Spectra and Photolysis of the 1-Oxides of the Pyridinecarboxylic Acids and Pyridinecarboxamides

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The ultraviolet absorption spectra of aqueous and alcoholic solutions of the pyridinemonocarboxylic acids and amides, of the vicinal pyridinedicarboxylic acids, and of the 1-oxides of these compounds, were measured and qualitatively interpreted. The photolysis of the 1-oxides in aqueous solution resulted principally in their deoxygenation. Photolysis of picolinamide 1-oxide also gave a rearrangement product, 1-formyl-2-pyrrolecarboxamide. The photolyses of the 2- and 4-monosubstituted 1-oxides were somewhat faster than those of the 3-substituted 1-oxides. The experimental results are discussed in terms of possible hydrogen-bonding effects.

Although the photochemistry of heteroaromatic 1-oxides and their functional derivatives has been extensively examined in recent years, these investigations have neglected the 1-oxides of the pyridinecarboxylic acids and their derivatives. The only relevant example for these compounds appears to be a 1963 report that the absorption spectrum of an alcoholic solution of nicotinamide 1-oxide is altered by ultraviolet radiation (2). As a part of a continuing series of studies on the chemistry of cyclic imides, we recently reported our findings on the photolyses of the pyridinedicarboximide 1-oxides (3). The absence of published information on the photochemistry of the 1-oxides of the pyridinemonocarboxylic acids and amides, with which we could compare our results, led us to undertake a study of this topic.

Since the technique used for following the course of the photolysis reactions involved determination of the absorption spectra of the photolysis mixtures, the absorption spectra of the 1-oxides and of their parent bases were first determined. Table I summarizes the features of the ultraviolet absorption spectra of the three pyridinemonocarboxylic acids and their amides and the two vicinal dicarboxylic acids and their imides, in water and in ethanol solutions. The corresponding data for the 1-oxides are presented in Table II.

For all compounds listed in Table I, the absorption bands were slightly broader for aqueous solutions than for alcoholic ones, with the result that absorptions appearing as minor peaks in ethanol tended to become shoulders in water. This effect was somewhat greater for the acids than for the amides and imides. The aqueous solutions also showed enhancement of absorption intensities, indicating protonation of the ring nitrogen (4). This enhancement was considerably greater with the acids than with the amides and imides, which may be taken as supporting evidence for earlier conclusions (5) to the effect that the pyridinecarboxylic acids are nonionic in alcoholic solution, but are converted to zwitterions in aqueous solution.

The absorption spectra of the 1-oxides (Table II) are dominated by the spectral characteristics of the pyridine 1-oxide function (6). In the near ultraviolet this function displays a strong absorption band below 300 nanometers, and a weaker band above this wavelength. Both bands undergo blue-shifts with increasing solvent polarity, the weaker band often disappearing or becoming submerged. This solvent effect may result from interaction of the negative end of the 1-oxide dipole with the positive end of a solvent dipole to stabilize the ground state and increase the excitation energy.

A recent molecular-orbital study (7) of the excited states of pyridine 1-oxide indicates that the weaker absorption band involves a polarization at right angles to the ground-state dipole, and the stronger band involves polarization in the opposite direction to that of the ground state. These findings suggest that substitution at the 2-position by an electron-attracting group in conjugation with the 1-oxide function should lower the excitation energy for the band above 300 nanometers, and that similar substitution at the 4-position should have a comparable effect on the shorter-wavelength band. Such decreases in the excitation energies would be manifested by redshifts of the affected bands. The spectra data are largely in agreement with these expectations. The higher-energy band is appreciably redshifted for the 4-substituted compounds, isonicotinic acid 1-oxide and isonicotinamide 1-oxide, in comparison with the 2- and 3-substituted 1-

TABLE I

Ultraviolet Absorption Spectra of Pyridinecarboxylic Acids and Pyridinecarboxamides

