

50. *γ-Substitution in the Resorcinol Nucleus. Part V. The Gattermann Reaction with 4-Acylresorcinols.*

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In continuation of previous work (J., 1939, 132, 300, 749) the behaviour of some 4-acylresorcinols in the modified Gattermann reaction has been studied.

(1) RESPROIOPHENONE gave a ketone-aldehyde whose constitution as 2 : 4-dihydroxy-3-formylpropiophenone was proved as follows: 2 : 4-Dihydroxy-3-methylpropiophenone, prepared by the Hoesch reaction from 2-methylresorcinol (Jones and Robertson, J., 1932, 1692) and propionitrile, gave by Clemmensen reduction 2-methyl-4-propylresorcinol, which was characterised by the preparation of 7-hydroxy-4 : 8-dimethyl-6-propylcoumarin. Reduction of the ketone-aldehyde by the Clemmensen method gave a phenol identical with 2-methyl-4-propylresorcinol.

2 : 4-Dihydroxy-3-formylpropiophenone on condensation with ethyl acetoacetate and cyanoacetic acid gave 5-hydroxy-3-acetyl-6-propionylcoumarin and 5-hydroxy-6-propionylcoumarin-3-carboxylic acid respectively.

(2) Resbutyrophenone gave a ketone-aldehyde whose constitution as 2 : 4-dihydroxy-3-formylbutyrophenone was established by reactions similar to those mentioned above. On condensation with cyanoacetic acid it afforded 5-hydroxy-6-butyrylcoumarin-3-carboxylic acid.

(3) 2 : 4-Dihydroxybenzophenone gave a ketone-aldehyde whose constitution as 2 : 4-dihydroxy-3-formylbenzophenone follows from its reduction by Clemmensen's method to a phenol identical with 4-benzyl-2-methylresorcinol prepared by reduction of 2 : 4-dihydroxy-3-methylbenzophenone (Jones and Robertson, *loc. cit.*). On condensation with cyanoacetic acid it afforded 5-hydroxy-6-benzoylcoumarin-3-carboxylic acid.

(4) 2 : 4-Dihydroxyphenyl benzyl ketone gave a ketone-aldehyde whose constitution as 2 : 4-dihydroxy-3-formylphenyl benzyl ketone was established as follows: 2 : 6-Dihydroxy-m-tolyl benzyl ketone, prepared by the Hoesch reaction from 2-methylresorcinol and phenylacetonitrile, gave on reduction by Clemmensen's method 2-methyl-4-β-phenylethylresorcinol, characterised by the preparation of a di-p-nitrobenzoyl derivative, and identical with the product of reduction of the ketone-aldehyde by the Clemmensen method. 2 : 4-Dihydroxy-3-formylphenyl benzyl ketone on condensation with cyanoacetic acid, ethyl malonate, and ethyl acetoacetate gave 5-hydroxy-6-phenylacetylcoumarin-3-carboxylic acid, ethyl 5-hydroxy-6-phenylacetylcoumarin-3-carboxylate, and 5-hydroxy-3-acetyl-6-phenylacetylcoumarin respectively.

EXPERIMENTAL.

The following compounds were prepared by methods already described (Part II; J., 1939, 132).

2 : 4-Dihydroxy-3-formylpropioiphenone.—To a solution of respropioiphenone (10 g.) in dry ethyl acetate, zinc cyanide (14 g.) and potassium chloride (1.5 g.) were added, followed by aluminium chloride (16 g.) in ether. Hydrogen chloride was passed for 4 hours. Water (200 c.c.) was then added gradually, and the mixture heated at 100° for $\frac{1}{2}$ hour. The precipitated *ketone-aldehyde* crystallised from alcohol (charcoal) in stout colourless needles (7.5 g.), m. p. 140—141° (Found : C, 62.1; H, 5.4. $C_{10}H_{10}O_4$ requires C, 61.9; H, 5.2%). It gave a bright yellow colour in alkali solution and a deep red coloration with alcoholic ferric chloride. The **2 : 4-dinitrophenylhydrazones** crystallised from glacial acetic acid in tiny yellow needles, m. p. 265—267° (decomp.) (Found : N, 15.1. $C_{16}H_{14}O_7N_4$ requires N, 15.0%).

5-Hydroxy-6-propionylcoumarin-3-carboxylic acid, prepared from cyanoacetic acid (1 g.) and the *ketone-aldehyde* (1 g.) in 20% sodium hydroxide solution (15 c.c.), crystallised from alcohol in straw-coloured needles (0.9 g.), m. p. 185—186° (efferv.) (Found : C, 59.9; H, 4.0. $C_{13}H_{10}O_6$ requires C, 59.5; H, 3.8%).

