Reactions of Active Methylene Compounds. IV. Synthesis of 2-Hydroxyphenyl Benzyl Ketones and 4-Hydroxy-3-phenylcoumarins (Continued)

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In the previous paper[1], 2-hydroxyphenyl benzyl ketones (III) and 4-hydroxy-3-phenylcoumarins (V) were prepared from 2-methoxybenzoyl-phenylacetonitriles (I) and ethyl 2-methoxybenzoyl-phenylacetates (II). Afterwards, it was known that Chatterjea and Roy[2] had reported a preparation of III (R, R′=H) and V (R, R′=H) from I (R, R′=H) by the action of hydrobromic acid in acetic acid.

The present paper describes a preparation of an analogous series of compounds (Ia, IIa, IIIa, IVa, b, b′ and Va, a′, b) by the same procedure described in the previous paper.

By the action of anhydrous aluminum chloride (2 moles) in nitrobenzene, 4-hydroxy-3-phenylcoumarin-2-imides (IVa, b) were obtained from nitriles Ia, b, methoxy groups of which all, except one in the *o*-position of the carbonyl group, were unaffected. 4-Hydroxy-3-phenylcoumarins (Va, b) were obtained from the imides IVa, b by acid hydrolysis, and Va was also obtained from IIa by means of aluminum chloride in nitrobenzene. By the use of an increased amount (4.5 moles) of aluminum chloride, small amounts of IVb′ and Va′ were obtained from Ib and IIa respectively, 4′-methoxy groups of which were demethylated. Attempted preparations of imide IVa′ from Ia, of coumarins Vb, b′ from IIb, and of IVa by ester condensation of methyl salicylate with *p*-methoxyphenylacetonitrile were unsuccessful.

1) Y. Kawase, This Bulletin, **31**, 390, 440 (1958).
2) J. N. Chatterjea and S. K. Roy, *J. Indian Chem. Soc.*, **34**, 155 (1957) [*Chem. Abst.*, **52**, 1987 (1958)]; cf. J. N. Chatterjea and S. K. Roy, *J. Indian Chem. Soc.*, **34**, 98 (1957) [*Chem. Abst.*, **51**, 16445 (1957)].

Experimental[3]

2-Methoxybenzoyl-4-methoxyphenylacetonitrile (Ia).—To a solution of methyl 2-methoxybenzoate (5.5 g.) and 4-methoxyphenylacetonitrile (4.5 g.) in anhydrous benzene (100 cc.), sodium hydride (1.5 g., 2 moles) was added and the mixture was heated for 4 hr. on an oil-bath (95~100°), most of the benzene being distilled off in the meantime. The well-cooled mixture was treated with water and extracted with ether. The alkaline aqueous solution was acidified and the solid product separated was collected, washed with aqueous sodium bicarbonate, and recrystallized from ethanol in colorless prisms, m.p. 109~110.5°; yield 6 g. or 70%.

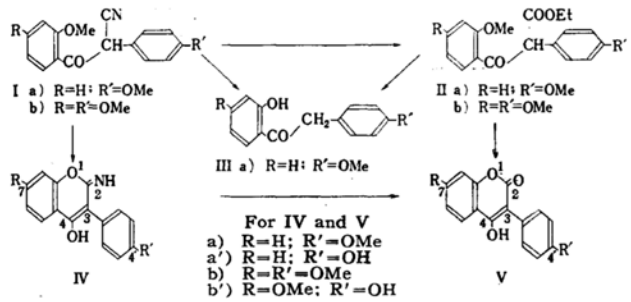
Anal. Found: C, 72.37; H, 5.27; N, 5.05. Calcd. for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.37; N, 4.98%.

Ethyl 2-Methoxybenzoyl-4-methoxyphenylacetate (IIa).—A solution of nitrile Ia (2.2 g.) in anhydrous ethanol (50 cc.) containing one mole of water (0.14 cc.) was saturated with hydrogen chloride with cooling. After three days at room temperature, water was added and ethanol was removed in vacuo. The gummy product separated was taken up in ether, washed with aqueous sodium hydroxide, and distilled to give colorless viscous oil, b. p. 180~200°/0.004mm. (bath-temperature); yield 1.6 g. or 62%.

Anal. Found: C, 69.23; H, 5.90. Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14%.

2-Hydroxyphenyl 4-Methoxybenzyl Ketone (IIIa).—(*a*) *From nitrile Ia.*—A solution of Ia (0.5 g.) in acetic acid (10 cc.) containing concentrated hydrochloric acid (5 cc.) was heated on a

3) Melting and boiling points are uncorrected.



steam-bath for 15 hr. The cooled solution was made alkaline with aqueous sodium hydroxide and extracted with ether. The residue obtained from the ether solution was distilled to give colorless oil, b. p. 160~180°/0.003 mm. (bath-temperature); yield 0.2g. 2,4-Dinitrophenylhydrazone, m. p. 198~199° (from ethanol).