	Acid				Amide or Imide			
	In Water		In Ethanol		In Water		In Ethanol	
Name	λ max, nm	log ε	λ max, nm	log ε	λ max, nm	log ε	λ max, nm	log ε
Picolinic	211	3.76	----	----	218	3.94	----	----
	258 (a)	3.71	258 (a)	3.53	259 (a)	3.59	258.5 (a)	3.54
	264	3.78	264	3.57	265	3.63	264	3.58
	271 (a)	3.67	272 (a)	3.39	274 (a)	3.41	273 (a)	3.35
Nicotinic	----	----	~215	----	~215	3.96	----	----
	256 (a)	3.42	256.5	3.41	256 (a)	3.44	257	3.40
	262	3.58	262	3.51	262	3.48	262	3.43
	269 (a)	3.37	269.5 (a)	3.32	269 (a)	3.35	270 (a)	3.36
Isonicotinic	----	----	----	----	203	3.92	----	----
	210 (a)	3.81	----	----	210	3.91	~218 (a)	----
	263	3.53	271	3.37	267	3.40	266	3.39
Quinolinic (b)	227 (a)	3.75	----	----	228 (a)	4.12	229.5 (a)	4.22
	----	----	259 (a)	3.37	235 (a)	3.96	236.5 (a)	4.01
	275	3.61	264	3.38	266	3.31	267	3.31
	----	----	271 (a)	3.16	271 (a)	3.20	272	3.37
Cinchomeronic (b)	----	----	----	----	224	4.08	223.5	4.09
	----	----	----	----	231.5	3.93	231.5	3.90
	262	3.68	271	3.15	279	3.44	271.5	3.48
	268 (a)	3.67	----	----	----	----	----	----

(a) Shoulder. (b) Data for Quinolinimide and Cinchomeronimide are quoted from Reference 3.

TABLE II

Ultraviolet Absorption Spectra of 1-Oxides

	Acid				Amide or Imide			
	In Water		In Ethanol		In Water		In Ethanol	
	λ max, nm	log ε	λ max, nm	log ε	λ max, nm	log ε	λ max, nm	log ε
Picolinic	204	4.16	~225	----	----	----	~225	----
	258.5	3.98	261.5	3.95	262	3.88	269	3.96
	----	----	308	3.11	303	3.09	312.5	3.21
	~313 (a)	2.65	~330 (a)	weak	----	----	----	----
Nicotinic	----	----	~220	----	----	----	----	----
	257.5	4.04	268	4.06	260	4.03	268.5	4.04
	~306 (a)	~2.6	312	2.89	~308 (a)	~2.7	~319 (a)	~2.7
Isonicotinic	212	4.20	~220	----	205.5	4.18	----	----
	273	4.21	287	4.23	278	4.21	287	----
Quinolinic (b)	210	4.27	~224	----	234	4.43	236	4.35
	259	3.99	268.5	3.98	273.5	3.98	282	3.96
	307	2.89	317.5	2.96	353	3.16	367	3.12
Cinchomeronic (b)	----	----	~230	----	239	4.02	241	4.23
	271	4.18	287	4.15	266	4.02	257	4.04
	----	----	----	----	330 (c)	2.7	331 (c)	3.67

(a) Shoulder. (b) Data for quinolinimide and cinchomeronimide 1-oxides are quoted from Reference 3. (c) Inflection.

oxides, and is also intensified. The same effects are observed for cinchomeronic acid 1-oxide. The difficulty in resolving the lower-energy band makes similar comparisons for it more difficult. This band is fully resolved for both aqueous and alcoholic solutions only for the 2-substituted compounds, picolinamide 1-oxide and quinolinic acid 1-oxide. It is completely undetectable, on the other hand, for the 1-oxides of isonicotinic acid and isonicotinamide, but this result may be due to a complete submergence beneath the end-absorption from the intense shorter-wavelength band. The effect of the imide moiety is peculiar. Both bands are redshifted for quinolinimide 1-oxide, the lower-energy band spectacularly, but neither is significantly enhanced; whereas neither band is significantly shifted with cinchomeronimide 1-oxide, but both show enhancement, at least in alcoholic solution.

The failure of most of these 2-substituted 1-oxides to show a redshifted lower-energy band may be attributed to two factors which would tend to increase the excitation energy for this band. First, intramolecular hydrogen-bonding of the carboxyl or amide protons to the 1-oxide oxygen atom would stabilize the ground state in the same fashion as a polar solvent. Second, ionization of the carboxyl group at the 2-position would decrease the tendency for electrons to be withdrawn in this direction. This may be the explanation for the absence of a clearly defined lower-energy band in the spectrum of picolinic acid 1-oxide in aqueous solution. None of these factors are present in the case of quinolinimide 1-oxide, the only one of the compounds displaying a substantially redshifted lower-energy band.

