*Reactions of Active Methylene Compounds. V. New Synthesis of Hydroxy Substituted 2-Hydroxyphenyl Benzyl Ketones and 4-Hydroxy-3-phenylcoumarins, and Structures of the Latter and Related 2-Imides**

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The present paper describes the action of anhydrous pyridine hydrochloride on methoxy substituted ethyl 2-methoxybenzoyl-phenylacetates (II) and 2-methoxybenzoyl-phenylacetonitriles (I) to give hydroxy substituted 2-hydroxyphenyl benzyl ketones (III) and 4-hydroxy-3-phenylcoumarins (V) respectively, and the structures of the latter and the intermediate, 2-imides IV of V are discussed through their infrared spectra.

Anhydrous pyridine hydrochloride is often used for demethylation of methyl ether of phenols⁽¹⁾; for instances, similar to the present work, 2-methoxybenzal-phenylacetonitriles were transformed into 3-phenylcoumarins⁽²⁾ and 4-hydroxy-2′-methoxy-3-phenylcoumarins into coumarino (3′, 4′: 3, 2) coumarones⁽³⁾.

The action of this reagent on nitriles Ia∼d⁽⁴⁾ under reflux caused demethylation of all the methoxy groups and subsequent cyclization to give the intermediate imides IV, which were readily converted into hydroxy substituted 4-hydroxy-3-phenylcoumarins (Va∼d) by acid hydrolysis. Methoxy substituted IV and V had been obtained⁽⁵⁾ by the action of aluminum chloride on I and II respectively, methoxy groups of which in the *p*-position of carbonyl group were unaffected. On the other hand, the action of pyridine hydrochloride on esters IIa∼d⁽⁴⁾ caused at first cleavage of ester group, decarboxylation, and then demethylation of all the methoxy groups to give hydroxy substituted 2-hydroxyphenyl benzyl ketones (IIIa∼d). Methoxy substituted III had been obtained⁽⁴⁾ by the action of hydrochloric acid on I and II, methoxy groups of which expect one in the *o*-position of the carbonyl group were unaffected.

It is reported that absorptions by carbonyl groups of 4-hydroxycoumarins⁽⁶,⁷⁾ are in a shorter region, and that of chromones⁽⁷,⁸⁾ are in a longer region, than 6 μ.

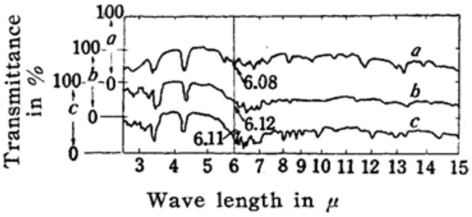

Fig. 1. Infrared spectra of VIII (a), VIa (b) and VIe (c).

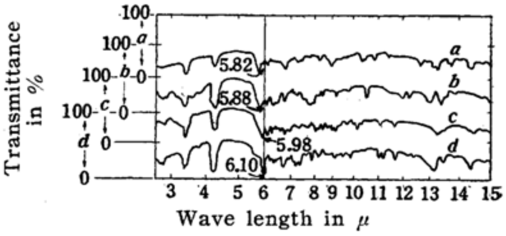

Fig. 2. Infrared spectra of IX (a), X (b), VIIa (c) and XIa(d).

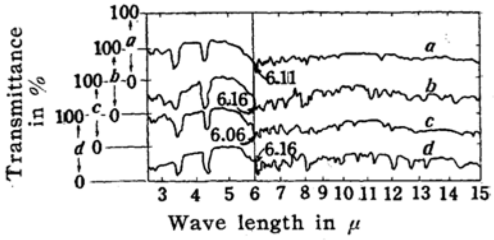

Fig. 3. Infrared spectra of VIIb (a), XIb (b), VIIe (c) and XIc (d).

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* Preliminary report: Y. Kawase, *Experientia*, **14**, Nov. (1958).

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6) T. R. Govindachari et al., *J. Chem. Soc*., **1956**, 629; F. M. Dean et al., ibid., **1957**, 3497.

7) a) C. H. Stammer et al., *J. Am. Chem. Soc*., **80**, 137, 140 (1958); b) A. Fujino and M. Yamaguchi, *J. Japan. Chem. (Kagaku no Ryôiki), Extra Voll*. **28**, 124, 126 (1958).

