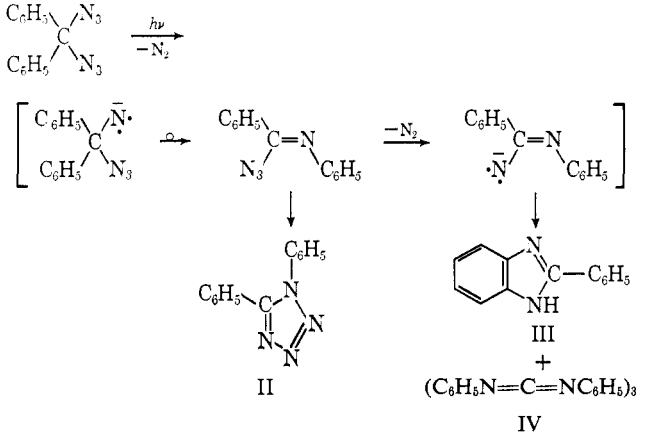
mediates drawn below in brackets, the following steps appeared to occur.

$$\text{diazide} \xrightarrow[-N_2]{h\nu} [\text{azidonitrene} \longrightarrow \text{iminoazide}] \longrightarrow$$

$$\text{1,5-disubstituted tetrazole} \xrightarrow[-N_2]{h\nu} [\text{iminonitrene}] \longrightarrow \text{products}$$

Recently Barash and co-workers reported epr evidence for the intermediacy of the azidonitrene in the photosensitized decomposition of benzophenone diazide (I) in a rigid matrix at 77°K.[2] Furthermore, they report that continued irradiation with light of wavelength 3650 A produced diphenylmethylene which was identified by observation of its epr spectrum. It should be noted, however, that 1,2-carbon-to-nitrogen migration of a phenyl group at the azidonitrene stage would yield an intermediate which *could not be* transformed to diphenylmethylene by any reasonable process. From this viewpoint, the benzophenone diazide system appeared to be a particularly interesting one for the purpose of comparing the course of a photochemical decomposition occurring in a rigid matrix relative to that in dilute fluid solution.

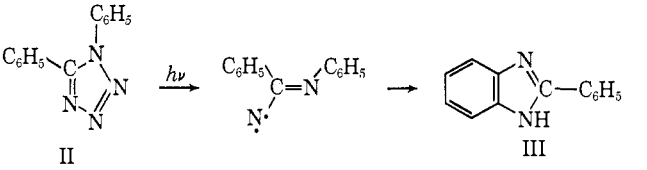
Irradiation[3] of 0.005 mole of benzophenone diazide[4] in 1% benzene solution for 8 hr yielded 2-phenylbenzimidazole (III),[5] 52%, 1,5-diphenyltetrazole (II),[6] 14%, N,N-diphenylcarbodiimide trimer (IV),[5] 10%, along with three unidentified products isolated in minor amounts.



II III + $(C_6H_5N{=}C{=}NC_6H_5)_3$ IV

The fact that 1,5-diphenyltetrazole (II) was obtained in the photolysis of I prompted the consideration that III and IV might result from photolysis of preformed II. This was shown not to be the case, however, since irradiation of 0.0033 mole of 1,5-diphenyltetrazole (II) (an amount equivalent to the 1,5-diphenyltetrazole (II) and 2-phenylbenzimidazole (III) produced in the photolysis of I under the same conditions) gave 0.0014 mole of 2-phenylbenzimidazole (III) in 42% yield as the sole product.[7]

It is important to note that no N,N-diphenylcarbodiimide trimer (IV) is formed in the photolysis of II. This result would tend to indicate some difference in the nature of the iminonitrene formed in the photolysis of I compared with the same intermediate which is presumed to be formed in the photolysis of II.



II III

Finally it is clear that a fundamental difference exists between the results obtained in the epr study[2] and those we have found in the fluid solution photolysis of I. The essential difference is that no major products derive from diphenylmethylene in the photolysis of I in dilute benzene solution. Assuming that diphenylmethylene is a major product in the epr study,[2] one must offer an explanation as to why the azidonitrene derived from photolysis of I in a rigid matrix does not undergo phenyl group migration but rather loses two additional molecules of nitrogen to yield the carbene.

