Tetrahedron Letters No.8, pp. 923-926, 1968. Pergamon Press. Printed in Great Britain.

UNEVEN DISTRIBUTION OF ^{18}O IN THE RESULTING ESTERS FORMED IN THE REACTION OF 2-PICOLINE, 2,6-LUTIDINE AND QUINALDINE N-OXIDE WITH ACETIC ANHYDRIDE.[1)]

S. Kozuka, S. Tamagaki, T. Negoro and S. Oae

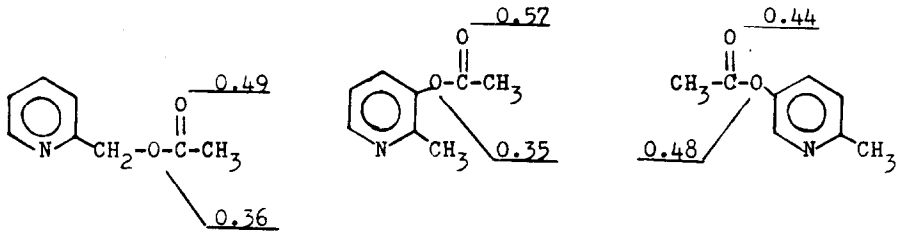
Department of Applied Chemistry, Faculty of Engineering
Osaka City University, Sugimoto-cho, Sumiyoshiku
Osaka, Japan

(Received in Japan 28 September 1967)

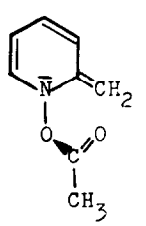
Earlier we have shown that 2-acetoxymethylpyridine, obtained by the reaction of 2-picoline N-oxide and ^{18}O labelled acetic anhydride, contained an excess ^{18}O concentration only as much as a half of that of the acetic anhydride applied while the excess ^{18}O was distributed nearly evenly on both carbonyl and etheral oxygens.[2)] We have noticed, however, that in no case the distribution of the excess ^{18}O was exactly even and attributed the anomaly to the technical loss during hydrolysis and the succeeding analysis.[3)] In fact, in the alkaline hydrolysis of 4-benxoyloxymethylquinoline, a small but noticeable loss of ^{18}O was found to be resulted in the hydrolyzed product i.e., lepidyl alcohol. We now have applied a better procedure to cleave the ester without any oxygen exchange that obscures the ^{18}O analytical results, namely, the reaction with phenylhydrazine to afford both 1-acetyl-2-phenylhydrazine and the corresponding alcohol. By analyzing the ^{18}O contents of the three components, i.e. the ester, 1-acetyl-2-phenylhydrazine and the alcohol, one can get accurate values of ^{18}O distributions on both carbonyl and etheral oxygens together with the range of the experimental error.

A crude ester obtained through a rough distillation is fractionated through GLC column into individual esters which were subjected separately to the cleavage reaction with phenylhydrazine. The reaction is complete in a few

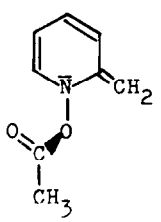
hours of gentle heating on a steam bath. 1-Acetyl-2-phenylhydrazine and the alcohol were isolated by fractional recrystallization from benzene. Alkaline hydrolysis was also employed to obtain the alcohol if it was difficult to isolate the alcohol by the above procedure. The ^{18}O content of these samples were analyzed by our modified Rittenberg-Pentecerlvo method. The ^{18}O distribution patterns of the esters obtained from the reaction of 2-picoline N-oxide with ^{18}O labelled acetic anhydride (^{18}O concentration = 0.92 excess atom %) are shown below:



One notices immediately that the excess ^{18}O is distributed unevenly in the two oxygens in the former two esters but not so much in the last one. This means that the recombination step, after the N-O bond cleavage, is fast that there is not enough time for acetoxy group to equilibrate and the oxygen atom that is relatively nearer to the methylenic carbon would have a better chance of combining together to be the etheral oxygen. These ^{18}O-distribution patterns can be explaind on the basis of conformational stability of the intermediate, anhydrobase. In the case of 2-picoline N-oxide, the prefered conformation would be Ib rather than Ia, because of the crowdness in the former conformer. Therefore, the oxygen atom originally combined to the nitrogen atom, being closer to both the methylenic carbon and the β-carbon will have a better chance



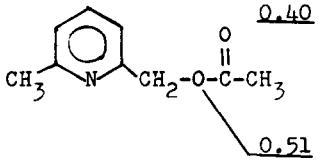
Ia

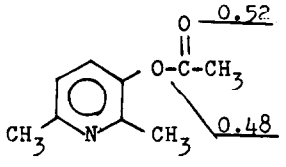


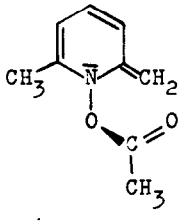
Ib

for recombination to become the etheral oxygen in both 2-acetoxymethylpyridine and 3-acetoxy-2-picoline, whereas both oxygens will have nearly equal chance of recombining with C-5 since the distances between position 5 and both oxygens would roughly be the same.

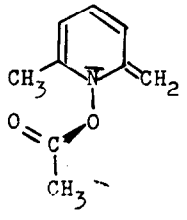
The plausibility of this hypothesis has been tested with other compounds. 2,6-Lutidine N-oxide gave both 2-acetoxymethyl-6-methylpyridine and 3-acetoxy-2,6-lutidine in the reaction with acetic anhydride. Here the prefered conformation of the anhydrobase is no longer IIb because of the steric crowdness due to 6-methyl group and the resulting 2-acetoxymethyl-6-methylpyridine contains more excess ^{18}O in the etheral oxygen atom than in the carbonyl. (Ac_2O^{18} ; excess 0.91 atom %)





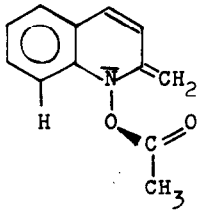


IIa

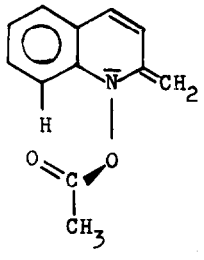


IIb

Apparently IIa is the more favorable conformer in this case. In the case of quinaldine N-oxide one would expect the conformer IIIa to have nearly equal stability as the other conformer IIIb due to the similar magnitude of steric interactions between acetoxy group with peri-hydrogen and with methylenic hydrogen.

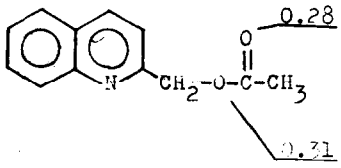


IIIa



IIIb

In fact, the resulting 2-acetoxymethylquinoline was found to contain the nearly same concentration of an excess ^{18}O in both the ether-oxygen and the carbonyl group, as shown below : (Ac_2O^{18} ; excess 0.67 atom %)



All these patterns of O^{18} distributions, the intramolecular nature of the rearrangement, together with the kinetic data, reported in the previous paper, suggest that both the cleavage of the N-O bond and the succeeding recombination are very rapid as compared to the 1st equilibrium and the succeeding deprotonation.

REFERENCES

1) Paper XX on Rearrangement of Tertiary Amine N-oxide.

2) S. Oae, T. Kitao and Y. Kitaoka, J. Am. Chem. Soc., 84 3359 (1962)

3) S. Oae, Y. Kitaoka and T. Kitao, Tetrahedron, 20 2685 (1964