

Kimiaki Imafuku* and Hiromichi Matsuura [1]

Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami,
Kumamoto 860, Japan
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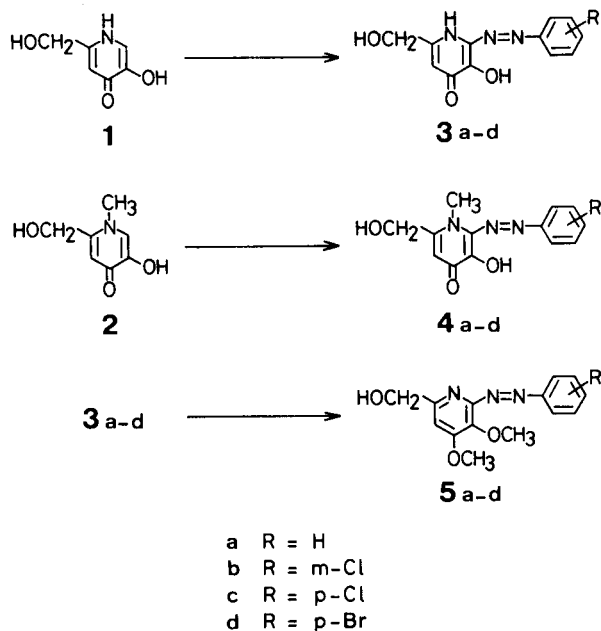
5-Hydroxy-2-hydroxymethyl-4-pyridone (**1**) and 5-hydroxy-2-hydroxymethyl-1-methyl-4-pyridone (**2**) reacted with arenediazonium salts to give 6-arylazo-substituted compounds **3a-d** and **4a-d**, respectively. Compounds **3a-d** were methylated with diazomethane to afford 6-arylazo-2-hydroxymethyl-4,5-dimethoxypyridines **5a-d**.

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Since kojic acid is an attractive material as a chemically and biologically important substance, many of its reactions have been carried out. Miyagawa *et al.* [2] and Quilico and Musante [3] independently obtained several 6-arylazo-substituted kojic acids, 6-arylazo-5-hydroxy-2-hydroxymethyl-4-pyrones, by the reaction of kojic acid with arenediazonium salts. It was reported that 6-arylazo-5-hydroxy-2-hydroxymethyl-4-pyrones were obtained except for 5-hydroxy-2-hydroxymethyl-6-phenylazo-4-pyrone [3]. The latter exists as its hydrate, which shows a tautomeric phenylhydrazono structure, and was not methylated with diazomethane.

Previously, we reported the tautomeric ratio of some 4-pyridones by measurement of dissociation constants of their *N*-methylated and *O*-methylated compounds [4]. The present communication deals with the synthesis of 6-arylazo-5-hydroxy-2-hydroxymethyl-4-pyridones and their *N*-methylated and *O*-methylated compounds, which are *N*-analogous to 6-arylazo-substituted kojic acids.

Scheme 1



5-Hydroxy-2-hydroxymethyl-4-pyridone (**1**) [5], which is an analogue of kojic acid, reacted with arenediazonium salts to give four 6-arylazo-5-hydroxy-2-hydroxymethyl-4-pyridones **3a-d**. Their *N*-methylated compounds, 6-arylazo-5-hydroxy-2-hydroxymethyl-1-methyl-4-pyridones **4a-d**, were obtained by the diazo-coupling reactions of 5-hydroxy-2-hydroxymethyl-1-methyl-4-pyridone (**2**) [6], while *O*-methylated compounds, 6-arylazo-2-hydroxymethyl-4,5-dimethoxypyridines **5a-d**, were obtained by methylation of the pyridones **3a-d** with diazomethane.

In addition, the spectrophotometric evaluation of the tautomeric ratio in the pyridones **3a-d** failed because these compounds might show a mixture of two pairs of tautomers as pyridone-pyridine and phenylazo-phenylhydrazono systems.

EXPERIMENTAL

Measurements.

The melting points were determined with a Yanagimoto MP-S2 apparatus and are uncorrected. The ir spectra were taken on a JASCO IRA-1 spectrophotometer, and the uv spectra on a Hitachi EPS-3T spectrophotometer. The ¹H nmr spectra were recorded with a Hitachi-Perkin-Elmer R-24 spectrometer (60 MHz).

6-Arylazo-5-hydroxy-2-hydroxymethyl-4-pyridones.

To an ice-cooled solution of 5-hydroxy-2-hydroxymethyl-4-pyridone (**1**) (280 mg, 2.0 mmoles) and sodium acetate (700 mg) in water (20 ml) was added arenediazonium salts solution, prepared from aniline derivative (2.1 mmoles), sodium nitrite (160 mg, 2.1 mmoles), and 1M hydrochloric acid (4.4 ml, 4.4 mmoles). After stirring for 2 hours, the precipitate was collected and recrystallized from methanol.