It appears most likely that the triplet azidonitrene obtained in the rigid matrix at 77°K very quickly loses any excess vibrational energy which may be required for the phenyl group migration. In benzene solution at room temperature a higher energy azidonitrene occurs which is capable of undergoing chemical reaction, namely, phenyl group migration, before it is deactivated to a ground-state molecule. Furthermore, the required orientation of the phenyl group with respect to the electron-deficient nitrogen may not obtain in the case of an azidonitrene locked in a rigid matrix. Also, the possibility cannot be excluded that the direct photolysis in benzene solution produces a singlet azidonitrene which may react differently from the triplet species. As far as products are concerned, the above results indicate clearly that the subsequent reactions of photochemically generated intermediates, such as azidonitrenes and iminonitrenes, depend strongly upon the mode of formation and environmental factors.

(2) L. Barash, E. Wasserman, and W. A. Yager, *J. Am. Chem. Soc.*, **89**, 3932 (1967).

(3) A Hanau high-pressure (Q81, 0.5 w at 2800 A) immersion lamp surrounded by a quartz water-cooled heat exchanger was placed directly into the solution to be irradiated.

(4) Benzophenone diazide was prepared according to the method of S. Götzky, *Ber.*, **64**, 1555 (1931). This compound is dangerous and may detonate upon shock or heat. Never should samples larger than 100 mg be handled.

(5) P. A. S. Smith and E. Leon, *J. Am. Chem. Soc.*, **80**, 4647 (1958). These workers carried out the thermal decomposition of benzophenone diazide and obtained diphenyltetrazole. Thermal decomposition of diphenyltetrazole yields the carbodiimide trimer and 2-phenylbenzimidazole.

(6) E. K. Harvill, R. H. Herbst, E. C. Schreiner, and C. W. Roberts, *J. Org. Chem.*, **15**, 662 (1950).

(7) A similar result has already been reported: W. Kirmse, *Angew. Chem.*, 71, 537 (1959).

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Intramolecular Nucleophilic Catalysis of Ester Hydrolysis by the Carboxylate Group

Sir:

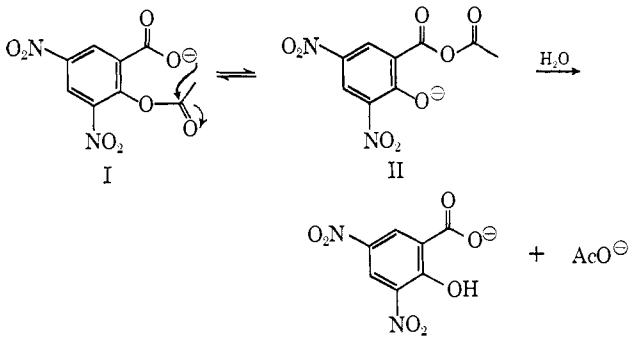
We have shown recently that the carboxylate group of aspirin anion is involved in the hydrolysis of the neighboring ester group not as a nucleophile but as a general base.[1] We now report an authentic example of

(1) A. R. Fersht and A. J. Kirby, *J. Am. Chem. Soc.*, **89**, 4853, 4857 (1967).

intramolecular nucleophilic catalysis in the hydrolysis of a substituted aspirin.

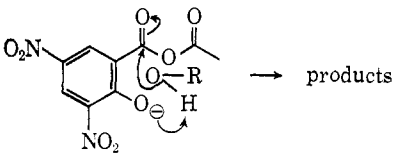
The carboxylate group of aspirin is not an effective nucleophilic catalyst because it is too weakly basic.[1] Gold has shown[2] that acetate ion does not catalyze the hydrolysis of substituted phenyl acetates by the nucleophilic mechanism if the leaving group is more than 3–4 pK units more basic than the catalyst. Other things being equal, the mechanism is determined by the difference in basicity between the nucleophile and the leaving group.

By an appropriate choice of substituents it is possible to lower the basicity of the leaving group of aspirin relative to that of the carboxyl group. The two nitro groups of 3,5-dinitro-aspirin (I), for example, would be expected to lower the pK_a of the carboxyl group by about $2\sigma_m$ = 1.4 pK units, whereas two nitro groups *ortho* and *para* to phenolic OH lower its pK_a by some 6 units. We find that the change in the relative basicities of nucleophile and leaving group is sufficient to change the mechanism to nucleophilic catalysis in the hydrolysis of 3,5-dinitro-aspirin.[3]



In the pH-independent region above pH 3[4] this ester is hydrolyzed in $H_2{}^{18}O$ at 39° with over 40% incorporation of labeled oxygen into the salicylic acid produced. On solvolysis in 50% aqueous methanol in this pH region the major product is methyl 3,5-dinitrosalicylate,[5] which is produced in 60 ± 2% yield[6] and can be isolated in 56% yield. It is evident that the anhydride II is an intermediate and lies on the major reaction pathway.

