Photochromic Nitrobenzylpyridines

AARON L. BLUHM, JULIUS WEINSTEIN, AND JOHN A. SOUSA

Pioneering Research Division, Quartermaster Research and Engineering Command, Natick, Massachusetts

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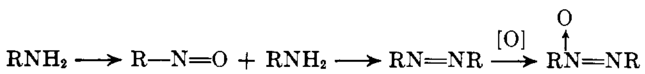
The synthesis of several nitrobenzylpyridines is presented. These compounds are all photochromic in solution and some are photochromic in the crystalline form. The visible spectra of the irradiated isomers are shown.

A kinetic study on the photoisomerization of 2-(2,4-dinitrobenzyl)pyridine and 2-(2-nitro-4-cyanobenzyl)-pyridine recently was reported.[1] When pale yellow crystals of 2-(2,4-dinitrobenzyl)pyridine or colorless crystals of 2-(2-nitro-4-cyanobenzyl)pyridine are exposed to light the crystals change to blue and green, respectively. When stored in the dark the crystals fade to their original color. Chilled solutions of these compounds also exhibit reversible photochromism.

In order to study this phenomenon, we have prepared a number of substituted benzylpyridines. All of these new compounds show a reversible photochromism in the solution phase and some also exhibit photochromism in the solid state.

The benzylpyridines synthesized are listed in Table I. Compounds I–III were prepared directly from 2-(2-nitro-4-cyanobenzyl)pyridine (VIII), the preparation of which was described by Sousa and Weinstein.[1] Amide III was obtained initially by alkaline peroxide treatment of VIII similar to a procedure reported by Radziszewski.[2] The amide also was obtained when cyano compound VIII was heated with isopropyl alcohol saturated with hydrogen chloride gas. It was not possible to prepare 2-(2-nitro-4-carboxybenzyl)pyridine (IV) by extended hydrolysis of VIII with either 50% sulfuric or 18% hydrochloric acid. However, treatment of the methyl ester (I) with hot 18% hydrochloric acid furnished the acid in good yield. Esters I and II were prepared by the acid-catalyzed alcoholysis of VIII. The azoxy compound V was obtained when 2-(2-nitro-4-aminobenzyl)pyridine was exposed at room temperature to a peroxidic glacial acetic acid solution containing a trace of sulfuric acid. This procedure has been utilized to oxidize aromatic amines to nitroso compounds.[3] It is likely that an intermediate nitroso compound is formed which then reacts with unchanged amine to form an azo compound which in the peroxidic medium oxidizes to the azoxy form.



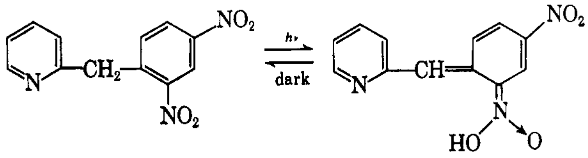
$$RNH_2 \longrightarrow R{-}N{=}O + RNH_2 \longrightarrow RN{=}NR \xrightarrow{[O]} R\overset{\overset{O}{\uparrow}}{N}{=}NR$$

Holmes and Bayer[3] reported that their nitroso compounds precipitated from the reaction mixture. However, in our preparation no material precipitated during the reaction, due to the solubility of the pyridine entity in the acid medium. This solubility factor most likely permits any intermediate nitroso compound to condense with unreacted amine.

