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Synthesis of Mercurated Pyridine-3-carboxylic Anhydride and Its Reaction with Nucleophilic Reagents

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Mercurated pyridine-3-carboxylic anhydride (III), obtained by the reaction of pyridine-2,3-dicarboxylic acid with mercuric oxide, showed a carbonyl absorption in the IR spectrum at extremely low wave number, indicating that the oxygen-mercury bond is ionic in nature, and thus that compound (III) takes an ionic structure (III′). The carbon bonded with mercury is reactive with nucleophilic reagents (SH^-, CN^-, I^-), as would be expected.

Keywords——pyridine-2,3-dicarboxylic acid; mercuric oxide; infrared spectrum; carbonium ion; oxygen-mercury bond; mercury compound; ionic structure pyridine ring

Previous papers[2,3] have reported the synthesis of mercury compounds of aromatic and aliphatic rings which contain a carbon-mercury bond.[4–7] In the present work, pyridine-2-mercuri-3-carboxylic anhydride (III) was obtained by the reaction of mercuric oxide with pyridine-2,3-dicarboxylic acid in acetic acid. The mercuration of pyridine-2,3-dicarboxylic acid (I) by a method similar to that used for the synthesis of mercurated naphthalic anhydride (IX) and mercurated norbornene (XII), was examined, and it was found that refluxing a mixture of sodium hydroxide solution of 1 with an acetic acid solution of mercuric oxide, maintained at pH 5.0—5.7, for a long time resulted in loss of the carboxyl group at the 2-position, and a compound (II) having mercury bonded to the carbon in the 2-position was obtained.

This mercury compound (III) was sparingly soluble in water and organic solvents but was stable in air. The results of elemental analysis of III supported the structure III or III′ (Chart 1), and the presence of mercury in III was confirmed by detection of mercury by the X-ray intensity method at 35600 cps, as well as by the peak of mercury absorption 2537 Å in atomic absorption spectrometry.

Treatment of III dissolved in sodium hydroxide solution with acetic acid gave pyridine-2-acetoxymercuri-3-carboxylic acid (IV), the nuclear magnetic resonance (NMR) spectrum of this compound exhibited a signal due to hydrogen in the methyl group $HgOCOCH_3$ as a singlet at δ 2.4 ppm. This evidence, together with the results of the X-ray intensity method and atomic absorption spectrometry, indicated that the structure of this mercurated compound can be represented by III in Chart 1.

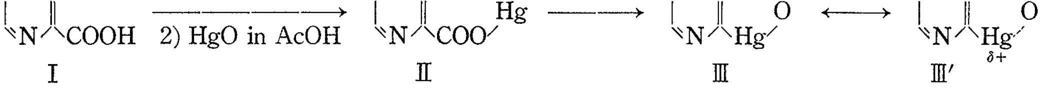

Chart 1

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[1] Location: *Miyama 2-2-1, Funabashi, Chiba-ken 274, Japan.*

[2] T. Takahashi, *Yakugaku Zasshi*, **98**, 358 (1978); **98**, 1568 (1978).

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[4] T. Swanney, C. Skeeters, and A.T. Shreve, *Ind. Eng. Chem.*, **32**, 360 (1940).

[5] C.A. Grob and G. Cseh, *Helv. Chim. Acta*, **47**, 194 (1964).

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For the of comparison, the infrared (IR) absorptions of the carbonyl group in the mercurated compounds (IX and XII) obtained earlier[2,3] are also shown in Table I, together with IR absorption data for III. A characteristic of the IR spectrum of this mercurated pyridine-3-carboxylic anhydride (III) is that the absorption of the carbonyl group appears at 1580 cm^{-1}, at considerably lower wave number than carbonyl groups in general.

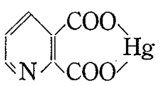
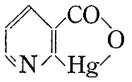
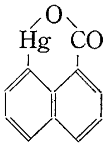
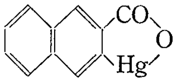
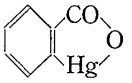
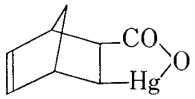
This indicates that this carbonyl is similar in nature to a carboxylate ion, and that the oxygen-mercury bond, which had been assumed to be covalent, is actually a highly polar ionic bond. This in turn has an inductive effect on the carbon atom of the aromatic ring δ-bonded with mercury, and is expected to lower the electron density at the bonding site. In other words, III takes the structure III′.