5-Hydroxy-3-acetyl-6-propionylcoumarin, prepared from the *ketone-aldehyde* (1 g.), ethyl acetoacetate (1 g.), and piperidine (4 drops), crystallised from dilute alcohol in yellow needles (0.6 g.), m. p. 188—190° (Found : C, 64.6; H, 4.7. $C_{14}H_{12}O_5$ requires C, 64.6; H, 4.6%).

2 : 4-Dihydroxy-3-methylpropioiphenone.—A solution of 2-methylresorcinol (1 g.) and excess of propionitrile (1 g.) in ether (30 c.c.) was saturated with hydrogen chloride in presence of fused zinc chloride (1 g.); a reddish viscous layer gradually separated. After 24 hours, ether (50 c.c.) was added, the ethereal layer decanted, and the viscous liquid washed twice with ether (30 c.c.). The residual material was heated with water (50 c.c.) on the steam-bath for $\frac{1}{2}$ hour, and the *ketone* collected on cooling. It crystallised from water in rosy needles (0.5 g.), m. p. 128—130° (Found : C, 66.6; H, 6.7. $C_{10}H_{12}O_3$ requires C, 66.7; H, 6.7%). Its reduction by the Clemmensen method gave **2-methyl-4-propylresorcinol**, which crystallised from ligroin in pearly prisms, m. p. 102—103° (Found : C, 72.4; H, 8.6. $C_{10}H_{14}O_2$ requires C, 72.3; H, 8.4%).

7-Hydroxy-4 : 8-dimethyl-6-propylcoumarin was prepared from 2-methyl-4-propylresorcinol (0.5 g.), ethyl acetoacetate (0.5 g.), and sulphuric acid (80%; 2 c.c.) and crystallised first from ligroin and then from 10% aqueous alcohol; it formed colourless needles, m. p. 160—162° (Found : C, 72.6; H, 6.9. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%).

Reduction of 2 : 4-Dihydroxy-3-formylpropioiphenone.—The *aldehyde* (1 g.), dissolved in acetic acid, was gradually added to a mixture of zinc amalgam (20 g.), dilute hydrochloric acid (1 : 1) (30 c.c.), and acetic acid (5 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 the evaporation of the ether, on neutralisation of the acetic acid, precipitated 2-methyl-4-propylresorcinol, which crystallised from ligroin in pearly prisms, m. p. and mixed m. p. with the above specimen 102—103°.

2 : 4-Dihydroxy-3-formylbutyrophenone.—Prepared from resbutyrophenone (10 g.), zinc cyanide (13 g.), potassium chloride (1.4 g.), aluminium chloride (14.7 g.), and hydrogen chloride, this crystallised from alcohol in stout yellow needles (3 g.), m. p. 42—43° (Found : C, 63.6; H, 5.9. $C_{11}H_{12}O_4$ requires C, 63.5; H, 5.8%). The *semicarbazone* crystallised from glacial acetic acid in colourless needles, m. p. 242—245° (decomp.) (Found : N, 15.3. $C_{12}H_{15}O_4N_3$ requires N, 15.9%).

5-Hydroxy-6-butyrylcoumarin-3-carboxylic acid, prepared by the condensation of the *ketone-aldehyde* with cyanoacetic acid, crystallised from alcohol in straw-coloured needles, m. p. 198—200° (efferv.) (Found : C, 60.7; H, 4.4. $C_{14}H_{12}O_6$ requires C, 60.9; H, 4.4%).

2 : 4-Dihydroxy-3-methylbutyrophenone, prepared from 2-methylresorcinol (1 g.), butyronitrile (1 g.), zinc chloride (1 g.), and hydrogen chloride in ether (30 c.c.), crystallised from water in straw-coloured needles, m. p. 155—157° (Found : C, 65.4, 65.4; H 6.2, 6.3. $C_{11}H_{14}O_3$ requires C, 68.1; H, 7.3%). The low carbon and hydrogen values appear to be due to the formation of methane in combustion).

2-Methyl-4-butyresorcinol was prepared by the reduction of 2 : 4-dihydroxy-3-methylbutyrophenone and 2 : 4-dihydroxy-3-formylbutyrophenone by the Clemmensen method. Both specimens crystallised from light petroleum (b. p. 80—90°) in pearly prisms, m. p. and mixed m. p. 74—76° (Found : C, 74.4; H, 9.3. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.9%).