Anal. of 2, 4-dinitrophenylhydrazone. Found: C, 59.66; H, 4.11; N, 13.28. Calcd. for $C_{21}H_{18}O_6N_4$: C, 59.71: H, 4.30; N, 13.27%.

(*b*) *From ester IIa.*—By the same procedure described for (a), 0.2 g. of IIIa was obtained from 0.5 g. of IIa; b. p. 160~180°/0.003 mm. (bath-temperature). 2, 4-Dinitrophenylhydrazone, m. p. 197~198°, was identical with the sample from (a).

4-Hydroxy-4'-methoxy-3-phenylcoumarin-2-imide (IVa).—A mixture of Ia (0.5 g.) and anhydrous aluminum chloride (0.5 g., 2.1 moles) in nitrobenzene (5 cc.) was heated on a steam-bath for 1 hr. The cooled solution was treated with water, and nitrobenzene was removed by steam-distillation. The semi-solid product separated from the residue was taken up in ethyl acetate, and extracted with dilute hydrochloric acid. The acid aqueous solution was made alkaline with aqueous sodium bicarbonate, and the precipitates obtained were crystallized from ethanol in colorless microcrystals, m. p. 214.5~215.5°; yield 0.1 g.

Anal. Found: C, 71.75; H, 5.34; N, 5.16. Calcd. for $C_{16}H_{13}O_3N$: C, 71.90; H, 4.90; N, 5.24%.

4-Hydroxy-4'-methoxy-3-phenylcoumarin (Va).—(*a*) *From imide IVa.*—A solution of IVa (ca. 0.05 g.) in 2 cc. of dilute hydrochloric acid (1 : 1) was heated on a steam-bath for 2 hr. The separated crystals were collected and recrystallized from dilute ethanol in colorless microcrystals, m.p. 228~229°; identical with the sample from (b).

(*b*) *From ester IIa.*—A mixture of IIa (0.5 g.) and aluminum chloride (0.5 g., 2.4 moles) in nitrobenzene (5 cc.) was heated for 1 hr. The cooled solution was treated with dilute hydrochloric acid, and nitrobenzene was removed by steam-distillation. The semi-solid product separated from the residue was taken up in ethyl acetate and extracted with aqueous sodium carbonate. The product obtained by acidifying the alkaline solution was recrystallized from dilute ethanol; m. p. 230~231°, yield 0.1 g.

Anal. Found: C, 71.63; H, 4.54. Calcd. for $C_{16}H_{12}O_4$: C, 71.63; H, 4.15%.

4, 4'-Dihydroxy-3-phenylcoumarin (Va').—A mixture of IIa (0.5 g.) and aluminum chloride (0.8 g., 4 moles) in nitrobenzene was worked up as before, and nitrobenzene was removed by steam-distillation. The residual aqueous mixture was filtered while hot, and the crystalline product formed from the filtrate on cooling was recrystallized from dilute ethanol; m. p. 254~255°, yield ca. 0.05 g. It was identical with the sample which will be described in the next paper.

The semi-solid precipitates obtained in the above mentioned filtration were dissolved in ethyl acetate, and treated as before to give Va (ca. 0.05 g.), m. p. 226~227° (from ethyl acetate); identical with the sample described before.

4-Hydroxy-4', 7-dimethoxy-3-phenylcoumarin-2-imide (IVb).—By the same procedure as described before, 0.1 g. of the compound was obtained from 0.5 g. of Ib and 0.5 g. (2.5 moles) of aluminum chloride; m. p. 214~215° (from ethanol).

Anal. Found: C, 68.59; H, 5.33; N, 5.55. Calcd. for $C_{17}H_{15}O_4N$: C, 68.67; H, 5.08; N, 4.71%.

4-Hydroxy-4', 7-dimethoxy-3-phenylcoumarin (Vb).—By hydrolysis of imide IVb with hydrochloric acid, Vb was obtained in colorless needles, m. p. 213~214° (from dilute ethanol). Reported m. p. is 219~220°[4].

Anal. Found: C, 68.10; H, 5.24. Calcd. for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73%.

4, 4'-Dihydroxy-7-methoxy-3-phenylcoumarin-2-imide (IVb').—By the same procedure as described before, a small amount of the compound was obtained from 0.8 g. of Ib and 1.5 g. (4.5 moles) of aluminum chloride; m. p. 287~288° (from ethanol), soluble in acid and in cold aqueous sodium hydroxide.

Anal. Found: C, 67.33; H, 4.66; N, 4.79. Calcd. for $C_{16}H_{13}O_4N$: C, 67.83; H, 4.59; N, 4.94%.

From the ethanolic mother liquor of recrystallization, 0.1 g. of IVb was obtained.

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4) J. Boyd and A. Robertson, *J. Chem. Soc.*, **1948**, 174.