

THE ACTION OF HEXAMETHYLENETETRAMINE ON THE METHYL ESTERS OF PHENOL-CARBOXYLIC ACIDS

Part V. The Derivatives of 2:4-Dihydroxy-5-Formylbenzoic Acid

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Received February 4, 1946

THE preparation as well as the characterisation of 2:4-dihydroxy-5-formylbenzoic acid has already been described by Desai and Radha.¹ Some of its important and interesting derivatives are being described in this communication. Attempts to esterify the carboxyl group by Fischer-Speier method resulted in the formation of some colouring matter. The action of either diazomethane, or dimethylsulphate in an alkaline medium or the action of methyl iodide on the silver salt of the acid resulted in the methylation of only one of the hydroxyl groups, and various other methods of methylation failed to give the dimethoxy derivative. The monomethoxy derivative may be either 2-methoxy-4-hydroxy-5-formylbenzoic or 2-hydroxy-4-methoxy-5-formylbenzoic acid.

Nitration of 2:4-dihydroxy-5-formylbenzoic acid gave a mixture of 2:4-dihydroxy-5-nitrobenzaldehyde and 2:4-dihydroxy-3:5-dinitrobenzoic acid, and it was not possible to isolate the nitro-derivative containing both the formyl and carboxyl groups in tact.

Clemmenson reduction gave readily 2:4-dihydroxy-5-methylbenzoic acid, while bromination of the aldehyde acid under various conditions gave a bromo-derivative which gave too low values for the halogen. Acetylation of the aldehyde acid with acetic anhydride in presence of either pyridine or anhydrous sodium acetate gave only the di-acetoxy derivative, not a trace of the coumarin which was expected in the latter method being formed.

Condensation of the aldehyde acid with ethyl malonate and ethyl acetoacetate by Knoevenagel's method gave respectively 3-carbethoxy-6-carboxy-7-hydroxy coumarin and 3-acetyl-6-carboxy-7-hydroxy coumarin, the alkaline solutions of which gave blue fluorescence. The formation of these two coumarin derivatives furnish the additional proof to establish the 5-position of the formyl group.

EXPERIMENTAL

Methylation of 2:4-dihydroxy-5-formylbenzoic acid and formation of 2 or 4-methoxy-4 or 2-hydroxy-5-formylbenzoic acid.—To the aldehydo-acid (1 gm.) dissolved in potassium hydroxide (100 c.c. of 20%), dimethylsulphate (20 c.c.) was gradually added with shaking and warmed on the water-bath for one hour. The yellow, flocculent precipitate obtained on the acidification with hydrochloric acid crystallised from methyl alcohol in small yellowish needles, m.p. 246–47. It gave an intense red coloration with alcoholic ferric chloride. (Found: C, 54.8; H, 3.9; $C_9H_8H_5$ requires C, 55.1; H, 4.0 per cent.)

Nitration of 2:4-dihydroxy-5-formylbenzoic acid and formation of 2:4-dihydroxy-5-nitrobenzaldehyde and 2:4-dihydroxy-3:5-dinitrobenzoic acid.—

Concentrated nitric acid (15 c.c.) was gradually added with constant stirring to the solution of the aldehydoacid (2 g.) dissolved in concentrated sulphuric acid (10 c.c.), and left in a frigidaire overnight. The solid that separated out was filtered, washed and crystallised from dilute alcohol in long, lustrous, golden-yellow needles, m.p. 146–47°. It did not dissolve in sodium bicarbonate solution, but readily reacted with 2:4-dinitrophenylhydrazine and identified as 2:4-dihydroxy-5-nitrobenzaldehyde of Gattermann.² (Found: N, 7.4; $C_7H_5O_5N$ requires N, 7.7 per cent.)

The 2:4-dinitrophenylhydrazone prepared in the usual manner crystallised from glacial acetic acid in small, orange needles, m.p. 258° (dec.). (Found: N, 19.5; $C_{13}H_9O_8N_5$ requires N, 19.3 per cent.)

The filtrate from which the nitro-aldehyde was removed was diluted with water, salted, and extracted with ether. On the removal of the solvent small yellow crystals of a solid, m.p. 195–96°, were obtained. It dissolved in sodium bicarbonate solution with effervescence, but did not react with 2:4-dinitrophenylhydrazone, and was identified as 2:4-dihydroxy-3:5-dinitrobenzoic acid by comparison with an authentic specimen prepared by Hemmel Meyer's³ method. (Found: N, 11.2; $C_7H_4O_8N_2$ requires N, 11.5 per cent.)

2:4-Dihydroxy-5-methylbenzoic acid was prepared by adding the alcoholic solution of the aldehydo acid (2 g.) to amalgamated zinc (40 g.) and dilute hydrochloric acid (50 c.c.) and warming the mixture on the water-bath for 2 hours. The hot liquid deposited small needles, m.p. 163–64° C. (Found: C, 58.2; H, 4.5; $C_8H_8O_4$ requires C, 58.3; H, 4.8 per cent.)

2:4-Diacetoxy-5-formylbenzoic acid was obtained by heating the mixture of the formyl acid (1 g.), acetic anhydride (10 c.c.) and pyridine (3 drops)

on a sand-bath for four hours. The pasty mass obtained on pouring the mixture into water crystallised from dilute alcohol in long, colourless needles, m.p. 158–59° C. and did not give any colouration with alcoholic ferric chloride. (Found: C, 53·8; H, 3·8; $C_{12}H_{10}O_7$ requires C, 54·1; H, 3·8 per cent.)

Ethyl 7-hydroxy-6-carboxy-coumarin-3-carboxylate.—A mixture of the aldehydo acid (2 g.), ethyl malonate (2 g.), pyridine (20 c.c.) and piperidine (4–5 drops) was kept overnight after heating on the water-bath for one hour. The pasty solid obtained on the addition of dilute hydrochloric acid crystallised from alcohol in pale-yellow needles, m.p. 235–36° C. (Found: C, 57·0; H, 4·2; $C_{15}H_{10}O_7$ requires C, 56·7; H, 3·9 per cent.)

7-Hydroxy-6-carboxy-3-acetylcoumarin was obtained by heating the mixture of the formyl acid (1 gm.), ethylacetoacetate (1 g.), pyridine (10 c.c.) and piperidine (4 drops) on the water-bath for one hour and keeping the mixture overnight. The solid obtained on acidification with dilute hydrochloric acid crystallised from dilute alcohol in needles, m.p. 167–68° C. The alcoholic solution of this substance as well as the one described above gave a reddish-brown colouration with alcoholic ferric chloride. (Found: C, 58·2; H, 4·0; $C_{12}H_8O_6$ requires C, 58·1; H, 3·8 per cent.)

SUMMARY

Some important and interesting derivatives of 2:4-dihydroxy-5-formylbenzoic acid have been prepared.

REFERENCES

1. Desai and (Miss) Radha .. *Proc. Ind. Acad., Sci.*, (A), 1940, 9, 423.
2. Gattermann .. *Annalen*, 357, 337.
3. Hemmel Meyer, M. .. 26, 190.