Compound **3a** was obtained in a yield of 83%, mp 193° dec; ir (chloroform): ν max 3100, 1635, 1595 cm⁻¹; uv (methanol): λ max 240 (sh, log ϵ 4.13), 371 (3.91), 435 nm (3.97); ¹H nmr (deuteriochloroform): δ 5.23 (s, 2H, CH₂), 7.30 (s, 1H, H-3), 7.3-8.2 (m, 5H, Ph).

Anal. Calcd. for C₁₂H₁₁N₃O₃: C, 58.77; H, 4.52; N, 17.14. Found: C, 58.67; H, 4.62; N, 16.94.

Compound **3b** was obtained in a yield of 58%, mp 176° dec; ir (chloroform): ν max 3150, 1595, 1590 cm⁻¹; uv (methanol): λ max 244 (sh, log ϵ 4.03), 455 nm (3.90); ¹H nmr (deuteriochloroform): δ 5.28 (s, 2H, CH₂), 7.35 (s, 1H, H-3), 7.6-8.1 (m, 4H, H-2',3',5',6').

Anal. Calcd. for C₁₂H₁₀ClN₃O₃: C, 51.53; H, 3.60; N, 15.02. Found: C, 51.41; H, 3.85; N, 14.72.

Compound **3c** was obtained in a yield of 62%, mp 178° dec; ir (chloroform): ν max 3150, 1605, 1580 cm⁻¹; uv (methanol): λ max 245 (sh, log ϵ 3.87), 458 nm (3.77); ¹H nmr (deuteriochloroform): δ 5.23 (s, 2H, CH₂),

7.32 (s, 1H, H-3), 7.63 (d, 2H, J = 9 Hz, H-3',5'), 8.03 (d, 2H, J = 9 Hz, H-2',6').

Anal. Calcd. for $C_{12}H_{10}ClN_3O_3$: C, 51.53; H, 3.60; N, 15.02. Found: C, 51.68; H, 3.85; N, 15.18.

Compound **3d** was obtained in a yield of 59%, mp 160° dec; ir (chloroform): ν max 3150, 1605, 1580 cm^{-1} ; uv (methanol): λ max 246 (log ϵ 4.17), 282 (sh, 4.00), 374 (4.02), 450 nm (sh, 3.89); 1H nmr (deuteriochloroform): δ 5.22 (s, 2H, CH_2), 7.32 (s, 1H, H-3), 7.76 (d, 2H, J = 9 Hz, H-3',5'), 7.88 (d, 2H, J = 9 Hz, H-2',6').

Anal. Calcd. for $C_{12}H_{10}BrN_3O_3$: C, 44.46; H, 3.11; N, 12.96. Found: C, 44.63; H, 2.87; N, 13.18.

6-Arylazo-5-hydroxy-2-hydroxymethyl-1-methyl-4-pyridones.

To an ice-cooled solution of 5-hydroxy-2-hydroxymethyl-1-methyl-4-pyridone (**2**) (155 mg, 1.0 mmole) and sodium acetate (350 mg) in water (10 ml) was added arenediazonium salt solution, prepared from aniline derivative (1.0 mmole), sodium nitrite (80 mg, 1.1 mmoles), and 1M hydrochloric acid (2.2 ml, 2.2 mmoles). After stirring for 2 hours, the precipitate was collected and recrystallized from methanol.

Compound **4a** was obtained in a yield of 21%, mp 154° dec; ir (chloroform): ν max 3250, 1610, 1605 cm^{-1} ; uv (methanol): λ max 286 (sh, log ϵ 3.78), 290 (sh, 3.82), 411 nm (3.71); 1H nmr (deuteriochloroform): δ 4.44 (s, 3H, CH_3), 5.30 (s, 2H, CH_2), 7.68 (s, 1H, H-3), 7.5-8.2 (m, 5H).

Anal. Calcd. for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: C, 60.05; H, 4.90; N, 16.25.

Compound **4b** was obtained in a yield of 26%; mp 182° dec; ir (chloroform): ν max 3260, 1620, 1590 cm^{-1} ; uv (methanol): λ max 286 (log ϵ 3.78), 324 (3.81), 422 nm (3.81); 1H nmr (deuteriochloroform): δ 4.46 (s, 3H, CH_3), 5.28 (s, 2H, CH_2), 7.67 (s, 1H, H-3), 7.5-8.1 (m, 4H).

Anal. Calcd. for $C_{13}H_{12}ClN_3O_3$: C, 53.16; H, 4.12; N, 14.31. Found: C, 53.06; H, 4.12; N, 14.25.

