PECHMANN CONDENSATION OF PHENOLS WITH ETHYL BUTYROACETATE

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In continuation of the previous work[1] to study the reactivity of γ-substituted acetoacetic esters in the Pechmann reaction, the reactivity of ethyl butyroacetate which is ethyl γ-ethyl aceto-acetate and which was prepared by the method of Bongert[2] has now been studied.

It has been found that ethyl butyroacetate condenses with resorcinol, orcinol, pyrogallol, phloroglucinol and α-naphthol in presence of sulphuric acid to give 4-propyl coumarin derivatives. The coumarin structure of the compounds was proved by the preparation of the cinnamic acid derivatives.

Phenol, β-naphthol, quinol, *m*-cresol, methyl β-resorcylate and resacetophenone did not condense with ethyl butyroacetate either in the presence of sulphuric acid or in the presence of phosphoryl chloride, phosphorous pentoxide and anhydrous aluminium chloride.

The results show that a γ-ethyl substituent in ethyl acetoacetate has considerable inhibiting effect on the course of the Pechmann reaction, for, phenol, *m*-cresol, quinol and methyl β-resorcylate which do not condense with ethyl butyroacetate do condense with ethyl acetoacetate to give coumarins in presence of sulphuric acid as found by previous workers.[3, 4, 5, 6] Further, the inhibiting effect of the γ-ethyl substituent in ethyl acetoacetate is greater than that of the α-ethyl substituent for it has been found that ethyl α-ethyl acetoacetate condenses with *m*-cresol and methyl β-resorcylate.[4, 7] The γ-ethyl substituent also seems to have a greater retarding effect than a negative substituent like the carbethoxy because ethyl acetone dicarboxylate which may be considered as ethyl γ-carbethoxy acetoacetate condenses with *m*-cresol and quinol[8] and also with methyl β-resorcylate.[9]

Experimental

7-Hydroxy-4-propyl coumarin.—To a mixture of ethyl butyroacetate (2·0 g.) and resorcinol (1·3 g.), sulphuric acid (75%, 15 c.c.) was slowly added. The reaction mixture was allowed to stand overnight and then poured in

powdered ice. The yellow solid (0·5 g.) obtained was crystallised from alcohol in needles, m.p. 130°. It gave blue fluorescence with alkali. (Found: C, 70·1; H, 5·8; $C_{12}H_{12}O_3$ requires C, 70·5, H, 5·8 per cent.)

The acetyl derivative.—7-Hydroxy-4-propyl coumarin (0·5 g.) was refluxed on a wire-gauze for 4 hours with anhydrous sodium acetate (1·0 g.) and acetic anhydride (5 c.c.). The product obtained on adding the reaction mixture to water was crystallized from rectified spirit in tiny needles, m.p. 118-19°. (Found: C, 68·1, H, 5·3; $C_{14}H_{14}O_4$ requires C, 68·3, H, 5·6 per cent.)

The methyl ether.—7-Hydroxy-4-propyl coumarin (0·5 g.) was dissolved in acetone (50 c.c.) and refluxed for twenty hours with fused potassium carbonate (1·0 g.) and methyl iodide (5 c.c.). The acetone was removed by evaporation and water was added. The product obtained was crystalised from very dilute alcohol in tiny shining needles, m.p. 145–46°. (Found: C, 71·3, H, 6·4; $C_{13}H_{14}O_3$ requires C, 71·5, H, 6·4 per cent.)

2 : 4-*dimethoxy β-propyl cinnamic acid.*—7-Hydroxy-4-propyl coumarin (1 g.) was dissolved in acetone, dimethyl sulphate (8 c.c.) was added and the reaction mixture heated on a boiling water-bath for 8 to 10 minutes. Sodium hydroxide (5%, 30 c.c.) was then added gradually with constant shaking, the heating being carried on all the time. More dimethyl sulphate (10 c.c.) and sodium hydroxide (40 c.c.) were added alternately with shaking. Finally, excess of sodium hydroxide was added and heating continued for about half an hour. It was then left overnight. Next day the solution was filtered and acidified with con. HCl. It was then kept in the frigidaire and on the next day the solid obtained was filtered, washed and treated with sodium bicarbonate solution. The product obtained on acidification of the sodium bicarbonate solution was crystallized from dilute alcohol in tiny shining silky needles, m.p. 83-85°. It decolourizes bromine water and dilute potassium permanganate solution. It dissolves in sodium bicarbonate solution with effervescence. (Found: C, 67·0, H, 7·0; $C_{14}H_{18}O_4$ requires C, 67·2, H, 7·1 per cent.)

