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4-Chloropyridine (**1**) converts to 1-(4'-pyridyl)-4-pyridone (**4**) in aqueous 2-propanol. The photo-initiated reaction of both of these compounds in acidic and non-acidic 4:1 2-propanol/water with and without benzophenone is reported.

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6-Membered monoazaaromatic compounds have been shown to undergo a number of interesting photochemical reactions in aqueous-alcoholic solution [1]. Depending on conditions and photophysical characteristics of the molecule, these reactions can involve either electron transfer or hydrogen atom abstraction processes. Moreover, when benzophenone is present, it can serve as a photosensitizer or an electron transfer agent through the formation of diphenyl ketyl by the photochemical reaction with 2-propanol. Both 2- and 4-pyridinecarbonitrile, for example, in the presence of benzophenone undergo electron transfer-substitution reactions resulting in the displacement of the cyano group [2,3], while 2-quinolinecarbonitrile undergoes triplet sensitization and dimerization [1].

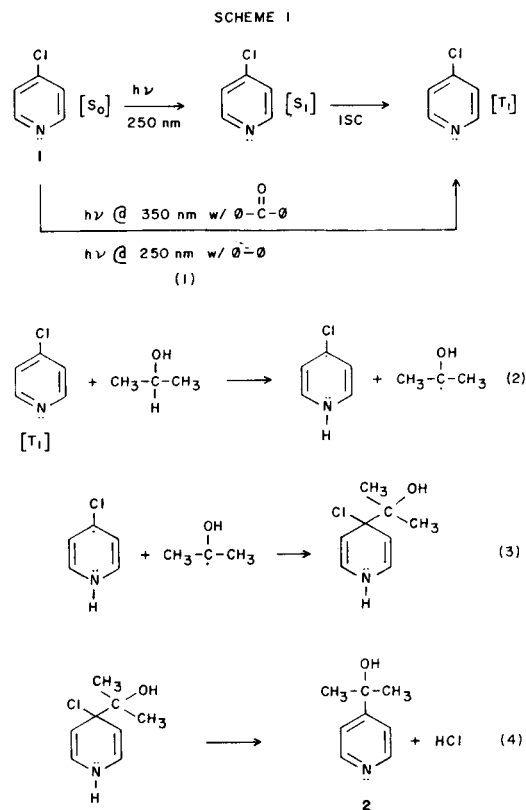
In our work with 6-membered nitrogen heterocycles we found that the reaction path depends to a large extent on the energy and η, π^* , or π, π^* nature of the reactive excited state, the latter being less reactive in hydrogen abstraction reactions [4,5]. Since substituent groups can have a pronounced effect on the excited state as well as the ground state of a molecule, keeping in mind the results with cyano substitution, we were interested in determining the effect that a 4-chloro substituent would have on the course of the reaction. Chlorine could either donate electrons through resonance or withdraw electrons through induction, though not as well as the cyano group.

When a solution of 4-chloropyridine (**1**) in 4:1 2-propanol/water is irradiated at 250 nm, a low yield (2%) of 2-(4'-pyridyl)-2-propanol (**2**) is formed. However, when this reaction is repeated with benzophenone and irradiated at 350 nm, the principal products formed are **2** (25% yield) and diphenyl-(4-pyridyl)methanol (**3**) (6% yield). Large amounts of benzopinacol were also formed in the reaction. The formation of benzopinacol suggests the possibility that diphenyl ketyl is involved in the reaction. Based on the reaction of 4-pyridinecarbonitrile [3], **3** would be the product expected from an electron-transfer substitution reaction, while **2** would be the product expected from a hydrogen atom abstraction reaction.

When the reaction of **1** with benzophenone was repeated under acidic conditions, **2** formed in 10% yield along

with **3** in 5% yield. A decrease in the amount of **2** formed under these conditions indicates that **2** probably forms by a hydrogen atom abstraction reaction of the photoexcited unprotonated pyridine base. Protonated pyridines do not undergo this abstraction process [6].

