

## HETEROCYCLIC COMPOUNDS

Part XVII. Coumarins from  $\beta$ -ketonic Esters and 5 methyl-2-ethyl, 5-methyl-2-propyl-, 5-methyl-2:4-diethyl-4-Ethyl-2-benzoyl-resorcinols, and Phlorobenzophenone

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IN continuation of the previous work of Desai and co-workers on the coumarins from substituted resorcinols, we have studied the coumarin condensation between some new resorcinols which we happened to synthesise and ethyl acetoacetate and its alkylated derivatives. Thus 5-methyl-2-ethyl-resorcinol and 5-methyl-2-propyl-resorcinol condensed readily with ethyl-acetoacetate giving 7-hydroxy-4:5-dimethyl-8-ethylcoumarin, and 7-hydroxy-4:5-dimethyl-8-propyl-coumarin in presence of concentrated sulphuric acid. The alkylated aceto-acetic esters behaved similarly. However, 5-methyl-2:4-diethyl-resorcinol gave the expected 7-hydroxy-4:5-dimethyl-6:8-diethyl-coumarin with aceto-acetic ester only in the presence of anhydrous aluminium chloride.

4-ethyl-2-benzoyl-resorcinol condensed with aceto-acetic ester ( $H_2SO_4$ ) with the formation of 4-methyl-6-ethyl-7-hydroxy-8-benzoyl-coumarin, the constitution of which was proved by its rational synthesis by the Fries migration of 7-benzoyloxy-4-methyl-6-ethyl-coumarin which was prepared by the benzoylation of 7-hydroxy-4-methyl-6-ethyl-coumarin.

Phlorbenzophenone condensed with aceto-acetic ester giving 5:7-dihydroxy-4-methyl-6 or 8-benzoyl-coumarin.

### EXPERIMENTAL

(A) Coumarins from 5-methyl-2-ethyl resorcinol.—5-methyl-2-ethyl-resorcinol was prepared by the method of Desai and Vakil.<sup>2</sup>

4:5-Dimethyl-7-hydroxy-8-ethyl-coumarin.—The mixture of 5-methyl-2-ethyl resorcinol (3 gms.), ethyl aceto-acetate (2.5 g.) and 73% sulphuric acid (50 c.c.) was kept at room temperature for twenty-four hours. On pouring the mixture over ice, the solid that separated out crystallised from alcohol in colourless needles m.p. 235° (yield 70 per cent). It dissolved in

caustic soda solution giving greenish pink fluorescence. (Found: C, 71.5; H, 6.6;  $C_{12}H_{14}O_3$  requires C, 71.6; H, 6.4%).

Its *acetyl* derivative crystallised from alcohol in lustrous needles m.p. 121°. (Found: C, 69.1; H, 6.3;  $C_{15}H_{16}O_4$  requires C, 69.2; H, 6.2%).

**3:4:5-Trimethyl-7-hydroxy-8-ethyl-coumarin.**—Prepared from 5-methyl-2-ethyl-resorcinol and ethyl methyl-aceto-acetate crystallised from alcohol in colourless silky needles m.p. 227° C. (Found: C, 72.3; H, 7.3;  $C_{14}H_{16}O_3$  requires C, 72.4; H, 7.1%).

**3:8-Diethyl-4:5-dimethyl-7-hydroxy-coumarin** crystallised from alcohol in needles m.p. 192° C. (Found: C, 73.0; H, 7.6;  $C_{15}H_{18}O_3$  requires C, 73.1; H, 7.4%).

**3-propyl-4:5-dimethyl-7-hydroxy-8-ethyl-coumarin** crystallised from alcohol in lustrous needles m.p. 172°. (Found: C, 73.6; H, 7.9;  $C_{16}H_{20}O_3$  requires C, 72.8; H, 7.8%).