In order to investigate the effects of this structure, reaction of III with nucleophilic reagents was carried out.

The two carboxyl groups in quinolinic acid appear at 1600 and 1590 cm^{-1} in the IR spectrum, *i.e*, at lower wave number than those bonded directyl to other aromatic rings.

Compound III reacted with hydrogen sulfide gas bubbled through a suspension of III in glacial acetic acid at room temperature, yielding a compound (V) by the replacement of mercury with SH. Reaction of III with cyanide resulted in the replacement of mercury with the CN group to form the compound (VII).

Table I. IR Spectra of Carboxylic Acid Mercuri-anhydride Compounds

	Compound	IR (in KBr) $\nu_{C=O}$ (cm^{-1})
II		1590
III		1580
IX		1530
X		1620
XI		1600
XII		1545

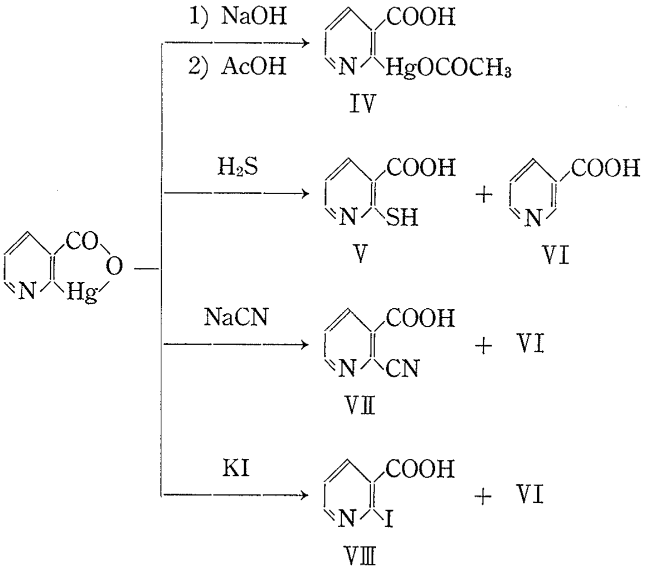


Chart 2

The reaction of III with potassium iodide gave the compound (VIII) in low yield, with iodide in the 2-position of the pyridine ring. The common feature in these reactions with nucleophilic reagents is the simultaneous formation of nicotinic acid (VI).

These results indicated clearly that mercurated pyridine-3-carboxylic anhydride was quite reactive with nucleophilic reagents, like mercurated naphthalic anhydride (IX) and mercurated norbornene anhydride (XII) reported earlier.

Experimental

Mercuration of Pyridine-2,3-dicarboxylic Acid (I)——A solution of 8 g of HgO dissolved in a mixture of 30 ml of glacial AcOH and 30 ml of H_2O was added to a solution of 10 g of I dissolved in 50 ml of 5% NaOH, with shaking, and the mixture was adjusted to a final pH of 5.0—5.8. This mixture was refluxed at 150—160° for *ca.* 20 hr, and CO_2 formed was absorbed in $Ba(OH)_2$ solution. Refluxing was continued until white turbidity was no longer formed. The mixture was filtered while hot, and the precipitate on the filter was washed consecutively with glacial AcOH, H_2O and MeOH, to yield 16.1 g of III as colorless fine crystals, mp>300°.

Detection of Hg in the Product: a) X-Ray Intensity Method: The apparatus used was a Hitachi GF-S unit. The specimen was formed under a pressure of 25 t/40. The value was 35600 cps at 30 kW, 10 mA.

b) Atomic Absorption Photometry: The apparatus used was a Hitachi 207 spectrophotometer. The sample was dissolved in 50% AcOH to saturation, and measured. Absorption was checked at 2537 Å. *Anal.* Calcd. for $C_6H_3HgNO_2$: C, 23.45; H, 0.98; N, 4.36. Found: C, 23.55; H, 1.01; N, 4.55.

