Notes

Decarboxylation of Some 2-Substituted Pyridinecarboxylic Acids

Russell J. Moser and Ellis V. Brown*

Department of Chemistry, University of Kentucky, Lexington, Kentucky 40506

Received September 3, 1970

Previous investigations have dealt with the decarboxylation of 2-pyridinecarboxylic acids in various solvents.[1-6]

We believed that 3- and 4-pyridinecarboxylic acids would not decarboxylate in 3-nitrotoluene at measureable rates since the rates of decarboxylation of these acids (266°, $k = 6.0 \times 10^{-5}$ sec^{-1}, and 288°, $k = 6.0 \times 10^{-5}$ sec^{-1}, respectively) in pyrene are so small.[7] We felt that by placing electron-withdrawing and -attracting groups at the 2 position we might be able to lower the temperature at which decarboxylation takes place.

We synthesized 2-chloro- and 2-nitro-*x*-pyridinecarboxylic acids (x = 3, 4, and 5) and 2-bromo-, 2-amino-, and 2-acetamido-3-pyridinecarboxylic acids and determined their rates of decarboxylation in 3-nitrotoluene. We then compared them with the rate of decarboxylation of 3-pyridinecarboxylic acid in 3-nitrotoluene. The rate constants are summarized in Table I. All of the rates reported have been duplicated. We wish to point out that the coefficients of variation are not so small as usually expected. The rates at the lowest temperature are at the lower limit for convenient measurement with our apparatus. This and the boiling point of 3-nitrotoluene (232°) contributed to the difficulty. However, we feel that the significant point is that at all temperatures used the relative order of the rates of decarboxylation was the same.

2-Substituted 3-Pyridinecarboxylic Acids.—2-Nitro-, 2-chloro-, and 2-bromo-3-pyridinecarboxylic acids decarboxylated below 227° in 3-nitrotoluene. We attempted to decarboxylate 3-pyridinecarboxylic acid in 3-nitrotoluene at 202 and 222°, but in neither case did the acid decarboxylate at a measureable rate. Some carbon dioxide did evolve at both temperatures; however, no accurate determination of a rate constant was possible. We found that the rate of decarboxylation decreased as the electron-withdrawing ability of the substituent decreased; consequently, electron-donating substituents should not encourage decarboxylation at these temperatures. This was found to be the case for a mixture of 2-amino-3-pyridinecarboxylic acid and 2-acetamido-3-pyridinecarboxylic acid.

Table I

Rate Data for the Decarboxylation of 2-Substituted Pyridinecarboxylic Acids in 3-Nitrotoluene

Compd (registry no.)	Temp, °C	Rate constant × 10^4 sec^{-1}	Coefficient variation
2-Nitro-3-pyridinecarboxylic acid (33225-72-8)	211	1.2	4.3
	216	2.0	2.1
	221	3.8	6.8
	227	6.5	5.3
2-Nitro-4-pyridinecarboxylic acid (33225-74-0)	217.2	N.R.[a]	
2-Nitro-5-pyridinecarboxylic acid (33225-73-9)	193.5	N.R.	
	216.0	N.R.	
2-Nitro-6-pyridinecarboxylic acid[b] (26893-68-5)	189.9	0.53	3.76
	195.0	0.78	1.26
	199.7	1.47	1.82
	204.8	2.16	4.10
	210.1	2.99	2.02
2-Chloro-3-pyridinecarboxylic acid (2942-59-8)	209	0.7	1.4
	215	1.0	1
	219	1.3	8
	227	1.7	1.4
2-Chloro-4-pyridinecarboxylic acid (6313-54-8)	225.0	<0.1	
2-Chloro-5-pyridinecarboxylic acid (5326-23-8)	224.4	≤0.1	
2-Chloro-6-pyridinecarboxylic acid[b] (4684-94-0)	190.3	0.93	0.70
	194.6	1.74	2.24
	200.4	2.12	4.04
	205.3	3.71	1.08
	210.9	6.39	2.17
2-Bromo-3-pyridinecarboxylic acid (35905-85-2)	210	0.58	9.2
	215	0.74	8.7
	220	0.91	9.2
	223	1.1	8.9
3-Pyridinecarboxylic acid (59-67-6)	202	<0.1	
	222	≤0.1	
Mixture of 2-amino-3-pyridinecarboxylic acid and 2-acetamido-3-pyridinecarboxylic acid	220.8	N.R.	

[a] No reaction. [b] R. J. Moser and E. V. Brown, *J. Org. Chem.*, **36**, 454 (1971).

Other 2-Substituted Pyridinecarboxylic Acids.—After observing that electron-withdrawing groups at the 2 position lower the activation energy of decarboxylation for the 3-pyridinecarboxylic acids, we decided to investigate if this electron-withdrawing effect would lower the temperature of decarboxylation of the other 2-substituted pyridinecarboxylic acids. We synthesized 2-nitro- and 2-chloro-*x*-pyridinecarboxylic acids (x = 4 and 5) and attempted to decarboxylate them. None of these acids decarboxylated in

---

(1) L. W. Clark, *J. Phys. Chem.*, **66**, 125 (1962).

