The Effect of pH on the Course
of the Photoreaction of 2,4-Pyridinedicarbonitrile
with Benzophenone in Aqueous 2 Propanol: Reduction vs Substitution.

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The photoinitiated reactions of 2,4-pyridinedicarbonitrile (1) and benzophenone in neutral, acidic, and basic 3:1 2-propanol-water and the kinetics of disappearance of 1, have been studied. Pyridinyl radical anion forms as an intermediate by an electron transfer. In acidic solution substitution of the cyano group in the 2 position and in the 2 and 4 positions with diphenylmethanol occurs. In neutral medium both substitution at the 2-position and reduction, in which the cyano group at the 4 position is replaced by hydrogen, are observed. In basic solution in which protonation of the radical anion is not likely, only reduction occurs. The rates of formation and relative yields of these products depends on the pH of the solution. A mechanism is discussed.

The photochemistry of six-membered monoazaaromatic heterocycles has been the subject of extensive investigations by us and by others [1]. The photochemical reactions of these bases are strongly dependent on both the solvent in which the reaction is carried out and on the substituents attached to the heterocyclic ring. A few years ago, we reported that the rate of formation of pyridinyl radical 2 from 2,4-pyridinedicarbonitrile (1) depends not only on the factors stated above, but on the pH of the solution as well (Equation 1) [2]. We proposed a mechanism that requires a simultaneous electron transfer from a molecule of alcohol to the triplet state of the heteroaromatic base and protonation of the nitrogen. The presence of benzophenone greatly increases the rate of formation of 2.


1

(1)

2
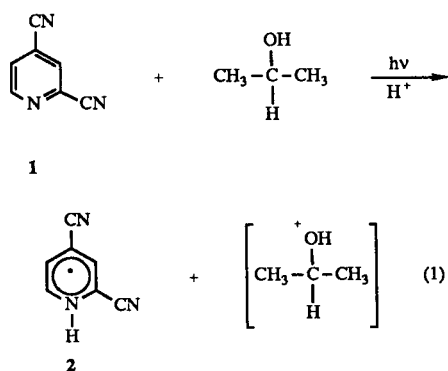
We have extended this work and now report the results of a study concerning the products obtained when 1 is irradiated in the presence of benzophenone at different pH's and on the rate of disappearance of this base under the different experimental conditions. Since the triplet states of 1 (71 kcal/mole) [2] and benzophenone (69 kcal/mole) lie close together, neither completely quenches the other and each participates in its own photochemistry. However, since the irradiations are carried out at 350 nm, most of the incident light is absorbed by the ketone which then in part transfers its energy to 1 in the ground state. Photochemical processes then follow leading to the formation of pyridinyl and diphenyl ketyl radicals.

When a solution of 1 in 3:1 (v/v) 2-propanol/water, buffered at pH 12, is irradiated at 350 nm, only 2-pyridine-carbonitrile (3) can be isolated from the reaction mixture. However, when this reaction is carried out in neutral solution, both 3 and 2-(α-hydroxydiphenylmethyl)pyridine (4) are obtained. If the reaction is repeated in acidic medium at pH = 3.5, the products formed depend on the irradiation time. At an irradiation time of 16 minutes 4 is the only product obtained, while at 120 minutes, 2,4-bis(α-hydroxydiphenylmethyl)pyridine (5) becomes the major product. The bis product is shown to form from 4 under the same experimental conditions as were used to form 5. It should be noted that benzophenone is recovered from all reaction mixtures, and benzopinacol is formed only at high conversion when the presence of 1 in the solution is greatly reduced.

It is important to stress that while in acidic medium mono and/or disubstitution of the cyano groups with diphenyl ketyl are the only reactions which occur, these reactions are completely suppressed in basic medium in which only decyanation is observed with the formation of the reduced product 3. In basic solution the radical anion

3

4
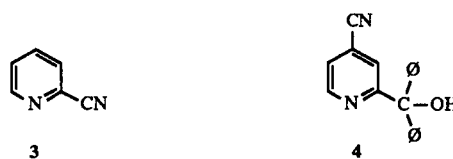
is not protonated and since the only product isolated from reactions run in basic medium is the reduced product, it may be concluded that the radical anion is the intermediate required for the elimination process.