Pyridine-2-acetoxymercuri-3-carboxylic Acid (IV)——A solution of 1.0 g of III dissolved in 20 ml of 2 N NaOH was heated on a water bath at 70° for 1 hr, acidified with glacial AcOH, and allowed to stand until the reaction product precipitated out as crystals. The crystals were collected and recrystallized form MeOH to give 0.7 g of IV, mp 208—211°. *Anal.* Calcd. for $C_7H_7HgNO_2$: C, 24.93; H, 2.08; N, 4.15. Found: C, 25.01; H, 2.33; N, 4.44. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1600 (COOH). NMR (in DMSO) δ: 2.3 (3H, singlet, $OCOCH_3$), 8.5 (1H, singlet COOH).

Pyridine-2-thio-3-carboxylic Acid (V)——H_2S gas was bubbled through a suspension of 1.0 g of III in a mixture of 20 ml of glacial AcOH and 1.0 ml of H_2O. Formation of a black precipitate of HgS was complete within *ca.* 20 min but H_2S was bubbled for a further 10 min. HgS was removed by filtration, the filtrate was evaporated under reduced pressure, and the residue was extracted with benzene. The benzene residue was recrystallized from benzene to give 100 mg of V, mp 177—180°. The residue left after benzene extraction was recrystallized from MeOH, yielding 40 mg of VI, mp 226—229°. V: *Anal.* Calcd. for $C_6H_5NO_2S$: C, 46.45; H, 3.23; N, 9.03. Found: C, 46.88; H, 3.36; N, 10.21. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 2100 (SH), 1600 (C=O). NMR (in DMSO) δ: 9.2 (1H, singlet, SH), 8.5 (1H, singlet, COOH). MS *m/e*: 155 (M^+). VI: This was identical with a commercial specimen (IR spectra). *Anal.* Calcd. for $C_6H_5NO_2$: C, 58.54; H, 4.88; N, 11.38. Found: C, 58.92; H, 5.04; N, 11.62.

Pyridine-2-cyano-3-carboxylic Acid (VII)——A suspension of 2.0 g of III in a mixture of 30 ml of glacial AcOH and 2.0 ml H_2O was treated with 0.5 g of solid NaCN, then shaken vigorously at room temperature until the reactants dissolved completely. The mixture was allowed to stand for *ca.* 2 hr, then heated on a water bath at 50—60° for *ca.* 30 min, and the solvent was evaporated off under reduced pressure. The residue was extracted with acetone the solvent was evaporated off, and the residue was recrystallized from MeOH to give 300 mg of VII, mp 192—203°. The residue left after acetone extraction was recrystallized from a mixture of MeOH and H_2O to give 150 mg of VI, mp 227—229°. VIII: *Anal.* Calcd. for $C_7H_4N_2O_2$: C, 56.76; H, 2.70; N, 18.91. Found: C, 57.02; H, 3.05; N, 19.11. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 2315 (CN), 1610 (C=O). NMR (in DMSO) δ: 8.55 (1H, singlet, COOH). MS *m/e*: 148 (M^+). VI was identical with an authentic commercial specimen.

Pyridine-2-iodo-3-carboxylic Acid (VIII)——One gram of KI was added to 1.0 g III suspended in a mixture of 20 ml of glacial AcOH and 1.0 ml H_2O, and the mixture was heated on a water bath at 70—80° until all the reactants dissolved, a scarlet precipitate of HgI_2 was simultaneously formed. This precipitate was removed by filtration the filtrate was concentrated under reduced pressure, and the residue was extracted with acetone. The solvent was evaporated off, and the residue was recrystallized from acetone to give 120 mg of VIII, mp 186—188°. The residue left after extraction with acetone was recrystallized from a mixture of MeOH and H_2O to give 80 mg of VI, mp 226—229°. VIII: *Anal.* Calcd. for $C_6H_4INO_2$: C, 29.03; H, 1.61; N, 5.65. Found: C, 29.13; H, 1.81; N, 5.87. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1610 (C=O). NMR (in DMSO) δ: 8.57 (1H, singlet, COOH). MS *m/e*: 249 (M^+). VI was identical with a commercial specimen (elemental analysis values and mp).