5-*Hydroxy*-4-*propyl*-7-*methyl coumarin.*—Prepared from orcinol (1·6 g.), ethyl butyroacetate (2 g.) and sulphuric acid (75%, 15 c.c.) as usual, was crystallized from alcohol in needles, m.p. 180°. It gave deep yellow colouration with sodium hydroxide. (Found: C, 72·1, H, 6·1; $C_{13}H_{14}O_3$ requires C, 71·7, H, 6·4 per cent.)

The acetyl derivative.—Prepared as before was crystallised from rectified spirit in tiny needles, m.p. 120–21°. (Found: C, 69·4, H, 6·1; $C_{15}H_{16}O_4$ requires C, 69·25, H, 6·25 per cent.)

The methyl ether.—Prepared as before, was crystallised from very dilute alcohol in tiny shining needles, m.p. 78–79°. (Found: C, 72·3, H, 6·8; $C_{14}H_{16}O_3$ requires C, 72·4, H, 6·9 per cent.)

2 : 6-*Dimethoxy*-4-*methyl*-β-*propyl cinnamic acid.*—Prepared as before, was crystallised from water with a few drops of alcohol in tiny fine silky needles, m.p. 165°. (Found: C, 68·3, H, 7·2; $C_{15}H_{20}O_4$ requires C, 68·2, H, 7·5 per cent.)

7 : 8-*Dihydroxy*-4-*propyl coumarin.*—Prepared from pyrogallol (1·6 g.), ethyl butyroacetate (2·0 g.) and sulphuric acid (75%, 15 c.c.); was crystallised from alcohol in needles, m.p. 198–200°. (Found: C, 65·8, H, 5·2, $C_{12}H_{12}O_4$ requires C, 65·5, H, 5·5 per cent.)

The diacetyl derivative.—Prepared as usual was crystallised from dilute alcohol in tiny needles, m.p. 150–52°. (Found: C, 62·8, H, 5·4; $C_{16}H_{16}O_6$ requires C, 63·1, H, 5·3 per cent.)

The dimethyl ether.—Prepared as usual, was crystallised from dilute alcohol in tiny shining needles, m.p. 95°. (Found: C, 67·9, H, 6·2; $C_{14}H_{16}O_4$ requires C, 67·8, H, 6·4 per cent.)

2 : 3-4-*Trimethoxy*-β-*propyl cinnamic acid.*—Prepared as usual was crystallised from aqueous alcoholic solution in fine silky needles, m.p. 134-36°. (Found: C, 64·4, H, 7·1; $C_{15}H_{20}O_5$ requires C, 64·4, H, 7·1 per cent.)

5:7-*Dihydroxy*-4-*propyl coumarin.*—Prepared from phloroglucinol (2 g.), ethyl butyroacetate (2 g.) and sulphuric acid (75%, 15 c.c.) was crystallised from alcohol in needles, m. p. 258°. (Found: C, 64·9; H, 5·2; $C_{12}H_{12}O_4$ requires C, 65·4, H, 5·4 per cent.)

The diacetyl derivative.—Prepared as usual was crystallised from rectified spirit in tiny needles, m.p. 145°. (Found: C, 62·8, H, 4·9; $C_{16}H_{16}O_6$ requires C, 63·1; H, 5·2 per cent.)

The dimethyl ether.—Prepared as usual was crystallised from dilute alcohol in needles, m.p. 150°. (Found: C, 67·6, H, 6·2; $C_{14}H_{16}O_4$ requires C, 67·8, H, 6·4 per cent.)

2 : 4 : 6-*Trimethoxy*-β-*propyl cinnamic acid.*—Prepared as usual was crystallised from water with a little alcohol in fine silky needles, m.p. 140°. (Found: C, 64·4, H, 7·2; $C_{15}H_{20}O_5$ requires C, 64·4, H, 7·1 per cent.)

α-*Naphtha* 4-*propyl* α-*pyrone.*—Prepared from α-naphthol (1·9 g.), ethyl butyroacetate (2 g.) and sulphuric acid (75%, 15 c.c.) was crystallised from alcohol (charcoal) in needles, m.p. 108–10°. (Found: C, 79·9, H, 5·8; $C_{16}H_{14}O_2$ requires C, 80·4, H, 5·8 per cent.)

Attempts to prepare the cinnamic acid derivative from this product by the usual method were unsuccessful.

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Summary

Ethyl butyroacetate has been found to condense with resorcinol, orcinol, pyrogallol, phloroglucinol and α-naphthol in presence of sulphuric acid to give 4-propyl coumarin derivatives. Phenol, *m*-cresol, quinol, β-naphthol, methyl β-resorcylate and resacetophenone however did not condense either in presence of sulphuric acid or in presence of phosphorous pentoxide, phosphoryl chloride or anhydrous aluminium chloride as condensing agents.

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