202. γ-*Substitution in the Resorcinol Nucleus. Part IV. The Gattermann Reaction with Polyhydroxy-acetophenones.*

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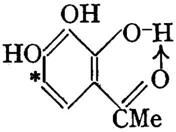
In continuation of previous work (Part II; this vol., p. 132) the behaviour of di- and tri-hydroxyphenyl methyl ketones in the modified Gattermann reaction has been studied. The non-condensation of gallacetophenone has been explained in the light of the mechanism of the reaction previously advanced (*loc. cit.*).

The behaviour of the following ketones in the modified Gattermann reaction has been studied.

(1) 2 : 4-Dihydroxy-5-ethylacetophenone afforded 2 : 4-*dihydroxy*-3-*formyl*-5-*ethylacetophenone*. This gave a 2 : 4-*dinitrophenylhydrazone* and a *dioxime* and its *o*-hydroxyaldehyde structure was proved by the formation of 5-*hydroxy*-3 : 6-*diacetyl*-8-*ethylcoumarin* and 5-*hydroxy*-6-*acetyl*-8-*ethylcoumarin*-3-*carboxylic acid* by condensation with ethyl acetoacetate and cyanoacetic acid respectively.

(2) 6-Methylresacetophenone gave a ketone-aldehyde which is regarded as 2 : 4-*dihydroxy*-3-*formyl*-6-*methylacetophenone* by analogy with the aldehyde obtained from resacetophenone (Shah and Shah, *loc. cit.*) and also on the following grounds : (*a*) The ketone-aldehyde on condensation with cyanoacetic acid gave 5-*hydroxy*-6-*acetyl*-7-*methylcoumarin*-3-*carboxylic acid*, which showed the typical property of a 5-hydroxycoumarin, *viz.*, non-fluorescence in alkaline and in sulphuric acid solution (Collie and Chrystall, J., 1907, **91**, 1804; Dey, J., 1915, **107**, 1614, 1621). (*b*) Reduction of the ketone-aldehyde by the Clemmensen method gave 2 : 5-*dimethyl*-4-*ethylresorcinol*, m. p. 95—97°, not 5 : 6-dimethyl-4-ethylresorcinol, m. p. 145—146° (Shah and Mehta, *J. Indian Chem. Soc.*, 1936, **13**, 358), which should have been formed, had the ketone-aldehyde been 2 : 4-dihydroxy-5-formyl-6-methylacetophenone.

(3) 2-Acetylresorcinol gave 2 : 6-*dihydroxy*-3-*formylacetophenone*. This, on condensation with cyanoacetic acid, ethyl malonate and ethyl acetoacetate, gave 7-*hydroxy*-8-*acetylcoumarin*-3-*carboxylic acid*, *ethyl* 7-*hydroxy*-8-*acetylcoumarin*-3-*carboxylate*, and 7-*hydroxy*-3 : 8-*diacetylcoumarin* respectively, and on reduction afforded 4-methyl-2-ethylresorcinol (Robinson and Shah, J., 1934, 1684).



(4) Phloroacetophenone afforded 2 : 4 : 6-*trihydroxy*-3-*formylacetophenone*.

Gallacetophenone, 5-nitroresacetophenone and *iso*pæonol were recovered unchanged after attempted condensation. The failure in the case of gallacetophenone can be explained on the view of the mechanism given in Part II (*loc. cit.*) : the carbon atom marked with an asterisk, where the condensation might be expected to take place, is not reactive, as it is united by a single bond to a carbon atom bearing a hydroxyl group.

EXPERIMENTAL.

The following compounds were prepared by methods already described (Part II, *loc. cit.*).

2 : 4-*Dihydroxy*-3-*formyl*-5-*ethylacetophenone*, obtained from 2 : 4-dihydroxy-4-ethylacetophenone (10 g.), zinc cyanide (13·7 g.), aluminium chloride (15·5 g.), and hydrogen chloride, crystallised from alcohol (charcoal) in colourless needles (4·5 g.), m. p. 77—78° (Found : C, 63·5; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·6; H, 5·8%). It gave a bright yellow colour with alkali solution and a deep red coloration with alcoholic ferric chloride. The 2 : 4-*dinitrophenylhydrazone* crystallised from glacial acetic acid in yellow needles, m. p. 261° (decomp.) (Found : N, 14·4. $C_{17}H_{16}O_7N_4$ requires N, 13·9%), and the *dioxime* from dilute alcohol in colourless needles, m. p. 189—190° (Found : N, 11·8. $C_{11}H_{14}O_4N_2$ requires N, 11·3%).

5-*Hydroxy*-3 : 6-*diacetyl*-8-*ethylcoumarin*, prepared from the preceding aldehyde (1 g.), ethyl acetoacetate (1 g.), and piperidine (4 drops), crystallised from alcohol in yellow needles (0·75 g.), m. p. 189—190° (Found : C, 65·3; H, 5·3. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1%).

5-*Hydroxy*-6-*acetyl*-8-*ethylcoumarin*-3-*carboxylic acid*, obtained from cyanoacetic acid (0·5 g.) and the aldehyde (0·5 g.) in 20% sodium hydroxide solution (20 c.c.), crystallised from alcohol in pale yellow needles (0·3 g.), m. p. 208—209° (efferv.) (Found : C, 60·9; H, 4·4. $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·3%).