The fact that **2** is formed when the reaction is run in neutral solution with or without benzophenone also supports a hydrogen atom abstraction process. The low yield of **2** formed in the absence of benzophenone indicates that the reaction involves the triplet state of **1**. If the triplet state is involved in an energy transfer reaction, then the amount of **2** formed should also be increased by using a sensitizer such as biphenyl, which can transfer energy but not an electron [7]. This was found to be the case as can be



seen from the data in Table 1. The mechanism that best explains these results is shown in Scheme 1.

Emission studies indicate that the singlet state is most likely η, π^* and that the intersystem crossing efficiency to the triplet manifold is quite low.

Table 1

Product Percentages for the Photoreaction of 4-Chloropyridine Under Various Conditions

Reaction Conditions Irradiation	% Yield of Dimethyl Product	% Yield of Diphenyl Product
250 nm, no H ⁺	2%	NONE
350 nm, no H ⁺ ; B	19%	6%
350 nm, 1 eq. HCl; B	10%	6% [a]
350 nm; 1 eq. HCl; B and 1 eq. H ₂ SO ₄	3%	1%
250 nm; no H ⁺ ; biphenyl	10%	NONE
thermal; w/benzopinacol	NONE	NONE

B = benzophenone

[a] Includes a 3% yield of 7

If **2** forms by an energy transfer-hydrogen abstraction mechanism, the question remains as to the origin of **3**.

In every reaction of 4-chloropyridine in aqueous 2-propanol there is also formed 1-(4'-pyridyl)-4-pyridone (**4**). It occurred to us that **3** may be a product of the reaction of **4** with diphenyl ketyl and may not involve **1** directly. The esr studies show that **4** forms a stable radical when irradiated in acidic primary or secondary alcohols [8]. However, when

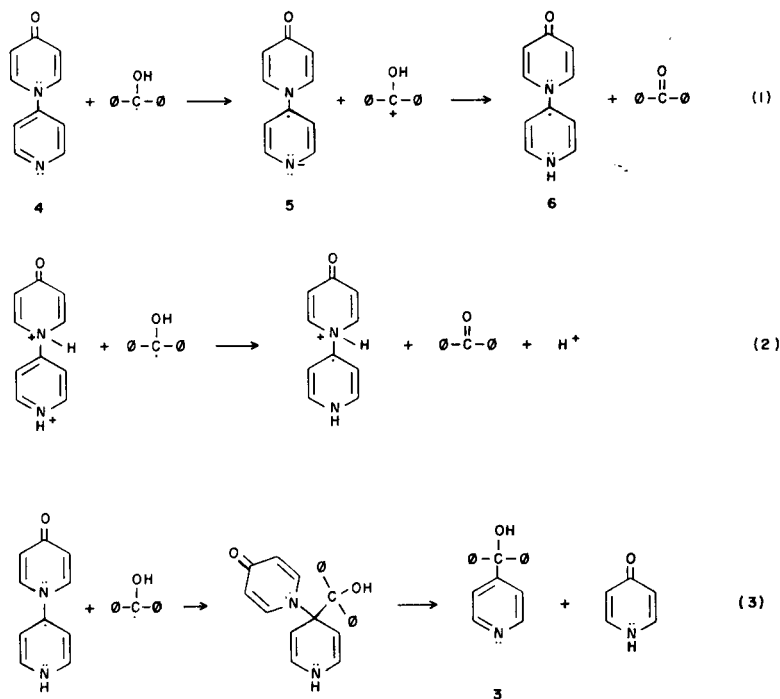
a neutral solution of **4** is irradiated in these solvents in the cavity of an ESR spectrometer, no signal is observed. This implies that **4** does not undergo H-atom abstraction reactions.

When a neutral, deoxygenated solution of **4** and benzophenone is aqueous 2-propanol is irradiated at 350 nm, **3** forms in 21% yield and 76% of **4** is recovered unchanged. Since **4** does not form a radical when irradiated in neutral solution, the 4-substituted pyridinyl radical (**6**, Scheme 2) most likely forms by an electron transfer from diphenyl ketyl to form the radical anion **5**, which then undergoes protonation [9]. Coupling of the radical **6** with another ketyl radical, followed by displacement of the 4-pyridone moiety, yields **3**. 4-Pyridone was isolated in 23% yield.

