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OXYGEN TRANSFER REACTIONS OF AROMATIC AMINE N-OXIDES

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Two reports (1,2) have recently appeared dealing with the reactions of aromatic amine N-oxides with phenylacetic anhydrides. We have also independently observed this reaction which stoichiometrically involves two equivalents of the N-oxide to one of the anhydride and which gives two equivalents of the corresponding amine and one each of carbon dioxide, phenylacetic acid and benzaldehyde as products. The reaction proceeds readily with both pyridine N-oxide and 4-picoline N-oxide but only to a minor extent with 2-picoline N-oxide (3). Benzaldehyde and carbon dioxide were formed in high yields (greater than 60%) in both of the former cases.

We have measured the kinetic dependence of the reaction of 4-picoline N-oxide with phenylacetic anhydride in acetonitrile with varying amounts of added phenylacetic acid. The data are summarized in Table I. The rates were followed by the decrease in infrared carbonyl adsorption of the anhydride. Linear rate plots for 60% reaction are obtained using the integrated rate expression corresponding to eq. 1.

TABLE I

Kinetics of the Reaction of 4-Picoline N-Oxide with Phenylacetic Anhydride at 75.4° in Acetonitrile[a]

Run	Acid Conc.[b]	$k \times 10^4$ sec^{-1}	t/2 min.
1	0	2.67	9.5
2	0.046 M	2.75	23
3	0.104 M	2.75	40
4	0.115 M[c]	3.60	
5	0.202 M	2.68	72

a) All runs initially 0.10 M in anhydride and 0.20 M in N-oxide. b) Initial phenylacetic acid concentration. c) 0.114 M pyridine added.

$$\frac{-d(\text{Anhydride})}{dt} = k\,\frac{(\text{N-Oxide})\,(\text{Anhydride})}{(\text{Acid})} \qquad (1)$$

A typical rate plot is shown in FIG. 1. The rate plots show a marked upward curvature after 60% reaction. Addition of pyridine at the beginning of the reaction produces an increase of about 30% in the apparent rate constant obtained from the first 60% reaction. These effects are probably a result of base catalysis by the amine product which is not important in the initial stages of the reaction.

The integrated form of eq. 1 predicts an inverse correlation of half time for reaction (t/2) with initial phenylacetic acid concentration. This correlation was verified experimentally as shown in FIG. 2. The slope of the line relating half time of the reaction to initial acid concentration gives another measure of the rate constant

FIG. 1

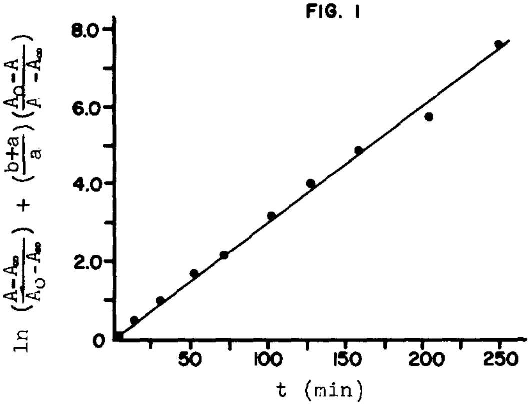


Figure 1. Kinetic plot of the reaction of 4-picoline N-oxide with phenylacetic anhydride in acetonitrile at 75.5° C. Initial N-oxide concentration equals twice the initial anhydride concentration (a) of 0.100 M. Initial phenylacetic acid concentration (b) is 0.202 M. A is infrared absorbance at 1815 cm^{-1}.

FIG. 2

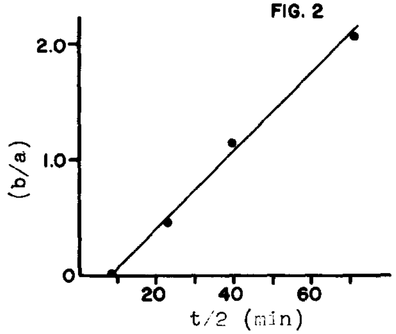
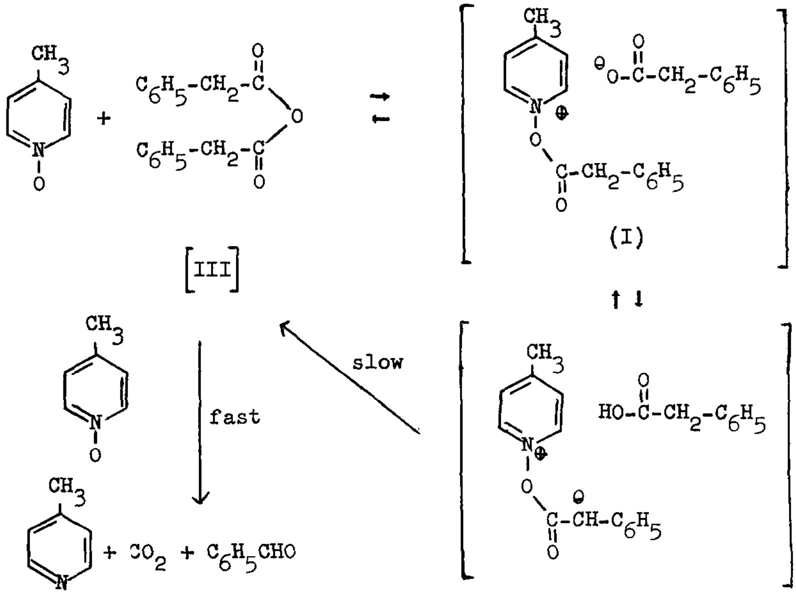


