

## FRIEDEL-CRAFTS REACTION

### Part IX. The Action of Propionic and Butyric Anhydrides on Orcinol and Further Evidence of $\gamma$ -Substitution in Resorcinol Derivatives

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As a result of the action of acetyl chloride and acetic anhydride on orcinol in presence of anhydrous aluminium chloride, it was observed by Desai and Vakil<sup>1</sup> that whereas the former gave a mixture of  $\gamma$ - and  $\beta$ -orcacetophenones the latter gave exclusively  $\beta$ -orcacetophenone. We have now found that propionic anhydride reacts with orcinol giving mainly 2-propionyl-5-methyl resorcinol ( $\gamma$ -orcpropiofenone) and a small quantity of 4-propionyl-5-methyl resorcinol ( $\beta$ -orcpropiofenone). Further, we have observed that butyric anhydride gives exclusively 2-butyryl-5-methyl resorcinol ( $\gamma$ -orcbutyrophenone). Thus this is a very convenient method of synthesising these inaccessible compounds, which have been characterised by their *p*-nitrophenylhydrazones.

As 2-propionyl-5-methyl- and 2-butyryl-5-methyl-resorcinols are unknown, we have studied their simple derivatives. They can be easily reduced to 2-propyl-5-methyl- and 2-butyl-5-methyl-resorcinols. Further action of the anhydrides give the diacyl derivatives which lose the acyl group in the 4-position on keeping them in contact with concentrated sulphuric acid. An attempt to condense them with ethylaceto-acetate in presence of sulphuric acid gave 5-hydroxy-4:7-dimethyl coumarin with the removal of the propionyl and butyryl groups. The opening up of the lactone ring of this coumarin in presence of dimethyl sulphate gave the trans-2:6-dimethoxy-4-methyl- $\beta$ -methylcinnamic acid which was unaffected by heat and light and gave 5-methoxy-4:7-dimethyl-coumarin by leaving in contact with concentrated sulphuric acid. Similarly the alkaline hydrolysis of 5-hydroxy-6-acetyl-4:7-dimethyl-coumarin gave the trans-2:6-dihydroxy-3-acetyl-4-methyl- $\beta$ -methyl cinnamic acid as it was unaffected by heat and light, and underwent ring closure in presence of concentrated sulphuric acid giving the original coumarin. The monobromo derivative of the coumarin gave, on mild hydrolysis by sodium carbonate solution, 4-hydroxy-3:6-dimethyl coumarone, and 4-hydroxy-3:6-dimethyl-coumarone-2-carboxylic acid.

## EXPERIMENTAL

*Action of propionic anhydride on orcinol and formation of 2-propionyl-5-methyl resorcinol ( $\gamma$ -orcpropiophenone).*

Propionic anhydride (13.0 g.) was slowly added to the solution of anhydrous orcinol (12.4 g.) and anhydrous aluminium chloride (26.7 g.) in dry nitrobenzene (150 c.c.). The contents were heated for one hour on the water-bath after keeping the mixture at the room temperature overnight. After decomposing the mixture with ice-cold hydrochloric acid, nitrobenzene was removed in steam. The solid that separated out on cooling crystallised from dilute acetic acid in pale yellow needles m.p. 132-133°. Its alcoholic solution gave greenish-black coloration with ferric chloride (yield, 40%). (Found: C, 66.5, H, 6.8.  $C_{10}H_{12}O_3$  requires C, 66.7; H, 6.7%.)

The acetic acid mother-liquor, on concentration gave a small quantity of a solid, the alcoholic solution of which gave reddish-brown coloration with ferric chloride, and was identified as 4-propionyl-5-methyl-resorcinol by the mixed m.p. with an authentic specimen (yield, 5%).

The *p*-nitrophenyl-hydrazone of  $\gamma$ -orcpropiophenone crystallised from alcohol in reddish micro needles m.p. 210°. (Found: N, 13.2.  $C_{16}H_{17}N_3O_4$  requires N, 13.3%.)

2-Propyl-5-methyl resorcinol was obtained by reducing the above ketone (1 gm.) with amalgamated zinc (5 g) and dilute hydrochloric acid (20 c.c.). The solid crystallised from petrol (60-80 bp) in colourless needles m.p. 105°. (yield, 70%). (Found: C, 72.3; H, 8.7.  $C_{10}H_{14}O_3$  requires C, 72.5; H, 8.5%.)

2:4-Dipropionyl-5-methyl-resorcinol was obtained by condensing propionic anhydride (1.5 g.) with  $\gamma$ -orcpropiophenone (2 g.) in presence of aluminium chloride (3.5 g) in nitrobenzene (30 c.c.) The substance crystallised from dilute acetic acid in colourless, long needles m.p. 85-86°. Its alcoholic solution gave deep-violet coloration with ferric chloride (Found: C, 65.8; H, 6.7.  $C_{13}H_{16}O_4$  requires C, 66.1; H, 6.8%.)

$\gamma$ -orcbutyrophene was obtained by the usual method using orcinol (12.4 g.), aluminium chloride (26.7 g.), and butyric anhydride (15.8 g.). The solid isolated as usual crystallised from dilute acetic acid in pale-yellow needles m.p. 120-121°. Its alcoholic solution gave greenish-black coloration with ferric chloride (yield, 40%). There was no trace of any isomeric compound. (Found: C, 68.1; H, 7.3.  $C_{11}H_{14}O_3$  requires C, 68.0; H, 7.2%.)