The hydroxy compound VI was prepared by the reduction of 2-(2,4-dinitrobenzoyl)pyridine with sodium borohydride in methanol. The benzoyl compound was prepared by the procedure of Nunn and Schofield.[4] The cyano compound VII was obtained from diazotization of 4-(2-nitro-4-aminobenzyl)pyridine[4] similarly to the preparation of VIII.[1]

Photochromic Properties

The reversible photochromic change from a pale yellow to a deep blue color observed when crystals of 2-(2,4-dinitrobenzyl)pyridine are exposed to light was first reported by Tschitschibabin and co-workers.[5] Since then other workers[1,6,7] have reported the reversible photochromism of cooled solutions of some benzylpyridines. It is believed that the color change shown by these compounds on irradiation is due to the formation of the tautomeric *aci*-nitro structure.[1,7,8]



This view is consistent with the observation that in compounds of this type the requirement for photochromism is the presence of a nitro and $-\overset{|}{\underset{|}{C}}-H$ group *ortho* to each other.[1,9] The criterion which is responsible for the apparent lack of photochromism in the crystalline form of some of the benzylpyridines is not clear at this time. In Table I are shown the colors obtained when the crystalline forms are irradiated with a Hanovia lamp. Compounds I–III give a colored form on irradiation at room temperature. In order to observe the photochromism of IV and V, the solid was cooled on Dry Ice. Compounds VI and VII did not show photochromism in the solid phase even when cooled.

The visible spectra of the irradiated colored forms of the benzylpyridines in solution are shown in Fig. 1. Their maxima are given in Table I. The benzylpyridine solutions are essentially colorless before irradiation and revert to the colorless form in the dark. The kinetics of the fading reaction are being investigated and will be the subject of a future paper.

Experimental[10]

Visible Absorption Measurements.—A Cary Model 14 spectrophotometer was used. Solutions were measured in absolute

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[1] J. A. Sousa and J. Weinstein, *J. Org. Chem.*, **27**, 3155 (1962).

[2] R. Radziszewski, *Ber.*, **18**, 355 (1885).

[3] R. R. Holmes and R. P. Bayer, *J. Am. Chem. Soc.*, **82**, 3454 (1960).

[4] A. J. Nunn and K. Schofield, *J. Chem. Soc.*, 5813 (1952).

[5] A. E. Tschitschibabin, B. M. Kuindshsi, and S. W. Benewolenskaja *Ber.*, **58**, 1580 (1925).

[6] R. Hardwick, H. S. Mosher, and P. Passailaigue, *Trans. Faraday Soc.*, **56**, 44 (1960).

[7] H. S. Mosher, C. Souers, and R. Hardwick, *J. Chem. Phys.*, **32**, 1888 1960).

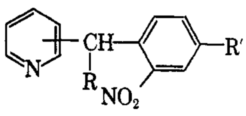
[8] R. Hardwick and H. S. Mosher, *J. Chem. Phys.*, **36**, 1402 (1962).

[9] G. Wettermark, *Nature*, **194**, 677 (1962).

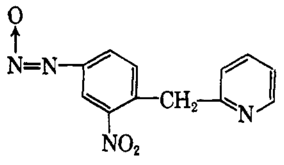
[10] Melting points were taken on a Fisher-Johns block and are not corrected.

TABLE I

WAVE LENGTHS OF THE VISIBLE ABSORPTION BANDS OF IRRADIATED BENZYLPYRIDINES IN ETHANOL SOLUTION AND COLOR OF THE IRRADIATED CRYSTALLINE FORMS



2-Benzylpyridines

Compound	R	R¹	Color (solid)	λ_{max}, mμ
I	H	$COOCH_3$	Dark blue-green	405, 460, 485, 575
II	H	$COOCH_2CH_3$	Pale blue-green	410, 460, 485, 585
III	H	$CONH_2$	Pale green	403, 450, 485, 580
IV	H	COOH	Pale gray[a]	405, 450, 470, 580
V	H		Med. blue-green[a]	610
VI	OH	NO_2	...	600
		4-Benzylpyridine		
VII	H	CN	...	448, 555, 590

[a] Observed by cooling solid on Dry Ice.