In acidic solution, **4** should be protonated and thus become a better electron acceptor, resulting in a higher yield of **3**. Electron transfer could occur directly from an alcohol molecule or from diphenyl ketyl to form **5**, which could then couple with diphenyl ketyl and ultimately form **3**. When the reaction was run in acidic solution the yield of **3** increased to 46%. An 8% yield of diphenyl-(4-pyridyl)-methane (**7**) was also formed. We previously reported that **7** is formed from **3** in photoreactions carried out in acidic, aqueous 2-propanol with benzophenone [3]. It can be assumed, therefore, that a 54% yield of **3** formed overall in this reaction [Scheme 2].

The isolation of **3** from **4** explains its formation in reaction mixtures of 4-chloropyridine. Since the formation of **4** begins immediately when **1** is placed in solution [10], the

SCHEME 2



photoreactions of **4** must also be considered with those of **1**.

EXPERIMENTAL

All reactions were run in 4:1 (v/v) 2-propanol/water unless otherwise stated. All solutions were deoxygenated by either bubbling dry nitrogen or argon gas through the solution for 30 minutes or more or by at least three freeze-vacuum-thaw cycles. Melting points were determined on either a Thomas-Hoover or a Mel-Temp capillary melting point apparatus and are uncorrected. The uv/vis spectra were recorded on a Cary 15 or 210 Model Recording Spectrophotometer. The ir spectra were recorded on a Beckman Acculab IV or a Perkin Elmer Model 821 infrared spectrophotometer. Liquid samples were run neat on sodium chloride windows and solids were run as pellets made with spectrograde potassium bromide. The proton nmr spectra were recorded on a Varian EM 360 A or a Em 390 A NMR spectrometer. The C ¹³nmr spectra were run on a Varian CFT 20 C13 NMR. All chemical shifts are reported in parts per million (ppm) from tetramethylsilane; all coupling constants (J) are reported in Hertz. Deuterated solvents were obtained from The Aldrich Chemical Company. The ESR spectra were recorded on a Bruker ER 220 D LR spectrometer available from Brown University.

Separation of most reaction mixtures was achieved by column chromatography with silica gel (Brinkmann Instruments, Silica Gel 60, 70-230 mesh) as the stationary phase. Thin layer chromatography (tlc) was done on commercially available sheets impregnated with a fluorescent indicator (Polygram Sil N-HR/UV).

Photochemical irradiations were carried out using either a 275 watt Sylvania Ultraviolet Sun Lamp or a Rayonet Model RPR-100 photochemical reactor. Elemental analyses were performed by Micro Analysis, Inc. of Wilmington, Delaware. Product yields are based on the amount of starting material used.

Materials.

4-Chloropyridine hydrochloride, 4-pyridone and benzophenone were obtained from the Aldrich Chemical Company, Inc. 4-Chloropyridine was prepared from the hydrochloride salt by dissolving the salt in distilled water and then neutralizing the acid with base. The aqueous layer was exhaustively extracted with ether and then the combined ether layers were washed with water and dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solvent by evaporation under reduced pressure leaving 4-chloropyridine as a colorless liquid. The 4-chloropyridine prepared in this manner was used without further purification. All other reagents and solvents were A.C.S. reagent grade.

Irradiation of 4-Chloropyridine (**1**) with Benzophenone.