Further kinetic data suggest that the nucleophilic reaction I → II is not the slow step of the reaction. The relative rates of solvolysis in various methanol–water mixtures, and in light and heavy water (k_H/k_D = 2.0), and the entropy of activation (−20.6 eu) are all similar to those observed for the hydrolysis of aspirin anion and are not consistent with rate-determining nucleophilic attack. We consider that the reaction is best described in terms of a rapid preequilibrium formation of the anhydride anion II, in very low concentration. This is then hydrolyzed by rate-determining attack of a molecule of water on the salicyloyl carbonyl group, in a reaction which very probably involves intramolecular general base catalysis by the phenolate oxygen.[7]



(2) D. G. Oakenfull, T. Riley, and V. Gold, *Chem. Commun.*, 385 (1966).
(3) Prepared by the method of G. Ciampa, *Ann. Chim.* (Rome), 54, 975 (1964).
(4) A. R. Fersht and A. J. Kirby, *J. Am. Chem. Soc.*, 89, 5961 (1967).
(5) The product had identical melting point, mixture melting point, and infrared spectrum as an authentic sample (mp 128–129°; T. Zincke, *J. Prakt. Chem.*, [2] 82, 23 (1910), reports mp 129°).
(6) Estimated spectrophotometrically. No methyl salicylate is produced on solvolysis of aspirin under these conditions.
(7) Ample precedent for this mechanism exists in work on the hydrolysis of substituted phenyl salicylates, by M. L. Bender, F. J. Kézdy, and B. Zerner, *J. Am. Chem. Soc.*, 85, 3017 (1963), and B. Capon and B. C. Ghosh, *J. Chem. Soc., Sect. B*, 472 (1966).

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Intramolecular General Acid Catalysis of Ester Hydrolysis by the Carboxylic Acid Group

Sir:

We have reported cases in which the carboxylate anion catalyzes the hydrolysis of a neighboring ester group by acting as a nucleophile[1] and a general base.[2] A third possible role for the carboxyl group in enzymic catalysis is that of a general acid. We report here an example of intramolecular catalysis of ester hydrolysis by the carboxylic acid group which appears to involve this mechanism.

The pH–rate profile for the hydrolysis of 3,5-dinitro-aspirin (see Figure 1) shows two pH-independent regions and differs strikingly from that of aspirin itself[3]

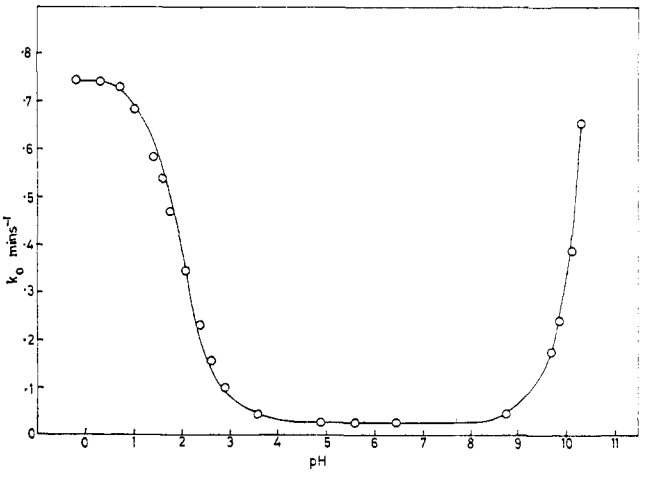

Figure 1. pH–rate profile for hydrolysis of acetyl-3,5-dinitrosalicylic acid at 39°, ionic strength 1.0.

in that the free acid is considerably more reactive (by 28 times) than the anion. The hydrolysis of the anion is subject to intramolecular nucleophilic catalysis by the carboxylate group,[1] so that the faster hydrolysis of the neutral species must be a result of catalysis also.[4] The pH–rate profile shows that this catalysis depends on a

(1) A. R. Fersht and A. J. Kirby, *J. Am. Chem. Soc.*, 89, 5960 (1967).
(2) A. R. Fersht and A. J. Kirby, *ibid.*, 89, 4857 (1967).
(3) L. J. Edwards, *Trans. Faraday Soc.*, 46, 723 (1950).
(4) Our preliminary results show that the methyl ester of 3,5-dinitro-aspirin is hydrolyzed over 200 times more slowly than the free acid.