2 : 4-Dihydroxy-3-formylbenzophenone.—Prepared from 2 : 4-dihydroxybenzophenone (10 g.),

zinc cyanide (16.4 g.), aluminium chloride (17.6 g.), and hydrogen chloride, this crystallised from alcohol in pale yellow needles (4 g.), m. p. 117—118° (Found : C, 68.7; H, 4.2. $C_{14}H_{10}O_4$ requires C, 69.4; H, 4.1%). The 2 : 4-dinitrophenylhydrazones crystallised from glacial acetic acid in yellow needles, m. p. 228—230° (decomp.) (Found : N, 13.1. $C_{20}H_{14}O_7N_4$ requires N, 13.3%).

5-Hydroxy-6-benzoylcoumarin-3-carboxylic acid, prepared by the condensation of the ketone-aldehyde with cyanoacetic acid, crystallised from alcohol in tiny needles, m. p. 244° (efferv.) (Found : C, 65.7; H, 3.4. $C_{17}H_{10}O_6$ requires C, 65.8; H, 3.2%).

4-Benzyl-2-methylresorcinol, prepared by Clemmensen reduction of the ketone-aldehyde, crystallised from ligroin in pearly prisms, m. p. 96—98° (Found : C, 78.4; H, 6.6. $C_{14}H_{14}O_2$ requires C, 78.5; H, 6.5%). The m. p. was not depressed by a sample prepared by the Clemmensen reduction of 2 : 4-dihydroxy-3-methylbenzophenone (Jones and Robertson, *loc. cit.*).

2 : 4-Dihydroxy-3-formylphenyl Benzyl Ketone.—Prepared from 2 : 4-dihydroxyphenyl benzyl ketone (10 g.), zinc cyanide (10.3 g.), aluminium chloride (11.2 g.), and hydrogen chloride, this crystallised from dilute alcohol in tiny colourless needles (6 g.), m. p. 110.5—112° (Found : C, 70.2; H, 4.7. $C_{15}H_{12}O_4$ requires C, 70.3; H, 4.7%). The 2 : 4-dinitrophenylhydrazones crystallised from glacial acetic acid in tiny yellow needles, m. p. 252—253° (decomp.) (Found : N, 12.6. $C_{21}H_{16}O_7N_4$ requires N, 12.8%), and the semicarbazone in tiny colourless needles, m. p. 248—249° (decomp.) (Found : N, 12.9. $C_{16}H_{15}O_4N_3$ requires N, 13.4%).

Ethyl 5-hydroxy-6-phenylacetylcoumarin-3-carboxylate, prepared from ethyl malonate (1 g.), the ketone-aldehyde (1 g.), and piperidine (4 drops), crystallised from alcohol in woolly yellow needles (0.6 g.), m. p. 200—201° (Found : C, 68.2; H, 4.6. $C_{20}H_{16}O_6$ requires C, 68.2; H, 4.6%).

5-Hydroxy-3-acetyl-6-phenylacetylcoumarin, prepared by the condensation of the ketone-aldehyde with ethyl acetoacetate in presence of piperidine, crystallised from alcohol in yellow needles, m. p. 198—200° (Found : C, 70.7; H, 4.4. $C_{16}H_{14}O_5$ requires C, 70.8; H, 4.4%).

5-Hydroxy-6-phenylacetylcoumarin-3-carboxylic acid, prepared by the condensation of the ketone-aldehyde with cyanoacetic acid, crystallised from alcohol in rectangular plates, m. p. 215—217° (efferv.) (Found : C, 66.6; H, 3.7. $C_{18}H_{12}O_6$ requires C, 66.7; H, 3.7%).

2 : 6-Dihydroxy-m-tolyl benzyl ketone was prepared from 2-methylresorcinol (1 g.), phenyl-acetonitrile (1.5 g.), zinc chloride (1 g.), and hydrogen chloride in ether (30 c.c.) and crystallised from benzene; m. p. 157—159° (Found : C, 70.9; H, 6.7. $C_{15}H_{14}O_3 \cdot 0.5H_2O$ requires C, 71.6; H, 5.9%).

2-Methyl-4-β-phenylethylresorcinol, prepared by Clemmensen reduction of the preceding ketone and of 2 : 4-dihydroxy-3-formylphenyl benzyl ketone, crystallised from hot water in colourless needles, m. p. 115—116° (Found : C, 78.9; H, 7.1. $C_{16}H_{16}O_2$ requires C, 78.9; H, 7.0%). The di-p-nitrobenzoyl derivative, prepared from the phenol (0.2 g.), p-nitrobenzoyl chloride (0.4 g.) in ether, and sodium hydroxide solution (3 c.c.), crystallised from alcohol in straw-coloured needles, m. p. 140—142° (Found : N, 5.3. $C_{23}H_{22}O_8N_2$ requires N, 5.5%).

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