With regard to the formation of the radical anion, we have reported that electron transfer from an alcohol to the triplet state of an unprotonated base is energetically unfavorable [2]. This indicates that a radical anion cannot form in basic solution by an electron transfer involving the alcohol as the electron donor. When benzophenone is present in these reaction mixtures, results have shown that even when benzopinacol is not formed that diphenyl ketyl does have a transient existance [3] and disappears by electron transfer to 1, thereby forming the radical anion. Evidence for this conclusion is found in the fact that electron transfer occurs readily from thermally generated dipenyl ketyl to 1 [4].

Once the radical anion forms, further reaction with ketyl results in substitution at the 2 position of 1. The highest spin density in the 2,4-dicyanopyridinyl radical resides at position 4, so that substitution cannot occur through a coupling reaction involving out-of-cage radicals, since this would result in initial substitution at position 4. The regiospecificity observed may be explained by a cyclic transition state in which the ketyl O-H hydrogen bonds to the ring nitrogen thus maintaining the ketyl group in a proper geometry for bonding at the 2 position as shown in structure 6 of Equation (2) [4].
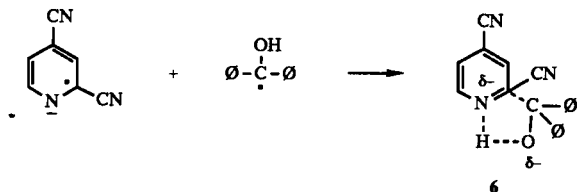
In summary, the course of these reactions depends on the acidity of the medium. At acidic pH's the radical anion is stabilized either by protonation yielding the pyridinyl radical or by coordination with ketyl yielding only substitution at the 2 position. The conversion of complex 6 to a dihydro intermediate leading to substitution is promoted by hydrogen ion [5]. The pyridinyl radical which forms on protonation of the radical anion does not couple with ketyl radical. In basic solution protonation of the intermediate radical anion does not occur and decyanation is the only reaction observed.

In an attempt to learn more about the mechanisms by which these reactions occur, rates of disappearance of 1 and the formation of products were measured under the same conditions used for the preparative reactions. Figure 1 shows the results obtained. In acidic and basic media the rates of disappearance of 1 corresponds, respectively, to the rates of formation of the monosubstitution and reduc-

tion products. In neutral medium, in which both products are formed, the overall rate of disappearance of 1 equals the sum of the rates of both reactions. In basic solution in which the protonation by the medium is not likely, the formation of the monosubstitution product is supressed and the rate of disappearance of 1 occurs 2.4 times faster than it does in acidic medium and 2.5 times faster than it does in neutral medium. This indicates that the decyanation process is rapid and competes well with the radical coupling reaction. Furthermore, from these results it may also be concluded that a mechanism exists by which the radical 2 can become 1 since in neutral medium, in which protonation of the radical anion is more probable, the rate of disappearance of 1 is slower. This supports the earlier conclusion that 2,4-dicyanopyridinyl radical does not react with diphenyl ketyl to give coupling products.
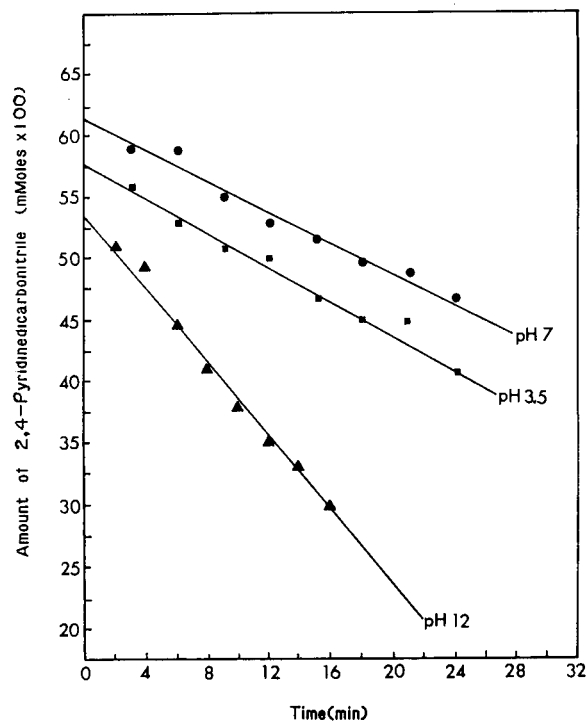