(B) *Coumarins from 5-methyl-2-propyl resorcinol.*—The above phenol was prepared by the clemmensen reduction of  $\gamma$ -orcpropiophenone which was prepared by the Fries migration of orcinol dipropionate as follows:—

A mixture of orcinol dipropionate (8 g.) and powdered anhydrous aluminium chloride (16 g.) was heated in an oil-bath at 145–150° C. for one hour and a half, and the cooled mass was decomposed with ice-cold water. The solid crystallised from dilute acetic acid in long, colourless needles m.p. 85–86°, and its alcoholic solution gave dark-red coloration with ferric chloride (yield, 60 per cent.). (Found: C, 65.9; H, 7.0;  $C_{13}H_{16}O_4$  requires C, 66.1; H, 6.8%).

The above *dipropionyl orcinol* (5 g.) was dissolved in 85 per cent. sulphuric acid (25 c.c.) and the solution was poured over ice after four hours, when a solid crystallising from dilute acetic acid in long needles m.p. 135° C. was obtained. The alcoholic solution of  $\gamma$ -orcpropiophenone gave green coloration with ferric chloride (yield = 3.0 g.). (Found: C, 66.5; H, 6.9;  $C_{10}H_{12}O_3$  requires C, 66.6; H, 66.6%).

The clemmensen reduction of the above  $\gamma$ -ketone with amalgamated zinc in the usual manner gave 5-methyl-2-propyl-resorcinol which crystallised from petroleum ether (b.p. 60–80°) in colourless needles m.p. 105°.

**4:5-dimethyl-7-hydroxy-8-propyl-coumarin** obtained from 5-methyl-2-propyl resorcinol and ethyl aceto-acetate using 73% sulphuric acid crystallised from alcohol in colourless needles m.p. 202°, and dissolved in dilute caustic soda with a yellow colour and greenish pink fluorescence. (Found: C, 72.2; H, 7.2.  $C_{14}H_{16}O_3$  requires C, 72.4; H, 7.1%).

**3:4:5-trimethyl-7-hydroxy-8-propyl-coumarin** prepared from 5-methyl-2-propyl resorcinol and ethyl methylacetate-crystallised from alcohol in soft, colourless needles m.p. 192°. (Found: C, 73.0; H, 7.2;  $C_{18}H_{18}O_3$  requires C, 73.2; H, 7.3%).

**3-Ethyl-4:5-dimethyl-7-hydroxy-8-propyl-coumarin** crystallised from alcohol in short needles m.p. 180° C. (Found: C, 73.5; H, 7.8;  $C_{16}H_{20}O_3$  requires C, 73.8, H, 7.7%).

**3:8-dipropyl-4:5-dimethyl-7-hydroxy-coumarin** crystallised from alcohol in needles m.p. 168°. (Found: C, 74.2; H, 8.2;  $C_{17}H_{22}O_3$  requires C, 74.5; H, 8.0%).

**2:4-Diethyl-5-methyl-resorcinol** was obtained by heating a mixture of 2:4-diacetyl-5-methyl resorcinol (2.5 g.), amalgamated Zinc (20 g.) and dilute hydrochloric acid (60 c.c.) for five hours under reflux. The solid that separated out on cooling crystallised from benzene in soft needles m.p. 122°. (Found: C, 73.2; H, 9.0;  $C_{11}H_{16}O_2$  requires C, 73.3; H, 8.9%).

**4:5-dimethyl-6:8-diethyl-7-hydroxy-coumarin.**—The solution of 2:4-diethyl-5-methyl-resorcinol (3.5 g.) ethylacetate-acetate (2.6 g.) and anhydrous aluminium chloride (6.0 g.) in nitro-benzene (40 c.c.) was heated in an oil-bath at 125–130° C. for two hours. After decomposing the mixture with ice-cold hydrochloric acid and removing the nitro benzene in steam, the residue crystallised from alcohol in straw-yellow needles m.p. 180°. Its yellow, alkaline solution gave green fluorescence. (Found: C, 73.0; H, 7.6.  $C_{15}H_{18}O_3$  requires C, 73.1; H, 7.4%).

