Cyclic Imides. VIII. The Azaphthalimides and Azaphthalimide-1-Oxides: A Near-Ultraviolet Study (1)

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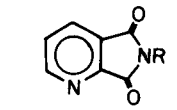
Received June 7, 1971

Earlier papers (3) in this series have dealt with the spectrophotometric properties of, and the action of bases on, a variety of phthalimide derivatives. These studies demonstrated that the imide portion of this structure exerts a sufficient electron-withdrawing effect to activate a 3-substituent to nucleophilic displacement (4). The effects of 3- and 4-substituents on the alkoxide-catalyzed Gabriel-Colman rearrangement of phthalimidoacetic esters were also examined (3,4,5).

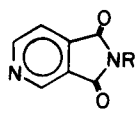
It was of interest to determine to what extent the characteristics of the phthalimide grouping carried over to the isoelectronic aza-analogs of phthalimide, quinolinimide (Ia) and cinchomeronimide (IIa), and to their derivatives, quinolinimidoacetic acid (Ib), cinchomeronimidoacetic acid (IIb), quinolinimide-1-oxide (III), and cinchomeronimide-1-oxide (IV). Of these compounds, only Ia and IIa have previously been described, although esters of Ib and IIb were long ago prepared by the Gabriel method. These esters have been shown to give the Gabriel-Colman rearrangement in the normal manner (6). This rearrangement, however, has also been observed for nonaromatic α-imidoesters (7), and is therefore not indicative of generally phthalimide-like properties. The preparations of Ib and IIb were accomplished by heating glycine with the appropriate anhydride in *N,N*-dimethylformamide. The azaphthalimide-1-oxides, III and IV, were prepared by oxidation of Ia and IIa with peracetic acid. The ultraviolet absorption spectra of these compounds were determined for solutions in 95% ethanol, distilled water, 0.1 *M* hydrochloric acid, 2.0 *M* hydrochloric acid, and 0.1 *M* sodium hydroxide. The characteristics of the absorption spectra are presented in Table I.

The spectral behavior of quinolinimide (Ia) and of quinolinimidoacetic acid (Ib) is similar to that of phthalimide, whose absorption spectrum also shows a slight weakening in the intensity of the long-wavelength band in dilute (0.1 *M*) hydrochloric acid as compared with ethanol (5). The general similarity of the spectra of Ia and Ib, together with the general similarity of behavior to that of phthalimide, argue against zwitterion formation to any significant degree in Ib, and against any significant protonation of the pyridine ring in these compounds, in 0.1 *M* hydrochloric acid. The increased molar absorptivities of Ia and Ib in 2.0 *M* hydrochloric acid indicate, on the other hand, that there is significant, but probably not complete, protonation of the pyridine ring at this acid concentration. This conclusion is based on observations by others (8) that pyridinium ions have enhanced absorptivities in comparison with the free bases, but very similar absorption wavelengths.



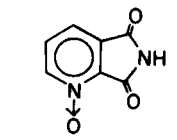
Ia R = H

Ib R = CH_2CO_2H

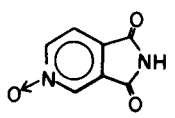


IIa R = H

IIb R = CH_2CO_2H



III



IV

Similar comparisons of the spectral behavior of IIa and IIb in alcohol and in 0.1 *M* hydrochloric acid with each other and with phthalimide likewise suggests an absence of zwitterionization in IIb, but the appreciable increases in the molar absorptivities in the acid solutions show appreciable protonation. The protonation is further enhanced in 2 *M* hydrochloric acid. It may be concluded that the 4-azaphthalimides are stronger bases than the 3-azaphthalimides. This conclusion is not surprising in view of the observations made elsewhere (4) upon the effects of imide moiety in activating a 3-substituent to nucleophilic displacement. Both the suppression of basicity in the 3-azaphthalimides and the nucleophilic activation of 3-substituents indicate a very strong electron-withdrawing effect upon the 3-position by the imide grouping. This effect evidently does not extend to the 4-position to a large degree.