Figure 2. Correlation of observed half time (t/2) for the reaction of 4-picoline N-oxide with initial phenylacetic anhydride (a) and phenylacetic acid (b) concentrations.

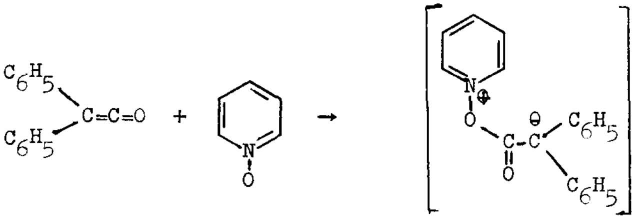
for the reaction which is in agreement with that found in the individual rate runs. A mechanistic sequence which is consistant with this rate expression is shown below.



The first equilibrium in this sequence is proposed by analogy with other pyridine N-oxide anhydride reactions (4). The observed inverse order in carboxylic acid indicates that the acid is formed reversibly prior to the rate determining step. When phenylacetic anhydride which contained 1.42 deuterium atoms per molecule (in the α-position) was allowed to react with pyridine N-oxide in acetonitrile the resulting benzaldehyde contained 0.35 deuterium atom per molecule in the aldehyde position. The product phenylacetic acid contained 1.10 deuterium atoms per molecule in the α-position.

These observations are consistant with reversible removable of the proton or deuteron from the α carbon of N-phenacyloxypyridinium ion (I) as shown.

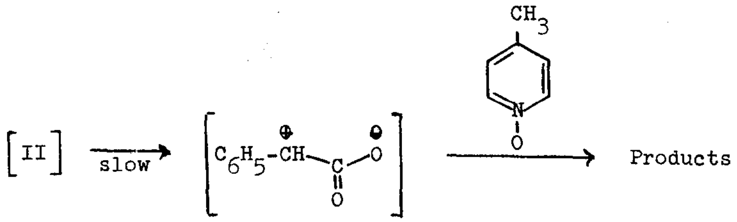
When pyridine N-oxide is added to a benzene solution of diphenylketene an exothermic reaction occurs and carbon dioxide is given off in 85% yield. Benzophenone is also formed in 45% yield (by g.l.c. and quantitative infrared). Some tetraphenylethylene was present in undetermined amount. The ketene might be expected to react with the N-oxide to give a zwitterion corresponding to II. The observation of a fairly high conversion of the ketene to benzophenone and the deuterium labeling experiments seem to support the intervention of zwitterions such as II or IIa as a type of intermediate common to both reactions.



IIa

The overall first order dependence of the rate of the reaction on N-oxide concentration indicates that the second mole of this reactant, demanded stoichiometrically, is involved after the rate determining step. This implies some other intermediate (III) intervenes between II and products. When the reaction is carried out in the presence of styrene or ethyl vinyl ether no cyclopropane products were found. This together with the reported (5) reluctance of carbene intermediates to deoxygenate N-oxides seems to rule against decarboxylative decomposition of the zwitterion (II) to give the carbene species.

Two electron transfer either through the π system or by intramolecular nucleophilic displacement on oxygen could give rise to a dipolar α-lactone as the missing intermediate. Such a species would be expected to react rapidly with a second mole of the N-oxide to give the observed products.



(III)

Our initial attempts at trapping the α-lactone have not been successful. The reported (1) isolation of α-acetoxyphenylacetic acid from the reaction when it is carried out in acetic anhydride might be a result of such a trapping process. The report (2) that *p*-nitrophenylacetic anhydride is more reactive than the corresponding *p*-methoxy compound is in good accord with the sequence proposed here. The observed inverse order of the reaction in acid concentration is not consistant with the other mechanisms which have been proposed for this reaction (1,2).

We have also (2) observed formation of benzhydryl diphenylacetate from slow addition of pyridine N-oxide to a refluxing solution of diphenylacetic anhydride. This product could arise from a carboxy inversion similar to that observed in a number of peroxide **decompositions** (6). This process bears a marked similarity to α-lactone formation proposed here. We are continuing our studies of these and related reactions.

Acknowledgement

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