The apparently anomalous spectral behavior of cinchomeronimide 1-oxide may be accounted for by our earlier suggestion (3) that the 266-nanometer band of aqueous solutions of this compound is an unresolved composite of the two 1-oxide absorptions. For dilute aqueous hydrochloric acid solutions, this composite was resolved into two broad bands peaking at 256 and 304 nanometers, which may be assumed to represent the approximate locations of the contributors to the composite.

Photolyses of the 1-oxides in dilute aqueous solutions by irradiation above 300 nanometers resulted in deoxygenation. The absorption spectra of the terminal reaction mixtures also showed the presence of additional photoproducts in the cases of the photolyses of the 1-oxides of picolinamide and picolinic acid. A preparative-scale photolysis of picolinamide 1-oxide resulted in the isolation of picolinamide and a second product in approximately equal amounts.

The second product from picolinamide 1-oxide was demonstrated by elemental analysis and mass-spectral molecular weight determination to be an isomer of picolinamide 1-oxide. A review of the photochemistry of pyridine 1-oxides (8) indicates that their photoisomerization may lead to 1-formylpyrroles, 2-formylpyrroles, 2-pyridones, and 3-hydroxypyridines. Two of the photoisomers of picolinamide 1-oxide predictable on the basis of these models, 6-carboxamide-2-pyridone (9) and 3-hydroxypicolinamide (10), have previously been described, and were not identical with the product. A third possible product, 5-hydroxypicolinamide, was eliminated from consideration by the fact that the absorption spectrum of the product was not altered by base. The AMX pattern in the nuclear magnetic resonance spectrum of the product, and the exchange of only two protons with heavy water, lead to identification of the product as 1-formyl-2-pyrrolecarboxamide. The infrared spectrum was consistent with this structure assignment.

The photolyses of the 2- and 4-substituted 1-oxides of quinolinimide 1-oxide were complete in two to three hours. Longer reaction times were required for the other 1-oxides. Two of the 1-oxides, picolinic acid 1-oxide and quinolinimide 1-oxide, were also photolyzed in absolute alcohol, with roughly two-fold and five-fold increases in the reaction times, respectively.

Hydrogen-bonding may have effects upon the course of the photolysis reactions as well as on the absorption spectra. The melting points of picolinimide 1-oxide and of picolinic acid 1-oxide are about a hundred degrees lower than those of their 3- and 4-substituted isomers, a good indication for intramolecular hydrogen bonding. That the photoproduct, 1-formyl-2-pyrrolecarboxamide, is also internally hydrogen bonded is shown by the wide separation of the amide proton signals (δ 12.08 and 9.85) and by the absence of the broad out-of-plane amide NH_2 wagging frequency from its infrared spectrum. It appears that, in aqueous solutions, photorearrangement of these compounds may be assisted by intramolecular hydrogen-bonding of a functional group to the *N*-oxygen. This assistance must be in the initial stages of the reaction, since internal hydrogen bonding could not be maintained throughout a photorearrangement following any of the currently accepted mechanisms (8). The greater ability of water to form hydrogen bonds, as compared with ethanol, provides an explanation for the significantly faster rates of photolysis of the 1-oxides of picolinic acid and of quinolinimide in water.

EXPERIMENTAL

Melting points were determined with an Electrothermal apparatus and are uncorrected. Ultraviolet absorption spectra were determined with a Cary Model 15 spectrophotometer, infrared spectra with a Perkin-Elmer 225 spectrophotometer, nuclear magnetic resonance spectra with a Varian A-60A spectrometer, and mass spectra with a Consolidated Electrodynamics 21-104 single-focus mass spectrometer. Microanalyses were done by Midwest Microlab, Inc., Indianapolis, Indiana.

Synthesis and Purification of 1-Oxides.

