Synthesis of Isoflavono$(7',8':6,5)$-α-pyrones and Formylation of 2,4-Dihydroxyphenyl Benzyl Ketone

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(Received June 5, 1958)

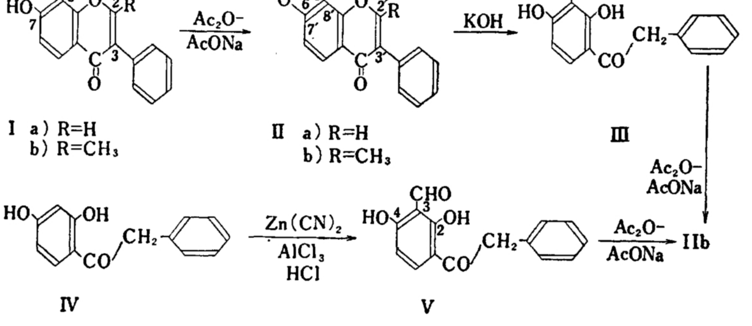
In previous papers[1,2], the authors reported the preparation of furano$(2',3':7,8)$-isoflavones. In connection with it, the present paper describes the preparation of isoflavono$(7',8':6,5)$-α-pyrones (IIa, b).

The synthesis of flavono$(7',8':6,5)$-α-pyrones has been carried out by two methods: that is, by α-pyrone-ring formation on 7-hydroxy-8-formyl-flavones[3], and by flavone-ring formation on 5-hydroxy-6-acyl-coumarins[4]. But, so far as the preparation of isoflavono$(7',8':6,5)$-α-pyrones is concerned, only the preparation of $2',4$-dimethyl-isoflavono-α-pyrone from 5-hydroxy-4-methyl-6-coumaryl benzyl ketone has been reported[5].

Here, isoflavono$(7',8':6,5)$-α-pyrone (IIa) and its $2'$-methyl homologue (IIb) were prepared from 7-hydroxy-8-formyl-isoflavones (Ia, b) by the Perkin reaction in the usual way. IIa and IIb were hydrolyzed to a same acid, 2,6-dihydroxy-3-phenylacetyl-cinnamic acid (III) (not a lactone of it, namely a coumarin-derivative), which was re-derived into IIb by the action of acetic anhydride and sodium acetate.

It has been reported recently[6] that formylation of 2,4-dihydroxyphenyl benzyl ketone (resbenzylphenone) (IV) by the Hoesch reaction gives isoflavone through the compound formylated in α-methylene group.

In the present work, formylation of IV by the same reaction as above in the presence of anhydrous aluminum chloride gave 2,4-dihydroxy-3-formyl-phenyl benzyl ketone (V), the structure of which was confirmed by deriving it into IIb. (α-Acylresorcinols are usualy substituted in the 3-position in the Hoesch[7] or the



I a) R=H
b) R=CH_3

II a) R=H
b) R=CH_3

III

IV

V

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1) T. Matsumoto, Y. Kawase, M. Nanbu and K. Fukui, This Bulletin, **31**, 688 (1958).

2) K. Fukui and Y. Kawase, ibid., **31**, 693 (1958).

3) S. Rangaswami and T. R. Seshadri, *Proc. Indian Acad. Sci.*, 9A, 7 (1939). [*Chem. Abstr.*, **33**, 4244 (1939)].

4) S. M. Sethna, N. M. Shah and R. C. Shah, *J. Chem. Soc.*, **1938**, 228.

5) C. V. Deliwala and N. M. Shah, ibid., **1939**, 1250.

6) L. Farkas, *Chem. Ber.*, **90**, 2940 (1957).

7) K. Nakazawa, *J. Pharm. Soc. Japan*, (*Yakugaku Zasshi*), **59**, 297 (1939); H. R. Shah and R. C. Shah, *J. Chem. Soc.*, **1939**, 132.