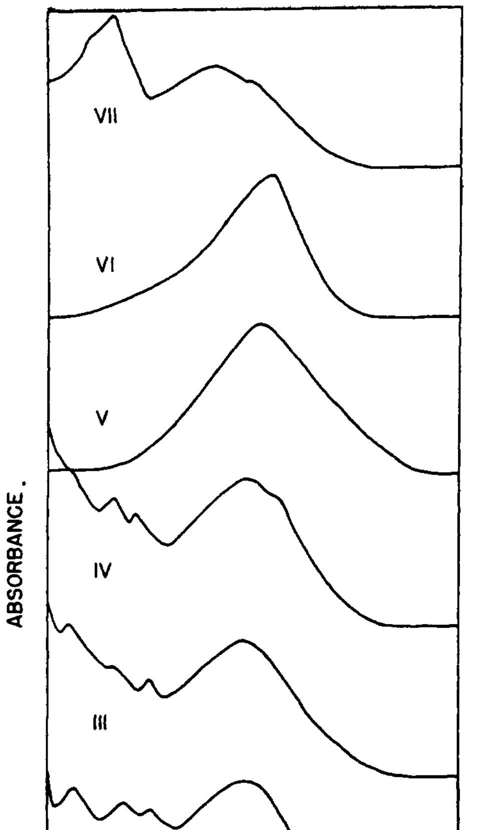


Fig. 1.—Visible absorption spectra of irradiated ethanol solutions measured at −91.0°. The ordinate is in arbitrary units.

"Spectro Grade" ethanol in a cryostated 2.5-cm. cell,[11] against a reference of pure solvent. The solutions at −91.0° were exposed for 2 min. to the unfiltered radiation from a Hanovia Type 16200 lamp with a quartz envelope.

2-(2-Nitro-4-cyanobenzyl)pyridine (VIII).—This cyano compound was prepared according to the procedure of Sousa and Weinstein.[1] The colorless crystals melted at 102–103°.

2-(2-Nitro-4-carbomethoxybenzyl)pyridine (I).—Dry hydrogen chloride gas was passed through 3 ml. of commercial absolute methanol in a 10-ml. round-bottom flask fitted with a condenser protected with a calcium chloride drying tube and a gas inlet tube, for 10 min. To this solution 0.20 g. of the preceding cyano compound VIII was added and the solution heated over a steam bath for 3 hr. On cooling a solid (the hydrochloride) deposited. To this mixture 3 ml. of water was added and the solution made alkaline with 28% ammonium hydroxide. The crystals which deposited were filtered after chilling and washed with water. Recrystallization from aqueous methanol furnished colorless lancelets melting at 67–68° in 75% yield. The infrared spectrum showed no C≡N group and the presence of a carboxylate group.

Anal. Calcd. for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.49; H, 4.32; N, 10.33.

2-(2-Nitro-4-carboethoxybenzyl)pyridine (II).—The procedure was similar to the preceding reaction, starting with 0.20 g. of VIII. Recrystallization of the product from aqueous ethanol furnished white crystals melting at 72–73° in 83% yield.

Anal. Calcd. for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.63; H, 4.70; N, 9.65.

2-(2-Nitro-4-carbamylbenzyl)pyridine (III).—In a 50-ml. erlenmeyer flask 0.30 g. of cyano compound VIII was dissolved in 15 ml. of acetone. Two ml. of 10% hydrogen peroxide and 0.10 ml. of 10% sodium hydroxide were added. The solution was placed in the dark at room temperature for 2 days and then evaporated in a current of air. Pale yellow crystals deposited which were filtered and washed with water. Recrystallization from 50% aqueous ethanol furnished cream colored needles melting at 169–170.5° in 70% yield. The infrared spectrum showed absence of C≡N group, and the presence of a carbonyl group at 1685 cm.$^{-1}$. The NH_2 group was observed at 3120 and 3305 cm.$^{-1}$ in a halocarbon mull and at 3411 and 3528 cm.$^{-1}$ in chloroform solution.

Anal. Calcd. for $C_{13}H_{11}O_3N_3$: C, 60.69; H, 4.31; N, 16.33. Found: C, 60.40; H, 4.43; N, 16.40.