Compound **4c** was obtained in a yield of 48%; mp 188° dec; ir (chloroform): ν max 3250, 1610, 1590 cm^{-1} ; uv (methanol): λ max 227 (log ϵ 4.32), 324 (3.81), 420 nm (3.81); 1H nmr (deuteriochloroform): δ 4.45 (s, 3H, CH_3), 5.28 (s, 2H, CH_2), 7.63 (s, 1H, H-3), 7.63 (d, 2H, J = 9 Hz, H-3',5'), 7.79 (d, 2H, J = 9 Hz, H-2',6').

Anal. Calcd. for $C_{13}H_{12}ClN_3O_3$: C, 53.16; H, 4.12; N, 14.31. Found: C, 53.22; H, 4.05; N, 14.47.

Compound **4d** was obtained in a yield of 38%; mp 175° dec; ir (chloroform): ν max 3250, 1610, 1590 cm^{-1} ; uv (methanol): λ max 227 (log ϵ 4.32), 338 (4.03), 422 nm (3.99); 1H nmr (deuteriochloroform): δ 4.47 (s, 3H, CH_3), 5.28 (s, 2H, CH_2), 7.66 (s, 1H, H-3), 7.80 (s, 4H, H-2',3',5',6').

Anal. Calcd. for $C_{13}H_{12}BrN_3O_3$: C, 46.17; H, 3.58; N, 12.42. Found: C, 45.98; H, 3.48; N, 12.23.

6-Arylazo-2-hydroxymethyl-4,5-dimethoxypyridines.

An excess of ethereal solution of diazomethane was added to a sus-

pended solution of 6-arylazo-5-hydroxy-2-hydroxymethyl-4-pyridone **3a-d** (1 mmole) in methanol (10 ml). The mixture was allowed to stand for 1 hour. After the evaporation of the solvent, the residue was chromatographed on a Wakogel B-10 plate (30 \times 30 cm) with ethyl acetate and recrystallized from benzene-petroleum ether to afford 6-arylazo-2-hydroxymethyl-4-pyridines **5a-d**.

Compound **5a** was obtained in a yield of 52%, mp 126-128°; ir (chloroform): ν max 3350, 1585 cm^{-1} ; uv (methanol): λ max 229 (log ϵ 4.20), 330 (3.94), 440 nm (sh, 2.96); 1H nmr (deuteriochloroform): δ 3.8-4.5 (br, 1H, OH), 3.92 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 4.77 (s, 2H, CH_2), 7.05 (s, 1H, H-3), 7.3-7.7 (m, 3H, H-3',4',5'), 7.8-8.2 (m, 2H, H-2',6').

Anal. Calcd. for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.65; H, 5.59; N, 15.34.

Compound **5b** was obtained in a yield of 12%, mp 139-142°; ir (chloroform): ν max 3350, 1590 cm^{-1} ; uv (methanol): λ max 233 (sh, log ϵ 4.22), 335 (3.92), 446 nm (sh, 2.93); 1H nmr (deuteriochloroform): δ 3.5-3.9 (br, 1H, OH), 3.98 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 4.75 (s, 2H, CH_2), 7.03 (s, 1H, H-3), 7.5-7.7 (m, 2H, H-4',5'), 7.9-8.2 (m, 2H, H-2',6').

Anal. Calcd. for $C_{14}H_{14}ClN_3O_3$: C, 54.63; H, 4.55; N, 13.66. Found: C, 54.78; H, 4.59; N, 13.54.

Compound **5c** was obtained in a yield of 18%, mp 181-182°; ir (chloroform): ν max 3350, 1590 cm^{-1} ; uv (methanol): λ max 232 (log ϵ 4.26), 335 (4.04), 450 nm (sh, 3.02); 1H nmr (deuteriochloroform): δ 3.5-3.8 (br, 1H, OH), 3.98 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.77 (s, 2H, CH_2), 7.03 (s, 1H, H-3), 7.51 (d, 2H, J = 9 Hz, H-3',5'), 7.95 (d, 2H, J = 9 Hz, H-2',6').

Anal. Calcd. for $C_{14}H_{14}ClN_3O_3$: C, 54.63; H, 4.55; N, 13.66. Found: C, 54.74; H, 4.63; N, 13.58.

Compound **5d** was obtained in a yield of 15%, mp 185-187°; ir (chloroform): ν max 3350, 1585 cm^{-1} ; uv (methanol): λ max 232 (log ϵ 4.23), 337 (4.05), 450 nm (sh, 3.03); 1H nmr (deuteriochloroform): δ 3.8-4.3 (br, 1H, OH), 3.98 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 4.79 (s, 2H, CH_2), 7.05 (s, 1H, H-3), 7.68 (d, 2H, J = 9 Hz, H-3',5'), 7.90 (d, 2H, J = 9 Hz, H-2',6').

Anal. Calcd. for $C_{14}H_{14}BrN_3O_3$: C, 47.74; H, 4.01; N, 11.93. Found: C, 47.89; H, 3.98; N, 12.05.

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