8) S. M. Sethna, N. M. Shah and R. C. Shah, *Current Sci.* (*India*), **6**, 93 (1937) [*Chem. Abstr.*, **32**, 549 (1938)].

Pechmann[4,5,8] reaction in the presence of anhydrous aluminum chloride.)

Experimental[9]

Isoflavono(7′, 8′ : 6, 5)-α-pyrone (IIa).—A mixture of Ia[2] (0.6 g.) and anhydrous sodium acetate (0.7 g.) in acetic anhydride (4 cc.) was refluxed for 10 hr. The cooled mixture was poured into water, and the solid product was recrystallized from ethyl acetate, colorless needles, m.p. 200∼200.5°C; yield 0.3 g. *Anal.* Found: C, 74.18; H, 3.55. Calcd. for $C_{18}H_{10}O_4$: C, 74.48; H, 3.47%.

2, 4-Dihydroxy-3-formyl-phenyl benzyl ketone (V).—A mixture of IV (5 g.), zinc cyanide (6 g.) and anhydrous aluminum chloride (5 g.) in anhydrous ether (100 cc.) was saturated with dry hydrogen chloride with stirring and cooling. By the usual treatment for the Hoesch reaction, the product was obtained in colorless microcrystals, m.p. 108∼109°C (from dilute ethanol); yield 3.5 g. *Anal.* Found: C, 70.51; H, 4.85. Calcd. for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72%.

2′-Methyl-isoflavono(7′, 8′ : 6, 5)-α-pyrone (IIb). (*a*) *From Ib.*—By the same procedure as described for IIa, starting from Ib[10] (1 g.), sodium acetate (1.1 g.) and acetic anhydride (6 cc.) the product IIb was obtained; m.p. 202∼203.5°C (from ethyl acetate), yield 0.3 g. *Anal.* Found: C, 75.03; H, 4.05. Calcd. for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97%.
(*b*) *From V.*—By the same treatment asd escribed for (a), starting from V (0.5 g.), sodium acetate (1 g.) and acetic anhyride (7 cc.) the product IIb (0.15 g.) was obtained; m.p. 202∼203.5°C, identical with the sample from (a).

Hydrolysis of IIa and IIb to 2, 6-dihydroxyl-3-phenyl-acetyl-cinnamic acid (III).—(*a*) A mixture of IIa (0.1 g.) and 10% aqueous potassium hydroxide (5 cc.) was heated on a steam-bath for 4 hr. After being cooled, the solution was acidified with dilute hydrochloric acid, and the precipitates were collected and recrystallized from ethanol to give III, m.p. 210∼211°C (decomp.), which was identical with the sample obtained from IIb. (*b*) A mixture of IIb (0.7 g.) and 10% aqueous potassium hydroxide (15 cc.) was treated similarly as described for a. Colorless microcrystals, m.p. 213∼214°C (decomp.). III gave a brown ferric reaction in ethanol, and dissolved slowly in aqueous sodium bicarbonate. III was not converted into a lactone (coumarin-derivative) by heating with dilute hydrochloric acid. *Anal.* Found: C, 67.95; H, 4.73. Calcd. for $C_{17}H_{14}O_5$: C, 68.19; H, 4.74%. The mixture of III (0.1 g.), acetic anhydride (3 cc.) and sodium acetate (0.4 g), when refluxed for 10 hr., furnished IIb, m.p. 197∼198°C (from ethyl acetate), which was identical with the sample described before.

An attempted preparation of IIa from III by the ethyl orthoformate-pyridine-piperidine method[11] was unsuccessful.

We are grateful to the Institute of Agricultural Chemistry, Faculty of Agriculture, Kyoto University for microanalyses.

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[9] Melting points are uncorrect.

[10] L. R. Row and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **34A**, 187 (1951) [*Chem. Abstr.*, **47**, 12374 (1953)].

[11] V. R. Sathe and K. Venkataraman, *Current Sci.* (*India*), **18**, 378 (1949) [*Chem. Abstr.*, **44**, 8916 (1950)].