The spectral behavior of the azaphthalimide-1-oxides (III and IV) in alcoholic and aqueous solution is generally

TABLE I

Ultraviolet Absorption Spectra of Azaphthalimides and Azaphthalimide 1-Oxides

Compound	In 95% Ethanol		In Water		In 0.1 *M* HCl		In 2.0 *M* HCl		In 0.1 *M* NaOH	
	λ max, nm	log ε max	λ max, nm	log ε max	λ max, nm	log ε max	λ max, nm	log ε max	λ max, nm	log ε max
Ia	229.5 (a)	4.22	228 (a)	4.12	228 (a)	4.18	228 (a)	4.15	----	----
	236.5 (a)	4.01	235 (a)	3.96	236 (a)	4.01	236 (a)	3.98	----	----
	267	3.31	266	3.31	266	3.27	269	3.41	265	3.49
	272	3.37	271 (a)	3.20	281 (a)	3.16	----	---	272 (a)	3.43
Ib	230 (a)	4.21	230 (a)	4.1	230 (a)	4.16	230 (a)	4.14	----	----
	238 (a)	4.03	238 (a)	4.0	238 (a)	4.01	238 (a)	3.99	----	----
	272	3.40	273	3.43	271	3.35	272	3.39	265	3.55
	281 (a)	3.32	281 (a)	3.31	281 (a)	3.27	280 (a)	3.32	272 (a)	3.50
IIa	223.5	4.09	224	4.08	224	3.99	225 (a)	3.87	----	----
	231.5	3.90	231.5	3.93	231	3.82	232 (a)	3.83	----	----
	271.5	3.48	279	3.44	272	3.65	272	3.74	265	3.42
IIb	224	4.4	224 (a)	4.0	224	4.04	221 (a)	4.05	----	----
	232	4.03	232 (a)	3.8	232	3.87	232 (a)	3.80	----	----
	280	3.54	272	3.48	275	3.62	277	3.75	262	3.52
III	236	4.35	234	4.43	235	4.45	235	4.42	224	4.24
	282	3.96	273.5	3.98	275	3.98	275	3.91	262	3.95
	367	3.12	353	3.16	353	3.11	352	3.13	307 (a)	2.81
IV	241	4.23	239	4.02	239	4.32	239	4.27	----	----
	257	4.04	266	4.02	256.5	4.11	256	4.10	272	4.12
	311	3.85	---	---	304	3.74	304	3.71	----	----
	331 (b)	3.67	330 (b)	2.7	---	---	329 (b)	3.48	----	----

(a) Shoulder. (b) Inflection.

more characteristic of the pyridine-1-oxide function than of the cyclic imide function. A blue-shift with increasing solvent polarity is observed for the two longest wavelength bands in the spectra of III in ethanol and in water. This effect is usual with pyridine-1-oxides (9), and identifies the two bands as corresponding to the 280-nm and 330-nm bands of pyridine-1-oxide. The spectrum of the aqueous solution of IV is less readily interpreted. We suggest that the band appearing at 266-nm for this solution is an unresolved composite of the bands appearing at 257 and 311-nm in alcohol. The latter band is the only one in the spectra of this compound which shows the shifts with solvent polarity characteristic of a 1-oxide. An additional band was also sometimes observed in the spectra of IV as a very poorly resolved inflection at about 330-nm.

Protonation of pyridine-1-oxide derivatives may result in either red-shifts or blue-shifts, but nearly always produces a large decrease in absorptivity (10). None of these effects are observed in the spectra of acidic solutions III and IV, which therefore must not be significantly protonated, even in 2 *M* hydrochloric acid.

All of the azaphthalimides and azaphthalimide-1-oxides showed blue-shifts in basic solution. This behavior is characteristic of the cyclic imide moiety, and is attributable to saponification of the imide ring to form an amate ion (5). The spectra of the basic solutions were indeed similar to that of the phthalamate ion, which shows a single peak at 269-nm (11).

Photolyses of III and IV were carried out with wavelengths above 300-nm, in aqueous solution. The choice of water as a solvent was dictated by the solubilities of these compounds, and the concentration used, 3×10^{-3} *M*, is close to the limit imposed by the solubility of III in water. The photolyses were followed by withdrawing samples at convenient intervals and measuring their absorption spectra. In the cases of both 1-oxides, the absorption spectra ultimately became identical with those of the parent compounds, Ia and IIa, indicating that deoxygenation was the major, and probably only, photolysis reaction occurring. The photolysis of III was complete in 2.2 hours, and that of IV in 5.3 hours.

EXPERIMENTAL

Melting points were determined with an Electrothermal apparatus and are uncorrected. Ultraviolet absorption spectra were determined with a Cary Model 15 recording spectrophotometer, and infrared spectra with a Beckman IR-5 spectrophotometer. Microanalyses were done by Midwest Microlab, Indianapolis, Ind.

Materials.

Commercially available pyridinedicarboxylic acids were converted to their anhydrides and imides by published methods (12). The 40% peracetic acid solution was purchased from the FMC Corporation.

Quinolinimidoacetic Acid (Ib).

