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ON THE MECHANISM OF THE PSCHORR CYCLIZATION

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Strong evidence has been presented (1) for the occurrence of an S_N1 mode of decomposition (2) in the uncatalyzed Pschorr cyclization in aqueous acid solution. On the other hand, the copper catalyzed reaction is thought to involve a homolytic mechanism (3,4,5). The simultaneous occurrence of both homolytic and heterolytic modes of cyclization in some cases has also been suggested (1,3). The only kinetic work carried out (1) measures the influence of substituents upon the rate-determining C-N bond cleavage, and not upon the ease of the subsequent ring closure. Recent work (6) raises strong doubts that a straightforward electrophilic attack is actually taking place in the uncatalyzed cyclizations. Two approaches are described here which attempt to distinguish between a homolytic and heterolytic mechanism for the cyclization. This represents the first report of a measure of the effect of substituents upon the actual rate of cyclization.

Attack by electrophilic reagents upon a pyridine (and more so a pyridinium) ring is very difficult e.g. the Friedel-Crafts reaction does not take place with pyridine. Conclusions based on the cyclization of 2-amino-N-methyl-N-3'-pyridylaniline (4) might be weakened by the fact that in this compound the pyridine ring bears an electron-donating amino-group. The cyclization of 3-(2'-aminobenzoyl)pyridine (I) under various conditions does not suffer from this ambiguity. The results are summarized in Table I. The cyclization catalyzed by ultraviolet light, as well as the copper catalyzed one, undoubtedly involve a homolytic process. The low yield of

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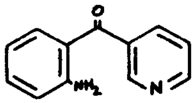
TABLE I

Decomposition of Diazotized 3-(2'-Aminobenzoyl)pyridine (I)
in Aqueous Acid Solution

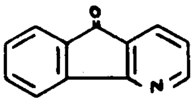
			% Yield of Products*				
Method of decomp.	Reaction temp.	Reaction time	4-Aza-fluorenone (II)	2-Aza-fluorenone (III)	3-Benzoyl-pyridine	Phenol**	Other
Thermal	80°	2 hr.	3.5	2.9	0	67	
Gattermann copper	4°	20 min.	30.3	19.5	13.0	10	
Ultraviolet light	30°	1 hr.	36.8	26.2	0	0	
Silver powder	4°, then r.t.	48 hr.	2.2	1.6	11.1	-	Dimer(?)
Iron filings	4°, then r.t.	42 hr.	4.8	2.5	22	-	Dimer(?) Azo-Compd.(?)
Zinc dust	4°	6 hr.	16.3	9.3	15.4	-	
Thermal (aq. NaOH)	40°	4 hr.	9.4	4.0	3.2	0	Dimer(?) Azo-Compd.(?)

* Estimated gas chromatographically.

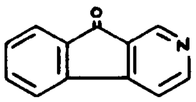
** Estimated by isolating and weighing the product; a dash means that phenol was not estimated. Calc. for $C_{10}H_9NO_2$: C, 72.35; H, 4.55. Found: C, 72.36; H, 4.63.



I



II



III

cyclized products in the thermal decomposition does not permit an unambiguous decision concerning the mechanism of the cyclization. That any cyclization has occurred at all, under these relatively mild conditions, upon a pyridine ring bearing, as well, a carbonyl function and in acid solution speaks against an attack by a cation. The results will be discussed in detail in the full paper.

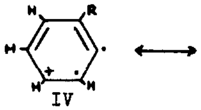
The relative rates of cyclization upon a phenyl and nitrophenyl nucleus have been estimated semi-quantitatively using a "competitive-like" technique. For two consecutive first order reactions of the type

$$A \rightarrow B^{+} \begin{array}{l} \xrightarrow{k_c} C \\ \xrightarrow[k_p]{} P \end{array}$$

in which the formation of the carbonium ion B^{+} is rate-determining it can be shown that $\frac{k_{CN}}{k_{CH}} = \frac{C_N}{P_N} \cdot \frac{P_H}{C_H} \cdot \frac{k_{PN}}{k_{PH}}$ where k_{CH} and k_{CN} are the rate constants for the cyclization of the intermediate carbonium ion onto unsubstituted and nitro-substituted phenyl, respectively, k_{PH} and k_{PN} are the corresponding rate constants for the formation of the two phenols at any moment during the reaction. Such a "competitive" cyclization of diazotized 2-amino- and 2-amino-3'-nitrobenzophenone has been carried out at 45° and the amounts of fluorenone (C_H), 2- and 4-nitrofluorenone (C_N), 2-hydroxy- (P_H) and 2-hydroxy-3'-nitrobenzophenone (P_N) at various intervals of time estimated simultaneously by gas chromatography. The average values of C_H/P_H and C_N/P_N thus obtained were 2.58 and 1.15, respectively. If it is assumed (as it seems reasonable to do since the nitro-group in the <u>meta</u>

position in another ring not in direct conjugation with the first would be expected to have only a slight effect upon the stability and reactivity of the phenyl cation) that the nitro-group has little effect on the rate of the hydroxylation reaction once the cation is formed *i.e.* $k_{PN}/k_{PH} \sim 1$, then $k_{CN}/k_{CH} = 0.45$: the phenyl nucleus is attacked only twice as fast as the nitrophenyl nucleus. Any influence the nitro-group might have would be in the direction of making k_{PN}/k_{PH} larger and hence make the ratio k_{CN}/k_{CH} larger as well, thus strengthening the argument which follows.

The concept of a highly reactive and non-discriminating carbonium ion (1) to explain the above results is not favoured. These and previous observations are best interpreted in terms of the formation of a diradical cation intermediate (IV) in the uncatalyzed Pschorr cyclization. The participation of structures such as (IV) in the transition state has already been postulated (7) to explain some aspects of the thermal decomposition of diazonium salts in aqueous solution and direct evidence for the intervention of radicals (of undetermined structure) in the uncatalyzed thermal decomposition of diazonium salts has been given (8). (IV) would behave like a strongly electrophilic radical, which is consistent with the present results and, as well, would possibly resolve the controversy concerning the mechanism of the demethylation and deamination observed in some cases (9).



other canonical structures

IV

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