2-(2-Nitro-4-carboxybenzyl)pyridine (IV).—2-(2-Nitro-4-carbomethoxybenzyl)pyridine (I) (0.25 g.) was refluxed with 18% hydrochloric acid for 8 hr. The cooled solution deposited fine white needles (hydrochloride) which were filtered and washed with a little ice–water. This product was dissolved in 15 ml. of

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[11] J. A. Sousa and J. Weinstein, *Rev. Sci. Instr.*, **34**, 150 (1963).

warm water and just neutralized with 5% sodium hydroxide. The white solid which precipitated was filtered and washed with a small amount of ice-water and recrystallized from 95% ethanol, m.p. 208–210°, white, 0.10 g.

Anal. Calcd. for $C_{13}H_{10}N_2O_4$: C, 60.46; H, 3.90; N, 10.85. Found: C, 60.26; H, 3.91; N, 10.98.

3,3′-Dinitro-4,4′-di(2-pyridylmethyl)azoxybenzene (V).—In a 125-ml. erlenmeyer flask 5 g. of 2-(2-nitro-4-aminobenzyl)pyridine (m.p. 118.5°, prepared according to the procedure of Nunn and Schofield[4]), 40 ml. of glacial acetic acid, 10 ml. of 30% hydrogen peroxide, and 2 drops of concentrated sulfuric acid were combined. The mixture was kept at room temperature for 48 hr., and 50 ml. of water was added followed by treatment with 20% sodium hydroxide. An oil which separated was extracted with toluene, the toluene extract washed with water and dried over anhydrous magnesium sulfate. After removal of the drying agent, the toluene was removed in a current of warm air. The solid yellow residue was recrystallized with a charcoal treatment from aqueous ethanol. The pure compound was yellow and melted at 135–136° (70% yield). The infrared spectrum showed no NH absorption bands.

Anal. Calcd. for $C_{24}H_{18}N_6O_5$: C, 61.27; H, 3.86; N, 17.87; mol. wt., 470.43. Found: C, 61.36; H, 3.97; N, 18.01; mol. wt., 464.0 (vapor pressure method).

2-(2,4-Dinitrobenzoyl)pyridine.—This material was prepared from 2-(2,4-dinitrobenzyl)pyridine by a procedure utilized by Nunn and Schofield[4] to oxidize analogous benzylpyridines. The 2-(2,4-dinitrobenzoyl)pyridine was obtained as white crystals melting at 149.5–151° (lit.[5] m.p. 148°).

2-(2,4-Dinitro-α-hydroxybenzyl)pyridine (VI).—In a 500-ml. round-bottom flask fitted with a condenser, stirrer, and addition funnel, a suspension of 2.75 g. (0.010 mole) of 2-(2,4-dinitrobenzoyl)pyridine in 150 ml. of commercial absolute methanol was cooled to 0° and an ice-cold solution of 1.04 g. (0.028 mole) of sodium borohydride in 15 ml. of methanol was quickly added. The reddish purple mixture was stirred at 0° for 1 hr. and then the temperature allowed to rise. After 1.5 hr. at room temperature the reaction mixture was heated at 50° for 1 hr. Dilute sulfuric acid was added and the inorganic material filtered. The filtrate was evaporated to one-fifth its original volume, an equal volume of water added, and the solution made basic with 2% sodium hydroxide. This mixture was extracted with ether, the ether extracts dried over anhydrous magnesium sulfate, and the drying agent removed. Evaporation of the ether afforded a yellow solid. Recrystallization from ethanol furnished pale yellow crystals melting at 134.5–135° dec. The infrared spectrum showed absence of C=O band and presence of OH band.

Anal. Calcd. for $C_{12}H_9N_3O_5$: C, 52.37; H, 3.30; N, 15.27. Found: C, 52.62; H, 3.36; N, 15.13.

