Tetrahedron Letters No.35, pp. 3117-3120, 1970. Pergamon Press. Printed in Great Britain.

CIDNP IN THE REACTION OF 2-PICOLINE N-OXIDE WITH ACETIC ANHYDRIDE

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(Received in Japan 10th June 1970; received in U.K. for publication 30th June 1970)

The mechanism of the reaction of 2-picoline N-oxide (I) with acetic anhydride to give 2-acetoxymethylpyridine (II) has been a subject of controversy.[1] On the basis of the observation that efficient ^{18}O scrambling between the two oxygen atoms in II was encountered when the reaction was started with natural I and ^{18}O-enriched acetic anhydride, Oae and co-workers[2] concluded the free radical pair mechanism in a solvent cage. Although the system has indeed been known to initiate the free radical polymerization of styrene,[3] the mechanism has been questioned by failure of the quenching of the rearrangement with such efficient free radical scavengers as DPPH, p-benzoquinone and m-nitrobenzene.[4] Furthermore it has recently been shown that, just as in 1,5-dienes, the [3,3]-sigmatropic shift is still the most favorable route in heteroatomic rearrangements.[5,6] In acetyl peroxide, for example, [3,3]-sigmatropic shift predominates over [1,3]-shift and homolytic cleavage, in scrambling the oxygen atoms.[7] Even [1,3]-sigmatropic rearrangement has been shown to be operative in acyl peroxides.[8]

In view of these findings, it seemed intriguing to reconsider the possible role of the sigmatropic mechanism for the rearrangement of I to give II. As an operational test, attempt was made to detect the intervention of a free radical pair by observing the chemically induced dynamic nuclear polarization[9] in the nmr spectrum of II in the reacting mixture of I with acetic anhydride.

In a typical run, 130 mg of I was mixed with 300 μl of acetic anhydride in the presence of 50 mg of benzene serving as an internal lock and as a diluent of the reaction, degassed and sealed in an nmr sample tube. At room temperature there were observed two singlet peaks at 2.33 and 1.95 ppm corresponding to the 2-methyl protons of I and those of acetic anhydride, respectively. As soon as the sample was introduced in the nmr probe which had been heated at 90°, a pair of intense emission lines appeared at 3.44 and 0.70 ppm (Figure 1). The amplitude reached their maximum (negative) at 130 and 160 sec, respectively, after the start of the reaction, and decayed as shown in Figure 2. The progress of the rearrangement could be followed by decrease in the 2.33 ppm peak as well as growth of the methylene proton signal at 5.12 ppm of II.

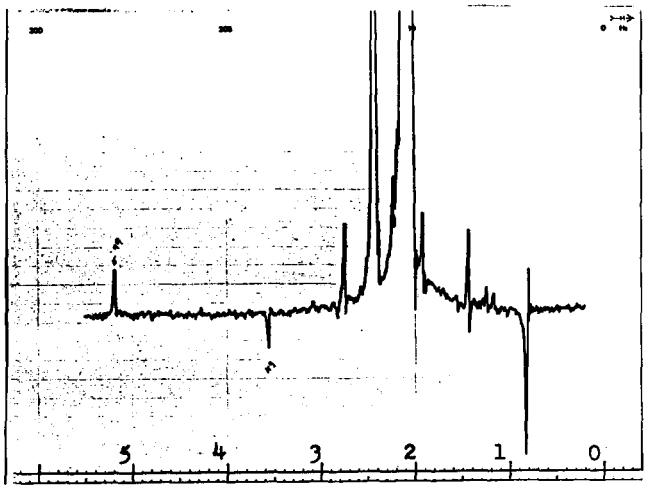

Figure 1. 100-MHz nmr spectrum of the reacting mixture of I with acetic anhydride at 90°. Since the sweep time was set at 250 sec (for 1000 Hz), the signals at 5.12, 3.44 and 0.70 ppm were scanned at 77, 119 and 187 sec after the start of the reaction.

By comparison with the spectra of the authentic samples, the emission was found to have nothing to do with II but owe their origin to the O-methyl protons (3.44 ppm) of methyl acetate and those of ethane (0.70 ppm). The latters are known and have now been confirmed to be formed as the by-products of the rearrangement in ca. 1 % yield. Since the development of the nmr polarization is critically dependent on the rate of radical formation and the spin-lattice relaxation time of the protons concerned,[9] the reaction was scrutinized at several temperatures between 70 and 130°. Under no circumstances was observed

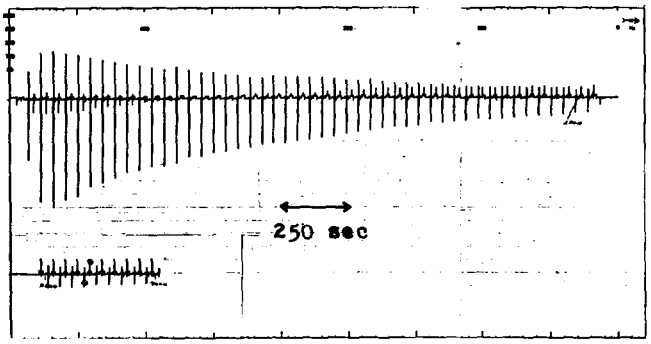

Figure 2. Time dependence of the amplitude of the emission lines. While the 3.44 ppm emission changed its sign at 800 sec of the reaction, the signal at 0.70 ppm was emitting even after 5000 sec.

any sign of either emission or enhanced absorption for the spectrum of II. The aromatic region of the spectra was explored in another run with 150 mg of I and 150 μl of acetic anhydride in 400 μl of 1,1,2,2-tetrachloroethane. No polarization was observed throughout the reaction.

Thus the rearrangement does not appear to proceed through the free radical pair mechanism, although acetoxyl radicals were confirmed to be actually formed during the reaction. The present findings together with the already established ^{18}O-scrambling[2] and intramolecularity of the rearrangement,[4] imply that [1,3]- and/or [3,3]-sigmatropic shift of the acetoxyl group may possibly be playing the role. It might be argued that the cage reaction must be exceptionally fast and that there might be no chance for the nuclear spin polarization to develop because of the tight singlet spin correlation between the two components of the radical pair. Empirically, however, CIDNP has been observed even for some Stevens and the related rearrangements[9] in which it is rather difficult to see a free radical character escaping from the solvent cage.

Experiments are in progress to determine whether a) [1,3]-sigmatropic shift of the nitrogen atom between the two oxygen atoms of the acetoxyl group before $N \rightarrow C_\alpha$ migration, or b) a competitive [1,3]- and [3,3]-sigmatropic rearrangement of the intermediate anhydro base is operative.

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