A mixture of 6.0 g. quinolinic anhydride, 3.3 g. glycine, and 24 ml. *N,N*-dimethylformamide was maintained with stirring for one hour at 80-100°. The mixture was then cooled to room temperature and filtered. Evaporation of the filtrate under reduced pressure gave 5.5 g. (66%) of material, which was triturated with hot chloroform and recrystallized once from tetrahydrofuran and once from acetone to give pure Ib, m.p. 240-244° with decomposition.

Anal. Calcd. for $C_9H_6N_2O_4$: C, 52.43; H, 2.93; N, 13.59. Found: C, 52.23; H, 3.09; N, 13.84.

Cinchomeronimidoacetic Acid (IIb).

A mixture of 4.5 g. cinchomeronic anhydride, 2.5 g. glycine, and 18 ml. *N,N*-dimethylformamide was stirred for one hour at 80-100°. The mixture was cooled to room temperature and filtered. Concentration of the filtrate under reduced pressure gave 4.0 g. (64.5%). Several recrystallizations by solution in hot *N,N*-dimethylformamide and addition of chloroform gave IIb, m.p. 243-245°.

Anal. Calcd. for $C_9H_6N_2O_4$: C, 52.43; H, 2.93; N, 13.59. Found: C, 52.34; H, 3.18; N, 13.48.

Quinolinimide 1-Oxide (III).

A mixture of 4 g. of quinolinimide and 40 ml. of 40% peracetic acid was maintained at 50° with stirring until the mixture became homogeneous. The mixture was then stirred at room temperature for four days, then filtered. The precipitate was washed with ice-water and dried, giving 2.16 g. (49%) of III, m.p. 271-275°. One recrystallization from water gave a pale-yellow powder, m.p. 278-279° with decomposition; ir (potassium bromide) 1230 cm^{-1} (*N*-oxide band).

Anal. Calcd. for $C_7H_4N_2O_3$: C, 51.22; H, 2.46; N, 17.07. Found: C, 50.94; H, 2.43; N, 17.19.

Cinchomeronimide 1-Oxide (IV).

A mixture of 2 g. of cinchomeronimide and 20 ml. of 40% peracetic acid was stirred at room temperature until the solid had completely dissolved, then at 35-40° for three hours. The precipitate was triturated with ice-water to give 0.9 g. (41%) of IV, m.p. 318-319° dec.; ir (potassium bromide) 1235 cm^{-1} (*N*-oxide band).

Anal. Calcd. for $C_7H_4N_2O_3$: C, 51.22; H, 2.46; N, 17.07. Found: C, 50.98; H, 2.65; N, 17.12.

Photolyses of III and IV.

Photolyses were carried out with a 100-watt Hanovia medium pressure mercury immersion lamp with a Pyrex thimble. All photolyses were done at ambient temperature, using 600 ml. of 3×10^{-3} molar solutions of III or IV in distilled water.

Acknowledgements.

We wish to thank Dr. Linda T. Creagh for assistance with the photolysis experiments, and Miss Allice Y. Chen for determining some of the absorption spectra.

REFERENCES

(1) The authors gratefully acknowledge financial support of this work in part by The Robert A. Welch Foundation, through Grant No. M-101, and in part by an Institutional Research Grant from The Texas Woman's University.

(2) To whom correspondence should be addressed.

(3) Most recent paper: L. R. Caswell, R. A. Haggard, and

D. C. Yung, *J. Heterocyclic Chem.*, 5, 865 (1968).

(4) L. R. Caswell and T. L. Kao, *ibid.*, 3, 333 (1966).

(5) L. R. Caswell and P. C. Atkinson, *ibid.*, 3, 328 (1966).

(6a) S. Gabriel and J. Colman, *Ber.*, 35, 1358 (1902); (b) E. Ochiai and I. Arai, *J. Pharm Soc. Japan*, 59, 458 (1939); *Chem. Abstr.*, 34, 108 (1940).

(7) T. Nagase, *Bull. Chem. Soc. Japan*, 37, 1175 (1964).

(8) R. J. L. Andon, J. D. Cox, and E. F. G. Herington, *Trans. Faraday Soc.*, 50, 918 (1954).

(9) E. Ochiai, "Aromatic Amine Oxides", Elsevier Publishing Co., Amsterdam, 1967, pp. 126-131.

(10) H. H. Jaffe, *J. Am. Chem. Soc.*, 77, 4451 (1955).

(11) L. R. Caswell, P. L. Wright, and D. D. Adams, *Texas J. Sci.*, 17, 334 (1965).

(12a) Y. Arata, S. Sakumoto, and R. Ito, *Yakugaku Zasshi*, 77, 1347 (1957); (b) J. C. Cochran and W. F. Little, *J. Org. Chem.*, 26, 808 (1961); (c) J. D. Crum and C. H. Fuchsman, *J. Heterocyclic Chem.*, 3, 252 (1966).