2 : 4-*Dihydroxy*-3-*formyl*-6-*methylacetophenone*, prepared from 6-methylresacetophenone (10 g.), zinc cyanide (14 g.), aluminium chloride (16 g.), and hydrogen chloride, was purified by steam-distillation (3 g.) ; it then crystallised from light petroleum (b. p. 80—90°) in long, stout, colourless needles, m. p. 98—99° (Found : C, 61·8; H, 5·2. $C_{10}H_{10}O_4$ requires C, 61·9; H, 5·2%), sparingly soluble in water but easily in alcohol and benzene. It gave a bright yellow colour in alkaline solution and a brownish-violet colour with alcoholic ferric chloride. The 2 : 4-*dinitrophenylhydrazone* crystallised from glacial acetic acid in tiny needles, m. p. 275° (decomp.) (Found : N, 15·1. $C_{16}H_{14}O_7N_4$ requires N, 15·0%).

5-*Hydroxy*-6-*acetyl*-7-*methylcoumarin*-3-*carboxylic acid*, prepared by condensation of the aldehyde with cyanoacetic acid, crystallised from dilute alcohol in pale yellow needles, m. p. 220—222° (efferv.) (Found : C, 59·5; H, 3·9. $C_{13}H_{10}O_6$ requires C, 59·5; H, 3·8%).

The aldehyde (1 g.), dissolved in hot alcohol, was gradually added to a mixture of zinc amalgam (prepared from 10 g. of zinc dust; Robinson and Shah, J., 1934, 1497) and dilute hydrochloric acid (1 : 1) (30 c.c.) at 100°. The heating was continued until an ethereal extract of a sample did not give a coloration with alcoholic ferric chloride. The cooled liquid was filtered and both it and the residual amalgam were extracted with ether. The oily residue left after evaporation of the combined extracts crystallised from light petroleum (b. p. 80—90°) in pearly needles of 2 : 5-*dimethyl*-4-*ethylresorcinol*, m. p. 95—97° (Found: C, 71·3; H, 8·3. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%), which decomposed on keeping.

2 : 6-*Dihydroxy*-3-*formylacetophenone*, prepared from 2-acetylresorcinol (10 g.), zinc cyanide (15·5 g.), aluminium chloride (18 g.), and hydrogen chloride, crystallised from dilute alcohol in colourless needles (9·5 g.), m. p. 105—106° (Found: C, 59·7; H, 4·6. $C_9H_8O_4$ requires C, 60·0; H, 4·4%). It did not give a yellow colour in alkaline solution. The *anil*, prepared from the aldehyde and aniline (1 mol.) at 100°, crystallised from dilute alcohol in yellow needles, m. p. 185° (Found: N, 5·6. $C_{15}H_{13}O_3N$ requires N, 5·5%).

Ethyl 7-*hydroxy*-8-*acetylcoumarin*-3-*carboxylate*, prepared from ethyl malonate (1 g.), the aldehyde (1 g.), and piperidine (4 drops), crystallised from dilute alcohol in woolly yellow needles (0·5 g.), m. p. 158—159° (Found: C, 60·8; H, 6·2. $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·3%). It gave a bluish-green fluorescence with alkali.

7-*Hydroxy*-8-*acetylcoumarin*-3-*carboxylic acid*, prepared by condensation of the aldehyde with cyanoacetic acid, crystallised from alcohol in long needles, m. p. 200—201° (efferv.) (Found: C, 53·8; H, 3·8. $C_{12}H_8O_6N_2$ requires C, 54·1; H, 3·8%), sparingly soluble in alcohol and moderately readily soluble in glacial acetic acid.

7-*Hydroxy*-3 : 8-*diacetylcoumarin*, prepared by condensation of the aldehyde with ethyl acetoacetate in presence of piperidine, crystallised from alcohol in yellow needles, m. p. 166—167° (Found: C, 63·1; H, 4·0. $C_{13}H_{10}O_5$ requires C, 63·4; H, 4·1%). The *acetyl* derivative, prepared by refluxing the coumarin (0·3 g.), acetic anhydride (50 c.c.), and pyridine (1 c.c.) for 3 hours and pouring the product into water, was crystallised from dilute alcohol and then from benzene; it formed tiny needles, m. p. 170—177° (Found: C, 62·7; H, 4·2. $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%).

2 : 6-Dihydroxy-3-formylacetophenone was reduced by the Clemmensen method and the oil obtained after ether extraction was purified by sublimation in a high vaccum at 100°, 4-methyl-2-ethylresorcinol being obtained in colourless woolly needles, m. p. 98—100° (Robinson and Shah, *loc. cit.*, give m. p. 98—100°). The *di*-p-*nitrobenzoyl* derivative, prepared by the Schotten–Baumann method, crystallised from alcohol in colourless needles, m. p. 174—175° (Found: N, 6·1. $C_{23}H_{18}O_8N_2$ requires N, 6·2%).

2 : 4 : 6-*Trihydroxy*-3-*formylacetophenone*, prepared from phloroacetophenone (10 g.), zinc cyanide (14 g.), aluminium chloride (16 g.), and hydrogen chloride, was crystallised from dilute alcohol and then from xylene; it formed tiny needles with an orange tinge (6 g.), m. p. 180—182° (Found: C, 54·5; H, 4·2. $C_9H_8O_5$ requires C, 55·1; H, 4·1%), easily soluble in alcohol and sparingly in benzene and xylene. The 2 : 4-*dinitrophenylhydrazone* crystallised from glacial acetic acid in deep red needles, m. p. 283° (decomp.) (Found: N, 14·7. $C_{15}H_{12}O_8N_4$ requires N, 14·9%).

All the analyses recorded are micro-analyses.

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