**Preparation of 4-Ethyl-2-Benzoyl resorcinol. Preparation of 7-Benzoyloxy-6-ethyl-4-methyl-coumarin.**—The benzoylation of 7-hydroxy-6-ethyl-4-methyl coumarin (Desai and Ekhlas<sup>3</sup>) by the Schotten-Baumann method gave 7-benzoyloxy-6-ethyl-4-methyl-coumarin, which crystallised from alcohol in lustrous needles m.p. 157°. (Found: C, 73.8; H, 5.3;  $C_{19}H_{16}O_4$  requires C, 74.0; H, 4.2%).

**8-Benzoyl-7-hydroxy-6-ethyl-4-methyl-coumarin.**—An intimate mixture of the above benzoyloxy-coumarin (3 gms.) and anhydrous aluminium chloride (3 gms.) was heated in an oil-bath at 150–160° for an hour and half, and the cooled mixture was decomposed with ice-cold hydrochloric acid. The resulting solid on treatment with warm benzene left a considerable amount of the solid which was 7-hydroxy-6-ethyl-4-methyl coumarin, while the benzene soluble substance was recrystallised from alcohol in needles m.p. 133°. Its alcoholic solution gave dark-violet coloration with ferric chlorides while its alkaline solution was yellow and devoid of fluorescence. (Found: C, 74.0; H, 5.3;  $C_{19}H_{16}O_4$  requires C, 74.0; H, 5.2%).

The yield of 8-benzoyl-7-hydroxy-6-ethyl-4-methyl coumarin was 40 per cent.

*Hydrolysis of 8-benzoyl-7-hydroxy-6-ethyl-4-methyl coumarin to 4-ethyl-2-benzoyl resorcinol.*—A solution of the above coumarin (1 g.) in 10 per cent. sodium hydroxide (15 c.c.) was heated under reflux for 4 hours. The filtered solution was acidified with hydrochloric acid, and the resulting solid was treated with sodium bicarbonate solution to remove some soluble impurities. The residue crystallised from alcohol in straw-yellow needles m.p. 128° (yield, 40 per cent.). Its alcoholic solution gave greenish coloration with ferric chloride. (Found: C 74.1; H, 5.9;  $C_{15}H_{14}O_2$  requires C, 74.4; H, 5.8%).

When the solution of the above phenol (1.2 g.) and ethyl aceto-acetate (0.7 g.) in 73% sulphuric acid (25 c.c.) was left at the ordinary temperature for 36 hours, and worked up as usual, the product that was obtained (1 g.) was identified by m.p. and mixed m.p. as 8-benzoyl-7-hydroxy-6-ethyl-4-methyl-coumarin.

*4-methyl-5:7-dihydroxy-6 or 8-benzoyl-coumarin.*—A solution of phloro-benzophenone (2 g.) and ethylaceto-acetate (1 g.) in 85% sulphuric acid (25 c.c.) was kept at the ordinary temperature for 36 hours. The solid obtained by pouring the solution in ice-cold water crystallised from alcohol in lustrous needles m.p. 322°. Its alcoholic solution gave reddish coloration with ferric chloride, while its yellow, alkaline solution was non-fluorescent. (Found: C, 68.6; H, 4.2;  $C_{17}H_{12}O_5$  requires C, 68.9; 4.0%).

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#### SUMMARY

Coumarins were prepared from  $\beta$ -ketonic esters and some new resorcinol derivatives which were prepared in connection with some other work, and it was observed that they varied in their capacity for condensation.

#### REFERENCES

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——— and Mavani .. *Ibid.*, 1941, 14, 100.
2. ——— and (Miss) Vakil .. *Ibid.*, 1940, 12, 393.
3. ——— and Ekhlas .. *Ibid.*, 1938, 8, 196.