Commercial (11) picolinic acid 1-oxide was recrystallized from water, m.p. 163-164° dec.; reported (12) 163-164° dec. The other monosubstituted 1-oxides were prepared by the method of Gardner, *et al.* (13) by oxidation of the parent bases with 40% peracetic acid. The compounds, yields, recrystallization solvents, and melting points were, respectively: picolinamide 1-oxide, 75%, acetone, 160-161° dec., reported (14) 161-162°; nicotinic acid 1-oxide, 84%, ethanol, 259-260° dec., reported (15) 254-255° dec.; nicotinamide 1-oxide, 71%, water, 285-286° dec., reported (16) 287°; isonicotinic acid 1-oxide, 69%, water, 270-271°, reported (17) 264-266°; and isonicotinamide 1-oxide, 55%, water, 312-313° dec., reported (18) 306°. The 1-oxides of quinolinic and cinchomeronic acids were prepared from the sodium salts by the method of Dunn and Heywood (19), giving quinolinic acid 1-oxide, 46%, water, m.p. 263-264° dec., reported (20) 260-261° dec.; and cinchomeronic acid 1-oxide, 51%, water, m.p. 248-249° dec., reported (20) 249-250° dec. The preparations of quinolinimide and cinchomeronimide 1-oxides have been described earlier (3).

Photolyses of 1-Oxides.

Photolyses were carried out with a 100-watt Hanovia medium pressure mercury immersion lamp with a Pyrex thimble, at ambient temperature, using 600 ml. of 3 x 10^{-3} molar solutions of 1-oxides in distilled water or absolute ethanol. Samples were withdrawn at intervals, diluted, and their ultraviolet absorption spectra were measured. Irradiations were stopped when the spectra were unchanged after a 10% extension of the irradiation time. These reaction times were as follows: picolinic acid 1-oxide in water, 2.5 hours, in ethanol, 5.5 hours; picolinamide 1-oxide in water, 2.5 hours; nicotinic acid 1-oxide in water, 5.5 hours; nicotinamide 1-oxide in water, >100 hours; isonicotinic acid 1-oxide in water, 1.8 hours; isonicotinamide 1-oxide in water, 3.0 hours; quinolinic acid 1-oxide in water, 16.9 hours; quinolinimide 1-oxide in water, 2.2 hours, in ethanol, 9.8 hours; cinchomeronic acid 1-oxide in water, 5.3 hours; and cinchomeronimide 1-oxide in water, 5.3 hours.

1-Formyl-2-pyrrolecarboxamide.

A solution of 5 g. (0.036 mole) of picolinamide 1-oxide in 600 ml. of water was irradiated for 55 hours. The solution was evaporated to dryness under reduced pressure, and the residue was dissolved in 95% ethanol. The ethanol solution was chromatographed on a neutral alumina column. Evaporation of the ethanol eluate gave 2.8 g. of dark reddish-brown material, which was extracted with hot benzene. Evaporation of the benzene extract gave 1.0 g. (23%) of picolinamide, which was identified by its uv and ir spectra.

The benzene-insoluble residue was redissolved in ethanol and chromatographed on basic alumina. The residue from the ethanol eluate was 1.1 g. (22%) of brownish-yellow powder. Four recrystallizations from water gave a white powder, m.p. 231-234°; uv max (95% ethanol) 249 nm (log ϵ 4.03), 257.5 nm (log ϵ 3.92), 310 nm (log ϵ 4.03), shoulder 335 nm (log ϵ 3.70); ir (potassium bromide) 3390, 3230 cm^{-1} (NH), 1663 cm^{-1} (formyl CO), 1655, 1647 cm^{-1} (amide CO), 1557, 1519 cm^{-1} (pyrrole), 740 cm^{-1} (CH=CH); nmr (DMSO-d_6) δ 12.08 (s, 1, NH), 9.85 (s, 1, NH), 8.63 (s, 1, CHO), 8.39 (q, 1, J_{AX} = 7.5 Hz), 7.73 (q, 1, J_{MX} = 5.6 Hz), 6.63 (q, 1, J_{AM} = 2.0 Hz); mass spectrum (70eV) m/e (rel intensity) 138 (36), 110 (100), 82 (30), 81 (28), 55 (30), 54 (20), 44 (17), 43 (18), 41 (19). The nmr signals at δ 12.08 and 9.85 disappeared on addition of a deuterium oxide solution of sodium deuteroxide.

Anal. Calcd. for $C_6H_6N_2O_2$: C, 52.17; H, 4.38; N, 20.28. Found: C, 52.15; H, 4.04; N, 19.96.

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