The *p*-nitrophenyl-hydrazone crystallised from alcohol in reddish micro-needles m.p. 180°. (Found: N, 12.5;  $C_{17}H_{19}N_3O_4$  requires N, 12.8%.)

2-Butyl-5-methyl-resorcinol obtained by the reduction of the above ketone crystallised from petrol (60–80 b.p.) in tiny needles m.p. 104° (yield, 70%). (Found: C, 73.1; H, 9.0.  $C_{11}H_{16}O_2$  requires C, 73.2; H, 8.9%.)

2:4-Dibutyl-5-methyl resorcinol obtained from the above ketone and butyric anhydride crystallised from dilute acetic acid in tiny needles m.p. 67°. Its alcoholic solution gave bluish-red coloration with ferric chloride. (Found: C, 67.9; H, 7.8.  $C_{15}H_{20}O_4$  requires C, 68.2; H, 7.6%.)

*Condensation of  $\gamma$ -orcpropiophenone and  $\gamma$ -orcbutyrophenone with Ethyl-acetoacetate and formation of 5-hydroxy-4:7-dimethyl coumarin.*

A solution of either of the above ketones (2 g.) ethyl acetoacetate (1.3 g.) in concentrated sulphuric acid (15 c.c.) was left overnight. The coumarin crystallised from alcohol in needles m.p. 248–250, and was identified as 5-hydroxy-4:7-dimethyl coumarin by comparison with an authentic specimen.

*Methylation and Hydrolysis of the above coumarin to 4-methyl-2:6-dimethoxy- $\beta$ -methyl-cinnamic acid.*

The mixture of the coumarin (2 g.) sodium hydroxide (20% 25 c.c.) and dimethyl sulphate (10 c.c.) was heated on water-bath for one hour. Further quantity of dimethyl sulphate (5 c.c.) and sodium hydroxide (10 c.c.) was added, and refluxing was continued for another one hour and half. The cooled alkaline solution was acidified, extracted with ether and the recovered solid purified through sodium bicarbonate solution. It crystallised from dilute alcohol in lustrous lemon-yellow needles m.p. 205°. (Found: C, 65.9; H, 6.7.  $C_{13}H_{16}O_4$  requires C, 66.1; H, 6.8%.)

*Conversion of the dimethoxy acid to 5-methoxy-4:7-dimethyl coumarin.*

A solution of the acid (0.5 g.) in concentrated sulphuric acid (10 c.c.) was allowed to stand for 48 hours, and worked up as usual. The solid crystallised from alcohol in needles m.p. 146°, and proved to be 5-methoxy-4:7-dimethyl coumarin by comparison with an authentic specimen.

3-Bromo-5-hydroxy-4:7-dimethyl coumarin was obtained by adding the solution of bromine (1 c.c.) in glacial acetic acid (5 c.c.) to the solution of coumarin (2 g.) in glacial acetic acid (20 c.c.) and crystallised from glacial acid in yellowish needles m.p. 217°. (Found: Br., 29.5.  $C_{11}H_9O_3$  Br, requires Br., 29.7%.)

*Hydrolysis of the above bromo-compound with 5 per cent. sodium carbonate solution and isolation of 3:6-dimethyl 4-hydroxy coumarilic acid and 3:6-dimethyl-4-hydroxy-coumarone.*

A solution of the bromo-coumarin (2 g.) in 5 per cent. sodium carbonate solution (40 c.c.) was heated on sand-bath under reflux for two hours. The solid that separated out on cooling was filtered, and the filtrate, on acidification gave an acid, which after purification through sodium bicarbonate solution slightly decomposed at 250°, but did not melt upto 320°. (Found: C, 63.8; H, 5.0.  $C_{11}H_{10}O_4$  requires C, 64.1; H, 4.9%.)

The solid which was insoluble in sodium carbonate, but soluble in sodium hydroxide crystallised from alcohol in small needles m.p. 320°. (Found: C, 74.0; H, 6.3.  $C_{10}H_{10}O_2$  requires C, 74.1; H, 6.2%.)

*Hydrolysis of 5-hydroxy-6-acetyl-4:7-dimethyl coumarin and Formation of 2:6-dihydroxy-3-acetyl-4-methyl- $\beta$ -methyl cinnamic acid.*

The solution of the coumarin (2 g.) prepared according to Desai and Ekhlās<sup>2</sup> in 20% sodium hydroxide (50 c.c.) was heated on a water-bath for one hour. The cooled solution was acidified with concentrated hydrochloric acid. The resulting acid after purification through sodium bicarbonate solution crystallised from alcohol in tiny needles m.p. 244–246°. Its alcoholic solution gave reddish coloration with ferric chloride. The acid was unaffected by heat and light, and reverted to the original coumarin on treatment with concentrated sulphuric acid in the cold. (Found: C, 62.1; H, 5.8.  $C_{13}H_{14}O_5$  requires C, 62.4; H, 5.6%.)

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#### SUMMARY

The study of the action of propionic and butyric anhydrides in presence of anhydrous aluminium chloride on orcinol shows that  $\gamma$ -substitution takes place almost exclusively. Therefore, this provides a convenient method for the synthesis of hitherto unknown  $\gamma$ -orc-propiofenone and  $\gamma$ -orc-butyrofenone. Some of their interesting derivatives have been prepared. A study has been made of some derivatives of 5-hydroxy-4:7-dimethyl-coumarin.

#### REFERENCES

1. Desai and (Miss.) Vakil .. *Proc. Ind. Acad. Sci.*, 1940, **12**, 391,
2. ——— and Ekhlās .. *Ibid.*, 1938, **8**, 567,