(2) L. W. Clark, *ibid.*, **69**, 2277 (1965).

(3) N. H. Cantwell and E. V. Brown, *J. Amer. Chem. Soc.*, **74**, 5967 (1952).

(4) N. H. Cantwell and E. V. Brown, *ibid.*, **75**, 4466 (1953).

(5) R. J. Moser and E. V. Brown, *J. Org. Chem.*, **36**, 454 (1971).

(6) A. Kandea and T. Hara, *Sci. Eng. Rev. Doshisha Univ.*, **7**, (4), 172 (1967).

(7) H. Schenkel and M. Schenkel-Klein, *Helv. Chim. Acta*, **31**, 924 (1948).

3-nitrotoluene at measurable rates below 227°. Thus, it seems clear that electron-withdrawing substituents at the 2 position will significantly increase the rate of decarboxylation of 3-pyridinecarboxylic acid only.

Experimental Section

Starting material, unless otherwise specified, is 2-amino-x-methylpyridine (x = 3, 4, and 5) purchased from Reilly Tar and Chemical Corp., Chicago, Ill. The apparatus and procedure used to collect the kinetic data has been described previously.[5] Melting points were determined with a Fisher-Johns block and are uncorrected.

Preparation of 2-Nitro-3-pyridinecarboxylic Acid.—This compound was prepared *via* oxidation of the amino group[8] followed by oxidation of the methyl group[9] of 2-amino-3-methylpyridine. It had mp 156° (lit.[10] mp 156°).

Anal. Calcd for $C_6H_4N_2O_4$: C, 42.8; H, 2.4; N, 16.7. Found: C, 42.7; H, 2.9; N, 16.4.

Preparation of 2-Nitro-4-pyridinecarboxylic Acid.—2-Nitro-4-pyridinecarboxylic acid was synthesized from 2-amino-4-methylpyridine by the same procedure as above. It had mp 174° (lit.[10] mp 175°).

Anal. Calcd for $C_6H_4N_2O_4$: C, 42.8; H, 2.4; N, 16.7. Found: C, 42.7; H, 2.3; N, 16.4.

Preparation of 2-Nitro-5-pyridinecarboxylic Acid.—This compound was prepared from 2-amino-5-methylpyridine by the same procedure as used to make 2-nitro-3-pyridinecarboxylic acid. It had mp 183° (lit.[10] mp 183°).

Anal. Calcd for $C_6H_4N_2O_4$: C, 42.8; H, 2.4; N, 16.7. Found: C, 42.4; H, 2.5; N, 16.3.

Preparation of 2-Chloro-3-pyridinecarboxylic Acid.—2-Chloro-3-pyridinecarboxylic acid was synthesized *via* diazotization of the amino group[11] followed by oxidation of the methyl group[9] of 2-amino-3-methylpyridine. It had mp 200–201° (lit.[10] mp ~192–193°).

Anal. Calcd for $C_6H_4ClNO_2$: C, 45.7; H, 2.5; N, 8.9. Found: C, 45.4; H, 2.8; N, 9.2.

Preparation of 2-Chloro-4-pyridinecarboxylic Acid.—This compound was prepared from 2-amino-4-methylpyridine by the same procedure as above. It had mp 249–251° (lit.[10] mp 245°).

Anal. Calcd for $C_6H_4ClNO_2$: C, 45.7; H, 2.5; N, 8.9. Found: C, 45.4; H, 2.8; N, 9.2.

Preparation of 2-Chloro-5-pyridinecarboxylic Acid.—2-Amino-5-methylpyridine was diazotized and oxidized to prepare 2-chloro-5-pyridinecarboxylic acid by the same procedure as used to make 2-chloro-3-pyridinecarboxylic acid. It had mp 194–195° (lit.[10] mp ~199°).

Anal. Calcd for $C_6H_4ClNO_2$: C, 45.7, H, 2.5; N, 8.9. Found: C, 45.9; H, 2.8; N, 9.0.

Preparation of 2-Bromo-3-pyridinecarboxylic Acid.—2-Bromo-3-pyridinecarboxylic acid was synthesized *via* diazotization[12] followed by oxidation[9] of 2-amino-3-methylpyridine. It had mp 254° (lit.[10] mp 249–250°).

Anal. Calcd for $C_6H_4BrNO_2$: C, 35.6, H, 2.0; N, 6.9. Found: C, 35.3; H, 2.0; N, 6.5.

3-Pyridinecarboxylic Acid.—This compound was purchased from Reilly Tar and Chemical Corp. It had mp 234° (lit.[10] mp 236°).