4-(2-Nitro-4-cyanobenzyl)pyridine (VII).—A magnetically stirred solution of 1.5 g. (0.0065 mole) of 4-(2-nitro-4-aminobenzyl)pyridine (m.p. 129–130°, lit.[4] m.p. 130–131°) and 1.68 ml. (0.020 mole) of concentrated hydrochloric acid in 5 ml. of water was cooled to 0° and the amine diazotized by gradual addition of 0.45 g. (0.0065 mole) of sodium nitrite in 4 ml. of water. The diazonium solution was then added to a magnetically stirred mixture of 0.58 g. (0.0065 mole) of cuprous cyanide, 0.85 g. (0.013 mole) of potassium cyanide, 5 ml. of water, and 75 ml. of toluene at 5–10°. The reaction mixture was heated at 80° for 2.5 hr., cooled, and made basic with 5% sodium hydroxide. Solids were collected on a filter. They and the water layer of the filtrate were extracted several times with toluene. The combined extracts were washed with 3% sodium hydroxide, water, and then dried over anhydrous magnesium sulfate. Evaporation of the toluene afforded 0.63 g. of amber residue which rapidly crystallized. Several crystallizations from toluene–ligroin (charcoal treatment) furnished pale yellow crystals melting at 73–74°. The infrared spectrum showed the presence of C≡N group.

Anal. Calcd. for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79. Found: C, 64.89; H, 3.95.

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Michael-Type Addition Reactions of 4-Chloropyrrolo[2,3-*d*]pyrimidines

ROBERT A. WEST

Burroughs Wellcome and Company (U.S.A.) Inc., The Wellcome Research Laboratories, Tuckahoe, New York

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4-Chloropyrrolo[2,3-*d*]pyrimidines react with acrylonitrile and ethyl acrylate under strong base catalysis giving N-7 adducts. These addition compounds are shown to be valuable synthetic intermediates.

It previously has been reported that 4-chloropyrrolo[2,3-*d*]pyrimidine and its 2-methyl relative were readily alkylated on the pyrrole nitrogen (N-7) using alkyl halides under alkaline conditions at room temperatures.[1]

The present investigation deals with the addition of these chloropyrrolopyrimidines, presumably as their anions, to acrylonitrile and to ethyl acrylate. These additions proceeded in excellent yields in refluxing ethanol with a catalytic amount of sodium ethoxide using excesses of the acrylic reagents (Table I). Paper chromatographic studies revealed that, with three moles of either ethyl acrylate or acrylonitrile to each mole of the pyrimidine, the additions were essentially complete after two hours. However, with four or five reactant molar ratios, much troublesome polymeric material resulted. With one or two reactant molar ratios of the acrylic reagents, unchanged materials were detected chromatographically even after four hours at reflux temperatures.[2]

Paper chromatographic studies failed to detect any di- or tri- addition products even after twenty-four hours at reflux. Further paper chromatographic studies revealed that strong base and moderately elevated temperatures were absolute requirements for these addition reactions to proceed within a reasonable length of time (twenty-four hours). The additions did not proceed in glacial acetic acid as shown by chromatography and by quantitative recovery of unchanged pyrrolopyrimidine.

Reaction of these adducts in alkaline media showed them to be reasonably stable. No retrogression was evident when they were heated in aqueous potassium hydroxide solutions (see experimental data and Reaction Scheme II) or when refluxed with an equimolar amount of sodium ethoxide for several hours. The chloro ester compounds under the former conditions yielded the chlorocarboxylic acids, however, as expected. The chloronitrile derivatives did not react under these

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(1) R. A. West and L. Beauchamp, *J. Org. Chem.*, **26**, 3809 (1961).

(2) The solvent system employed in these chromatographic studies was a mixture of 5 ml. of isopropyl alcohol and 95 ml. of a 5% aqueous ammonium sulfate solution using 1.5-in.-wide Whatman no. 1 paper strips using the ascending technique. The spots were detected on the dried papers, in a darkroom, using a Fisher Mineralite ultraviolet lamp (2537 Å.).