A solution of **1** (1.15 g, 0.010 mole) and benzophenone (3.70 g, 0.020 mole) in 75 ml of 2-propanol/water was irradiated at 350 nm for 24 hours. After this time the solution was dark purple in color and contained a large amount of both a white and dark precipitate. The solid was collected by filtration and the solvent was removed from the filtrate by evaporation on a rotary evaporator leaving a brown oil as residue. This oil was dissolved in chloroform and subjected to chromatography on a 50 × 1.5 cm column packed with silica gel. Successive elutions with benzene, ether, and methanol gave 0.16 g of benzopinacol, mp 191-193° (ethanol), (lit. 193-195° [11], 90% total yield); ir (potassium bromide): 3480 (OH), 3030 (Ar C-H), 1450-1500 (2 peaks), 1020 (C-O), 690 (2 peaks) and 748 cm⁻¹; nmr (deuteriochloroform): δ 3.0 (s, OH, 2) and 7.20 (s, Ar, 20), 0.16 g of diphenyl(4-pyridyl)methanol (**3**), mp 235-236° (acetone) (lit 235° [12], 6% yield); ir (potassium bromide): 3100 (Ar and OH), 1600 (C=C), and 800-700 cm⁻¹ (two peaks, Ar); nmr (deuteriochloroform): δ 6.7 (s, OH, 1), 7.2 (d, pyridine H, 2, J = 7 Hz), 7.25 (s, Ar, 10), and 8.50 (d, pyridine H, 2, J = 7 Hz), and 0.27 g of 2-(4'-pyridyl)-2-propanol (**2**), mp 136-138° (methanol-acetone) (lit 135-136° [13], 19% yield); ir (potassium bromide): 3200 (OH), 2990 (C-H), 1610 (C=C), 1180 (C-O), and 850 cm⁻¹ (Ar); nmr (deute-

riochloroform): δ 2.32 (s, CH₃, 6), 5.1 (s, OH, 1), 7.6 (d, Ar, 2, J = 7 Hz), and 8.5 (d, Ar, 2, J = 7 Hz). Infrared and nmr spectra were superimposable on those of known samples. The precipitate which had been collected was shown by ir and nmr to be benzopinacol.

Irradiation of 4-Chloropyridine and Benzophenone Under Acidic Conditions.

A solution of 4-chloropyridine hydrochloride (3.00 g, 0.020 mole) and benzophenone (7.29 g, 0.040 mole) was irradiated at 350 nm for 24 hours. At the end of this time the solution was dark purple and contained a large amount of both a white and dark solid. This precipitate was collected on a filter, and the white solid was shown by mp, and ir and nmr spectroscopy to be benzopinacol, 6.28 g. The dark solid had characteristics of a polymer, 0.42 g. The volume of the reaction mixture was reduced on a rotary evaporator, and the residue made basic with 10% sodium hydroxide. The aqueous layer was then extracted several times with chloroform. The chloroform extracts were combined, dried over anhydrous magnesium sulfate, and the solvent removed under vacuum.

The resulting red oil was subjected to chromatography on a 40 × 2.5 cm silica gel column. Elution was affected with a series of solvents including benzene, chloroform-ether (1:1), ether, ether-methanol (10:1) and methanol. The compounds isolated in order of elution from the column were benzopinacol (0.53 g), unreacted **1**, 0.14 g, 6.1% recovery, diphenyl(4-pyridyl)methane (**7**), 0.14 g, mp 123-124° (lit 125° [12], 3% yield); ir (potassium bromide): 3010 (Ar C-H), 1580 (C=C), 1400-1500 (3 peaks, C-H), and 700-800 cm⁻¹ (2 peaks, Ar); nmr (deuteriochloroform): δ 5.5 (s, C-H, 1), 7.2 (d, pyridine H, 2, J = 7 Hz), 7.25 (s, Ar, 10), and 8.50 (d, pyridine H, 2, J = 7 Hz), **3**, 0.12 g (3% yield), and **2**, 0.27 g, (10% yield). The nmr and ir spectra are the same as those of known samples.

Irradiation of 4-Chloropyridine and Benzophenone with Excess Acid.

A solution of 4-chloropyridine hydrochloride (1.00 g, 6.67 × 10⁻³ mole) and benzophenone (2.43 g, 1.33 × 10⁻² mole) in 40 ml of 2-propanol, 8 ml of distilled water, and 2 ml of reagent grade concentrated sulfuric acid was irradiated at 350 nm for 24 hours. After this time, the solution was yellow and the flask contained a considerable amount of white solid. The solid was collected on a filter and shown by the usual methods to be benzopinacol, 2.19 g. The filtrate was treated by the same procedure as described above. The compounds isolated from the column were benzopinacol, **1**, 0.61 g (81% recovery), **2**, 0.028 g (3% yield), and **3**, 0.017 g (1% yield). All melting points and ir data were consistent with the assigned structures.