Anal. Calcd for $C_6H_5NO_2$: C, 58.5; H, 4.1; N, 11.4. Found: C, 58.1; H, 4.0; N, 11.3.

Preparation, Determination of Per Cent Composition and Kinetics of 2-Amino- and 2-Acetamido-3-pyridinecarboxylic Acid Mixture.—This mixture was synthesized *via* acetylation[11] followed by oxidation[13] of 2-amino-3-methylpyridine. In the oxidation step partial hydrolysis of the amide linkage took place. The per cent composition was determined by titrating a given amount of sample with standardized NaOH and solving two simultaneous equations. The mixture was found to be 15% 2-acetamido-3-pyridinecarboxylic acid and 85% 2-amino-3-pyridinecarboxylic acid. The kinetics were run as described above; however, a twofold excess of the mixture was used as compared to the above acids in an effort to determine if any CO_2 was evolved. The reaction was run for over 1 hr. During this time no CO_2 was detected.

---

(8) R. H. Wiley and J. L. Hartman, *J. Amer. Chem. Soc.*, **73**, 494 (1951).

(9) E. V. Brown, *ibid.*, **76**, 3167 (1954).

(10) E. P. Oliveto, *Heterocycl. Compounds*, **14** (3), Chapter 10 (1962).

(11) S. M. McElvain, "The Characterization of Organic Compounds," Rev. Ed., Macmillan, New York, N. Y., 1964, p 210–201.

(12) L. C. Craig, *J. Amer. Chem. Soc.*, **56**, 231 (1934).

(13) G. Ferrari and E. Marcon, *Educ. Sci.*, **14**, 594 (1959); *Chem. Abstr.*, **54**, 6709*a* (1960).

Preparation and Photolysis of Esters of Perphthalic Acid[1]

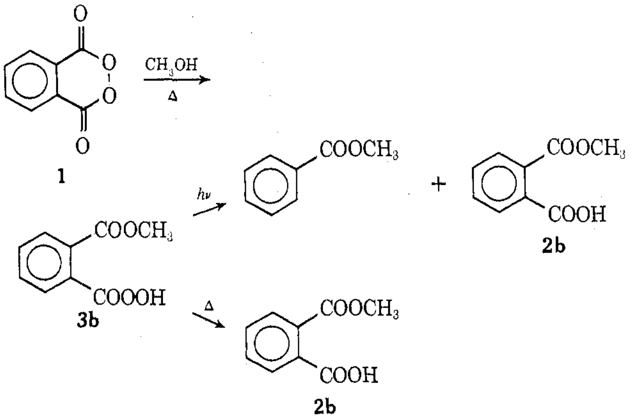
MARK R. DECAMP[2] AND MAITLAND JONES, JR.*

Department of Chemistry, Princeton University, Princeton, New Jersey 08540

Received May 10, 1972

Phthaloyl peroxide (**1**)[3,4a] has long been recognized as a highly reactive species. Greene and coworkers discovered the facile addition of **1** to unsaturated systems[4b–f] and attributed its reactivity to the inherent strain of a planar six-membered array containing a peroxide linkage. Horner and Brüggemann[5] studied thermal decompositions of **1** in a variety of substrates and found that the reactivity and rate of decomposition of **1** was considerably greater than that of its acyclic relative, benzoyl peroxide. Although they allude to the basic hydrolysis of **1**,[6] Horner and Brüggemann do not report any further reactions with hydroxylic oxygen nucleophiles. Greene[4a] also briefly mentioned the slow dissolution of **1** in water "with concomitant hydrolysis to monoperphthalic acid." We describe here the reaction of **1** with water and alcohols to give monoperphthalic acid and its esters. We further report the photolytic decomposition of these compounds.

Upon overnight refluxing of **1** in methanol, a quantitative conversion to phthalic acid monomethyl ester (**2b**) was effected. Ester **2b** was identified by inspection of spectra, conversion to phthalic anhydride on gas chromatography, and formation of dimethyl phthalate



---

[1] Support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged (5528 AC1, 4).

[2] National Science Foundation Trainee, 1970–1971; *Petroleum Research Fund Fellow*, 1971–1972.

[3] K. E. Russell, *J. Amer. Chem. Soc.*, **77**, 4814 (1955).

[4] (a) F. D. Greene, *ibid.*, **78**, 2246 (1956); (b) *ibid.*, **78**, 2250 (1956); (c) F. D. Greene and W. W. Rees, *ibid.*, **80**, 3432 (1958); (d) F. D. Greene, *ibid.*, **81**, 1503 (1959); (e) F. D. Greene and W. W. Rees, *ibid.*, **82**, 890 (1960); (f) *ibid.*, **82**, 893 (1960).

[5] L. Horner and H. Brüggemann, *Justus Liebigs Ann. Chem.*, **635**, 22 (1960).

[6] Phthaloyl peroxide was dissolved in 0.1 *M* NaOH to form sodium phthalate and the sodium salt of monoperphthalic acid.