Figure 1. A plot of the millimoles of 2,4-pyridinedicarbonitrile (1) remaining as a function of time in minutes for the photoreaction of 1 with 2-propanol at pH 3.5, 7, and 12. The rates of disappearance calculated from the slopes are 6.4×10^{-3} (r = 0.976), 6.0×10^{-3} (r = 0.985), and 1.53×10^{-2} (r = 0.995) Ms^{-1} respectively.

EXPERIMENTAL

All preparative reactions were run in 3:1 (v/v) 2-propanol-water. The solutions were deaerated either by three freeze-vacuum-thaw cycles or by nitrogen bubbling for 30 minutes or more. Photochemical irradiations were carried out using a Rayonet RPR-100 photochemical reactor equipped with 16 lamps with a maximum emission at 350 nm. The reaction mixtures were separated by column chromatography with silica gel as the stationary phase and mixtures of hexane-ethyl acetate as eluents. Melting points are

uncorrected. The proton nmr spectra were recorded on a Varian FM 390 MHz spectrometer using deuteriochloroform as the solvent. All chemical shifts are reported in parts per million (ppm) from tetramethylsilane as the internal standard and all coupling constants (J) are reported in Hertz. Mass spectra were recorded with a Hitachi-Perkin-Elmer RMV 6 D single focusing spectrometer. The hplc analyses were carried out on a Jasco VL-614 using a Hibar column RP-18 packed with LiChrosorb and eluting with a 40/60 mixture of acetonitrile/water.

Materials.

2,4-Pyridinedicarbonitrile and benzophenone were available in a reasonably pure state and were used without further purification. All other reagents and solvents used were of an analytical grade.

Irradiation of a Mixture of 2,4-Pyridinedicarbonitrile (1) and Benzophenone in Neutral Medium.

A solution of 1 (1 g, 0.0078 mole) and benzophenone (2.8 g, 0.0154 mole) in 60 ml of 2-propanol-water was irradiated at 350 nm for eight hours. After this time the reaction mixture was extracted several times with methylene chloride and the combined extracts dried over anhydrous magnesium sulfate and the solvent removed by evaporation at reduced pressure. The residual brown oil was subjected to chromatography on a column packed with silica gel and eluted with hexane-ethyl acetate (80:20). The compounds isolated in order of elution were 2.2 g of benzophenone (79% recovery), 0.63 g (35% yield) of 2-(α-hydroxydiphenylmethyl)pyridine-4-carbonitrile(4) [6], mp 77° (benzene-hexane); ir (nujol); 3460 (OH), 2220 (CN), 1640 (heteroaromatic ring) cm⁻¹; ¹H nmr: 8.66 (dd, pyridine H₆, 1, $J_{6,5}$ = 5 Hz, J = 1.2 Hz), 7.35 (dd, pyridine H,1, $J_{5,3}$ = 2 Hz), 7.31 (m, 10 ArH and pyridine H₃, 11), 5.5 (s, O-H 1); ms: 286, 269, 209, 183, 105, 103, 77; 0.15 g of unreacted 2,4-pyridinedicarbonitrile and 0.20 g of 2-pyridine-carbonitrile (31% yield). When the column was eluted with methanol, a mixture of polar products was obtained which was not examined further, Benzopinacol was not detected among the reaction products.