Irradiation of 4-Chloropyridine at 250 nm with Biphenyl.

A solution of **1** (1.39 g, 0.012 mole) and biphenyl (Aldrich Chemical Company) (3.79 g, 0.025 mole) in 10 ml of 2-propanol/water was irradiated at 250 nm in a quartz vessel for 24 hours. After two hours of irradiation, the solution was purple and all the biphenyl had dissolved. After 24 hours, the polymer was filtered from solution and the volume of the filtrate was reduced under vacuum. Some white crystals formed which were collected on a filter and shown to be biphenyl by ir and nmr analysis. The residue was extracted several times with chloroform and the extracts combined and the products isolated as usual by column chromatography on a 45 × 2.5 cm silica gel column. The products isolated included recovered biphenyl, 2.69 g, 0.033 g of pinacol, mp 38-40° (lit [14] 40-43°), and 0.017 g of **2**, (10% yield). Ultraviolet analysis of the liquid evaporated from the reaction mixture indicated the presence of pyridine (max 247, 255, and 260 nm).

Total Emission Studies of 4-Chloropyridine.

Total emission spectra were recorded on a Farrand Spectrofluorometer MK2 equipped with a 150 watt lamp. The excitation monochrometer was set at 255 nm and 2.5 mm excitation and 1.0 mm emission slits were used. Methylcyclohexane (Matheson, Coleman, and Bell) and acetonitrile (Aldrich) were distilled before use. Ten 3M solutions of **1** in these solvents were used to obtain total emission spectra at liquid nitrogen temperature. In methylcyclohexane, **1** fluoresces at 310 nm and in acetonitrile at 273 nm. No phosphorescence was observed.

Synthesis of 1-(4'-Pyridyl)-4-Pyridone (**4**) from 4-Pyridone.

1-(4'-Pyridyl)-4-pyridone (**4**) was synthesized according to the procedure described by F. Arndt and A. Kalischek [15]. A solution of 4-pyridone (2.0 g, 0.02 mole) and acetic anhydride (3 ml, 0.04 mole) was heated at reflux for 3 hours. After this time the brown solution was allowed to cool slowly to room temperature, at which time the mixture had solidified. The solid was washed from the flask with ether and collected on a filter. The material on the filter was placed in a Soxhlet extractor and extracted overnight with 500 ml of boiling benzene. The volume of benzene was then reduced to 50 ml under vacuum, and the residual liquid was then cooled in an ice bath causing the product to crystallize. The resulting 1-(4'-pyridyl)-4-pyridone was recrystallized twice from benzene, the first time with activated charcoal. The yield of **4** was 1.29 g, mp 176-177° (lit 177-178° [15], 71% yield); ir (potassium bromide) 3010 (Ar C-H), 1630 (C=C), 1580 (C=O), and 830 cm^{-1} ; nmr (deuteriochloroform): δ 6.5 (d, d, Ar, 2, J = 8 Hz), 7.4 (d, d, Ar, 2, J = 6 Hz), 7.8 (d, d, Ar, 2, J = 8 Hz), and 8.8 (d, d, Ar, 2, J = 6 Hz).

Irradiation of 1-(4'-Pyridyl)-4-Pyridone (**4**) with Benzophenone.

A solution of **4** (0.34 g, 0.002 mole) and benzophenone (0.73 g, 0.004 mole) in 15 ml of 2-propanol/water was irradiated at 350 nm for 24 hours. After this time there was a white solid present in a light yellow solution. This precipitate was collected on a filter and shown by mp, ir, and nmr to be benzopinacol, 0.41 g. The solvent was removed from the solution under vacuum and the residue taken up in 5 ml of chloroform. This solution was chromatographed on a 40×1.5 cm silica gel column. Successive elutions with benzene, ether, and methanol gave 0.25 g of benzopinacol, **3**, 0.12 g (21% yield), 4-pyridone, 0.04 g (23% yield) and 0.26 g of unreacted **4** (76% recovery). Melting points and ir and nmr spectra were consistent with all assigned structures.

