

A ROUTE TO ALDEHYDES AND KETONES BY A FOUR-ELECTRON
DECARBOXYLATIVE OXIDATION UTILIZING PYRIDINE N-OXIDE

Theodore Cohen, Il Hwan Song, and John H. Fager

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15213

(Received 3 December 1964)

One-electron (Kolbe reaction) and two-electron decarboxylative oxidations are well known reactions which have been of great mechanistic and synthetic interest. We now wish to report the discovery of a four-electron decarboxylative oxidation and to suggest a probable reaction path which involves the novel and potentially useful mechanistic concept of functionalization of the the α -position of a carboxylic acid by nucleophilic rather than electrophilic attack.



The reaction, which is shown for the case of phenylacetic acid, can be performed either on the anhydride or on a mixture of the corresponding acid with acetic anhydride. The oxidizing agent is pyridine N-oxide, two moles of which are consumed per mole of aldehyde or ketone formed. The yields in the oxidation of several acids in the refluxing solvents indicated (for 10-48 hrs.) are listed in the table. Carbon dioxide and pyridine are also formed. In the case of phenylacetic acid, a small quantity of diphenylmaleic anhydride (DPMA) is produced. Isobutyric and butyric anhydrides fail to react at an appreciable rate

in benzene and toluene, respectively. Very little carbon dioxide is produced under similar conditions from acetic anhydride (xylene), cyclohexanecarboxylic acid (toluene), cyclohexanedicarboxylic and glutaric anhydrides (diethyl Carbitol, b.p. 195°), and trimethylacetic anhydride (xylene).

TABLE I

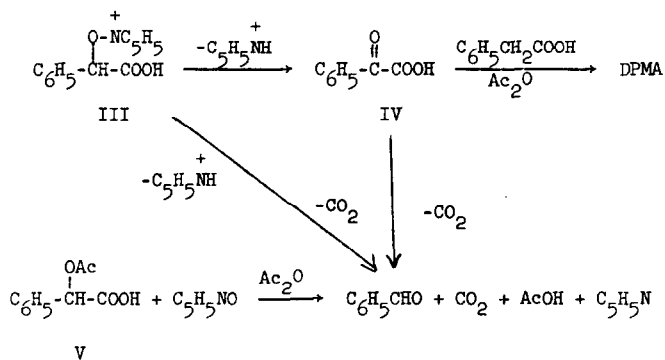
Reactions of Anhydrides and Acids with Pyridine N-Oxide

<u>Run</u>	<u>Anhydride or acid^a</u>	<u>Solvent</u>	<u>Products (% Yield)</u>
1	Phenylacetic anh.	Benzene	Benzaldehyde (60)
2	Phenylacetic acid ^b	Benzene	Benzaldehyde (68)
3	Diphenylacetic anh.	Benzene	Benzophenone (68)
4	Diphenylacetic acid ^b	Benzene	Benzophenone (62)
5	Isobutyric anh.	Toluene	Acetone (39)
6	Butyric anh.	Xylene	Propionaldehyde ^c (12.4)
7	Acetic anh.	Xylene	2-Acetoxy pyridine (d)

^aFour moles of pyridine N-oxide per mole of anhydride or acid was used. ^bAcetic anhydride (1.5 moles per mole of acid) was employed.

^cInfrared examination revealed the presence of an undetermined quantity of 2-pyridone. ^dNot determined.

The reactivity sequence indicated in the table could be interpreted as favoring a carbonium ion cleavage reaction of the initially formed N-acyloxy pyridinium ion, I, (dotted arrows)(1) followed by oxidation of the carbonium ion by pyridine N-oxide (2). However, militating against such a mechanism are the findings (a) that acetone could not be detected (v.p.c.) in run 6, (b) that benzyl phenylacetate was not



Further support for this mechanism has been obtained by the detection of the methyl esters of the proposed intermediates, IV (0.6-3%) and V (6.3-10.5%) in the esterified acid fractions of some of the product mixtures from the reaction of pyridine N-oxide with phenylacetic acid.

Further study of the synthetic and mechanistic implications of the several novel reactions reported here is now under way.

Acknowledgment. This work was supported by Contract AF 49(638)-788 and Grant AF-AFOSR 344-63 from the Air Force Office of Scientific Research of the U. S. Air Force and by Grant PRF-1788-A4 from the Petroleum Research Fund of the American Chemical Society.

References and Footnotes

1. An excellent analogy for this fragmentation is the acid catalyzed decomposition of certain diacylperoxides and peresters: P. D. Bartlett and J. E. Leffler, J. Am. Chem. Soc., 72, 3030 (1950); H. Hart and R. A. Cipriani, ibid., 84, 3697 (1962); C. Rüchardt and H. Swarzer, Angew. Chem., 74, 251 (1962).
2. W. Feely, W. L. Lehn and V. Boekelheide, J. Org. Chem., 22, 1135 (1957).
3. (a) The detection of 0.5% of this ester would have been possible. (b) However, this ester was detected by Rüchardt, Eichler and Krätz (4) under somewhat different reaction conditions. This presumably indicates that a carbonium ion fragmentation is not precluded under all conditions. (c) In a run in which the molar ratio of N-oxide to phenylacetic acid was 1.0 and in which a large excess of acetic acid and acetic anhydride was present, less than 0.15% of benzyl acetate (the reaction product of benzyl carbonium ions with acetic acid) was produced.
4. C. Rüchardt, S. Eichler and O. Krätz, Tetrahedron Letters, 4, 233 (1965)
5. (a) Small quantities (ca. 1%) of 2- and 4-benzylpyridine were, however, produced in this reaction. (b) See ref. 4 for other evidence against a radical reaction.
6. I. Lillien, J. Org. Chem., 29, 1631 (1964). However, several alternative paths for the production of III and V can also be envisioned.
7. The mechanistic implications of this novel decarboxylation will be discussed in a separate paper.