, upon treatment with perchloric acid, butanone forms acetone, 2-pentanone, 3-pentanone, 3-hexanone and a number of other as yet unidentified compounds. Similarly, 3-pentanone forms acetone, butanone, 2-pentanone, 3-hexanone and several unidentified compounds; acetone forms butanone, mesityl oxide and other compounds; 4-heptanone forms 3-hexanone, probably an octanone and other compounds. Clearly straight chain saturated ketones of molecular weight both higher and lower than the starting material are formed. *A disproportionation reaction must have taken place. These results cannot possibly be explained in terms of the mechanism mentioned above, or any other intramolecular mechanism.*

The ketones were stirred with 70% perchloric acid (10 g of ketone per 50 ml of acid) for appropriate times (one hr to 72 hr) at appropriate temperatures (room temperature to 100°). The reaction mixture was poured onto ice, and the solution was made basic with sodium hydroxide, saturated with sodium chloride and extracted with ether. After removal of the ether, the remaining volatile material was collected by distillation. Recovery of volatile material was essentially quantitative for short time low temperature experiments and ranged downward to a few percent (the rest being polymeric material) for high temperature long time experiments. The volatile material was analyzed by gas chromatography and preliminary identification of the various compounds was made by comparison of retention times with those of known compounds. Several columns of differing polarity were used, but most analyses were run on a 10' x 1/4" column of 20% triethylene glycol on firebrick.

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[5] A. Fry, I. Ookuni, G. J. Karabatsos, J. D. Graham and F. Vane, *J. Org. Chem.* **27**, 1914 (1962).

In the shortest time low temperature experiments, barely detectable amounts of rearrangement products were formed. As the conditions became more drastic, increasing amounts of rearrangement were found (up to 15% of 2-pentanone in 3-pentanone), but the amount of volatile material recovered decreased drastically. Nevertheless, in larger scale experiments on butanone, macro amounts of 3-hexanone (semicarbazone m.p. 110-12°, reported[6] m.p. 113°) and a 2-pentanone-3-pentanone fraction (shown by infra red comparison[5] with known mixtures to be 10% 3-pentanone-90% 2-pentanone) were isolated by preparative gas chromatography.

The butanone recovered after treatment of 2-butanone-1-C^{14} with 70% perchloric acid for 48 hr at 50° was degraded by the iodoform reaction. The molar activity of the iodoform obtained was only 95% of that of the starting material while that of the propionic acid (as the p-toluidide) was 5.0%. Obviously, the label rearranges away from the one position. Before separation of the butanone, holdback carriers of acetone, 2- and 3-pentanone and 3-hexanone were added. Subsequently, the acetone, the mixture of 2- and 3-pentanone, and the 3-hexanone were isolated by preparative gas chromatography and were shown to be radioactive.

The mechanism for this disproportionation reaction is not completely established, but the following aldol condensation-carbonium ion rearrangement working hypothesis is in accord with all of the facts known at this time. Here, if $R = CH_3$ and $R' = C_2H_5$, the starting material is 3-pentanone, and the disproportionation products are butanone and 3-hexanone. Other modes of condensation and alkyl group shifts would give other products, and the products formed in the first step could obviously condense again to give secondary products.

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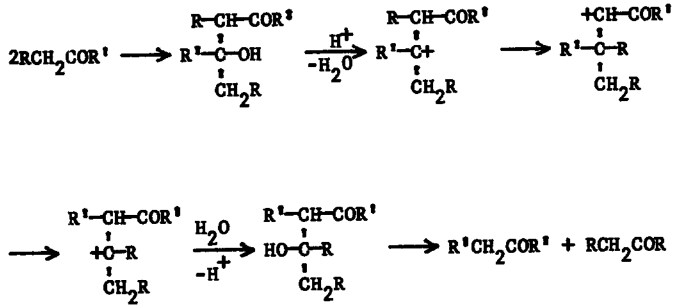
[6] C. D. Hodgman, Ed., "Tables for Identification of Organic Compounds", Chemical Rubber Publishing Company, Cleveland, Ohio, 1960.



These bimolecular ketone rearrangements bear a striking resemblance to the case of carbonium ion formation from alkyl halides where Karabatsos, Vane and Meyerson[7] have recently demonstrated the existance of a bimolecular path. Experiments are planned to test the above hypothesis and to investigate the relationships between the mechanisms given in the first paragraph and the disproportionation reaction.

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[7] G. J. Karabatsos, F. M. Vane and S. Meyerson, J. Amer. Chem. Soc. 83, 4297 (1961).