Irradiation of 2,4-Pyridinedicarbonitrile and Benzophenone in Acidified 2-Propanol-Water.

A solution of 1 (1 g, 0.078 mole) and benzophenone (2.8 g, 0.0154 mole) in 60 ml of 2-propanol-water and 1 ml of hydrochloric acid (36%) was irradiated at 350 nm for 2 hours. The solution was then made basic with 10% sodium hydroxide solution and then extracted several times with methylene chloride. The extracts were combined and dried and the solvent removed as usual. The resulting oil was subjected to column chromatography on silica gel and eluted with 80:20 hexane-ethyl acetate. The products isolated in order of elution from the column are benzophenone (2.7 g, 96% recovery), 0.42 g of 1 (21%

yield), 0.54 g of 5 (16% yield), mp 152° (ethyl acetate); ir (potassium bromide): 3560 (O-H), 1640 (Ar ring) cm⁻¹; ¹H nmr: 8.5 (dd, pyridine H₆, $J_{6,5}$ = 6 Hz), 7.2 (broad, 4 ARC-H and 2 pyridine C-H, 22), 6.3 (s, O-H, 1) and 3.2 (s, OH, 1); ms: 443, 366, 182, 105; 0.10 g of 1 was also detected. A complex mixture of products (0.20 g) was also isolated when the column was eluted with methanol. These products were not examined further.

Irradiation of 2,4-Pyridinedicarbonitrile and Benzophenone in Basic 2-Propanol-Water.

A solution of 1 (1 g, 0.0078 mole) and benzophenone (2.8 g, 0.0154 mole) in 60 ml of 2-propanol-water, buffered at pH = 12, was irradiated at 350 nm for two hours. The reaction mixture was treated as usual and yielded 2.7 g of benzophenone (96% recovery) and 2-pyridinecarbonitrile (0.60 g, 82% yield), 0.10 g of unreacted 1 was also isolated.

Kinetic Experiments.

For the kinetic experiments, three stock solutions of 1 were prepared with various pH's as follows: a) pH 7, 0.042M in 7:3 2-propanol-water; b) pH 3.5, 0.041 M in 7:3 2-propanol-water acidified with hydrochloric acid; and c) pH 12, 0.039 M in a solution composed of 7 parts of 2-propanol and 3 parts of a buffered solution made by mixing 50 ml of 0.05M disodium hydrogen phosphate and 26 ml of 0.1 M sodium hydroxide. Eight 15 ml samples of each solution were then deaerated by nitrogen bubbling and then irradiated at 350 nm using a merry-go-round apparatus in a Rayonet photochemical reactor for the indicated times. After the usual work-up the samples were analyzed by hplc using 2-chloropyridine as an internal standard. The values reported are averages of three independent analyses.

REFERENCES AND NOTES

[1] For a review of the photochemical reactions of six-membered-ring aromatic monoazaheterocycles with hydrogen containing solvents, see A. Lablache-Combier, Elements de Photochemie Advancee, P. Courtot, ed, Hermann, Paris, 1972, p 289; see also the references therein.

[2] T. Caronna, S. Morrocchi and B. M. Vittimberga, J. Am. Chem. Soc., 108, 2205 (1986).

[3] A. L. Riger and B. M. Vittimberga, work to be submitted for publication.

[4] B. M. Vittimberga and P. McDevitt, work to be submitted for publication.

[5] A similar result was obtained in the reaction of 1 with thermally generated diphenyl ketyl.

[6] The structure of product was determined via reductive decyanation of 4 by titanium trichloride: A. Clerici and O. Porta, Tetrahedron Letters, 21, 1675 (1980). The product obtained for the reaction was identified as 2-(α-hydroxydiphenylmethyl)pyridine by comparison with an authentical sample; T. Caronna, S. Morrocchi and B. M. Vittimberga, J. Heterocyclic Chem., 17, 399 (1980).