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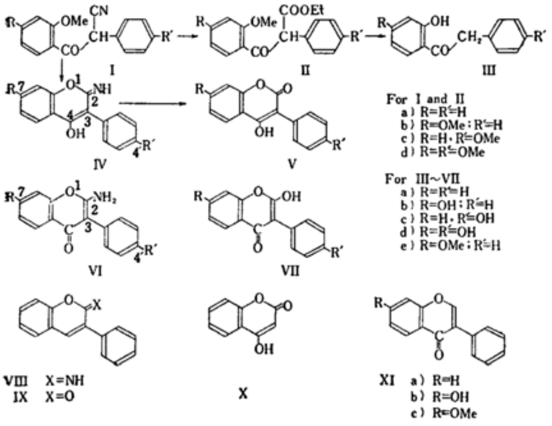
The infrared spectra of IVa, e and Va, b, e were measured in Nujol and compared* with those of related 3-phenylcoumarin-2-imide (VIII), 3-phenylcoumarin (IX), 4-hydroxycoumarin (X) and isoflavones (XIa~c). (see Figs. 1—3). (Preparation of IVa, e and Va, e was reported in the previous paper[5]). It seems that 4-hydroxycoumarin structures of IV and V will rather be replaced by chromone structures, namely 2-amino- (VI) and 2-hydroxy-isoflavones (isoflavonols) (VII) respectively, from the whole shapes of their infrared spectra, and from the absorptions by their carbonyl groups in a longer region than 6 μ.



Experimental[9]

2-Hydroxyphenyl Benzyl Ketone (IIIa).—A mixture of ester IIa (0.3 g.) and anhydrous pyridine hydrochloride (1.5 g.) was refluxed for 20 min. on an oil-bath (ca. 220°). The cooled mixture was treated with dilute hydrochloric acid and heated for several minutes on a steam-bath. After being cooled, the solid product separated was collected and recrystallized from ethanol; m. p. 57~58°, identical with the authentic sample[4]; yield 0.1 g. The three following ketones were prepared in the same way.

2, 4-Dihydroxyphenyl Benzyl Ketone (IIIb).—From 0.3 g. of IIb, 0.1 g. of IIIb was obtained, m. p. 110~113° (from water), identical with the authentic sample[10].

2-Hydroxyphenyl 4-Hydroxybenzyl Ketone (IIIc).—From 0.3 g. of IIc, 0.1 g. of IIIc was obtained, m. p. 106~107° (from oqueous ethanol, and dried at 80°).

Anal. Found: C, 73.58; H, 5.30. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30%.

2, 4-Dihydroxyphenyl 4-Hydroxybenzyl Ketone (IIId).—From 0.3 g. of IId, 0.1 g. of IIId was obtained, m. p. 183~184° (from dilute ethanol, and dried at 120°). Reported m. p. is 191~192°[11].

Anal. Found: C, 68.78; H, 5.20. Calcd. for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95%.

2-Hydroxyisoflavone (Isoflavonol) (VIIa).—A mixture of nitrile Ia (0.3 g.) and anhydrous pyridine hydrochloride (1.5 g.) was refluxed for 20 min. on an oil-bath. The cooled mixture was treated with dilute hydrochloric acid and heated on a steam-bath for 1 hr. After being cooled, the deposits were collected and crystallized from ethanol; m. p. 228~229°, yield 0.15 g.; identical with the authentic sample[5]. The following compounds were prepared in the same way.

2, 7-Dihydroxyisoflavone (VIIb).—From 0.3 g. of Ib, 0.15 g. of VIIb was obtained; m. p. 277~278° (from ethanol). Reported m. p. is 284~285°[12] or 285°[13].

Anal. Found: C, 70.68; H, 4.06. Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96%.

2-Amino-4'-hydroxyisoflavone (VIc) and 2, 4'-Dihydroxyisoflavone (VIIc)—In the case of Ic, intermediate imide VIc was isolated together with VIIc by the same procedure as described before. Ic (0.3 g.) was treated with pyridine hydrochloride and with dilute hydrochloric acid, and the precipitates thus formed were crystallized from ethanol to give VIc in colorless microcrystals, m. p. ca. 330° (decomp.); yield 0.1 g.

Anal. Found: C, 71.15; H, 4.50; N, 5.42. Calcd. for $C_{15}H_{11}O_3N$: C, 71.14; H, 4.37; N. 5.53%.

From the ethanolic mother liquor of crystallization, VIIc (0.1 g.) was obtained; m. p. 255~256° (from dilute ethanol, and dried at 150°).

Anal. Found: C, 70.64; H, 3.98. Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96%.

VIIc was also obtained from imide VIc by hydrolysis with dilute hydrochloric acid for a longer time; m. p. 252~254°.

2, 4', 7-Trihydroxyisoflavone (VIId).—From Id (0.5 g.) and pyridine hydrochloride (2.5 g.), 0.2 g. of VIId was obtained; m. p. ca. 340° (decomp.) (from methanol, and dried at 150°).

Anal. Found: C, 66.63; H, 3.84. Calcd. for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73%.

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* λ_{max} (C=O) of coumarin and umbelliferone are 5.80 and 5.95 μ respectively (A. Fujino and M. Yamaguchi, loc. cit.), and that of 2,7-dihydroxychromone is 6.0 μ (C. H. Stammer et al., loc. cit.).

[9] Melting points are uncorrected.

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