Irradiation of 1-(4'-Pyridyl)-4-Pyridone (**4**) and Benzophenone in Acidic Solution.

A solution of **4** (0.34 g, 0.002 mole) and benzophenone (0.73 g, 0.004 mole) in 12 ml of 2-propanol, 1.5 ml water, and 1.5 ml reagent grade concentrated hydrochloric acid was irradiated at 350 nm for 24 hours. At the end of this time the white solid which formed was separated from the yellow solution by filtration and shown to be benzopinacol by mp and ir and nmr spectroscopy, 0.36 g. The filtrate was made basic with 10% sodium bicarbonate and extracted several times with chloroform. The combined extracts were treated as usual. The volume was reduced to about 5 ml and the residue chromatographed on a 40×1.5 cm silica gel column. The column was eluted with benzene which gave 0.17 g of benzopinacol,

then with ether which gave 0.04 g (8% yield) of **7**. The final fractions were eluted with ether/methanol 10:1 and methanol giving 0.24 g (46% yield) of **3** and 0.027 g of unreacted **4** (8% recovery).

Ultraviolet analysis of the aqueous layer showed one absorption at 255 nm which was due to 4-pyridone, 0.18 g (95% yield). Identification was confirmed by ir and nmr spectroscopy after evaporation of the water.

REFERENCES AND NOTES

- [1] For example, see T. Caronna, S. Morrocchi and B. M. Vittimberga, *J. Org. Chem.*, **46**, 34 (1981) or T. Furihata and A. Sugimori, *J. Chem. Soc., Chem. Commun.*, 241 (1975).
- [2] T. Caronna, S. Morrocchi and B. M. Vittimberga, *J. Heterocyclic Chem.*, **17**, 399 (1980).
- [3] B. M. Vittimberga, F. Minisci and S. Morrocchi, *J. Am. Chem. Soc.*, **97**, 4377 (1975).
- [4] N. J. Turro, "Modern Molecular Photochemistry", Benjamin Cummings Publishing Co., Menlo Park, Calif., 1978, p 368.
- [5] D. G. Whitten and Y. J. Lee, *J. Am. Chem. Soc.*, **93**, 961 (1971).
- [6] A. Castellano, J. P. Catteau, and A. LaBlache-Combiere, *Tetrahedron*, **31**, 2255 (1975).
- [7] Biphenyl is a less efficient photosensitizer than benzophenone with a triplet energy of 65.8 Kcal and $\phi_{isc} = 0.81$ compared to 69.2 Kcal and $\phi_{isc} = 1.00$ respectively.
- [8] The photochemistry and photophysics of **4** along with its derivatives will be submitted for publication in the near future.
- [9] We have found that this type of mechanism predominates when the heteroaromatic ring is highly electron deficient and the lowest triplet state is π, π^* .
- [10] For a discussion of the reaction converting **1** to **4** see M. H. Palmer, "The Structure and Reactions of Heterocyclic Compounds", St. Martins Press, New York, NY, 1967, p 38.
- [11] H. Zeldes, R. Livingston, *J. Phys. Chem.*, **77**, 2076 (1973).
- [12] A. E. Tschitschibabin and S. W. Benewolenskaja, *Chem. Ber.*, **61B**, 547 (1928).
- [13] J. Drillet, L. Torres and E. Bordier, *C. R. Acad. Sci., Paris, Ser. C*, **266** 1381 (1968).
- [14] Aldrich Handbook of Fine Chemicals, 1982-1983, Aldrich Chemical Company, Inc., Milwaukee Wisconsin.
- [15] F. Arndt and A. Kalischek, *Chem. Ber.*, **63B**, 587 (1930); See also, F. Arndt, *ibid.*, **65B**, 92 (1932).