

# REACTIVITY OF THE DOUBLE BOND IN COUMARINS AND RELATED UNSATURATED CARBONYL COMPOUNDS

## Part VII. Action of Mercuric Acetate on Hydroxy and 4-Methyl Coumarins

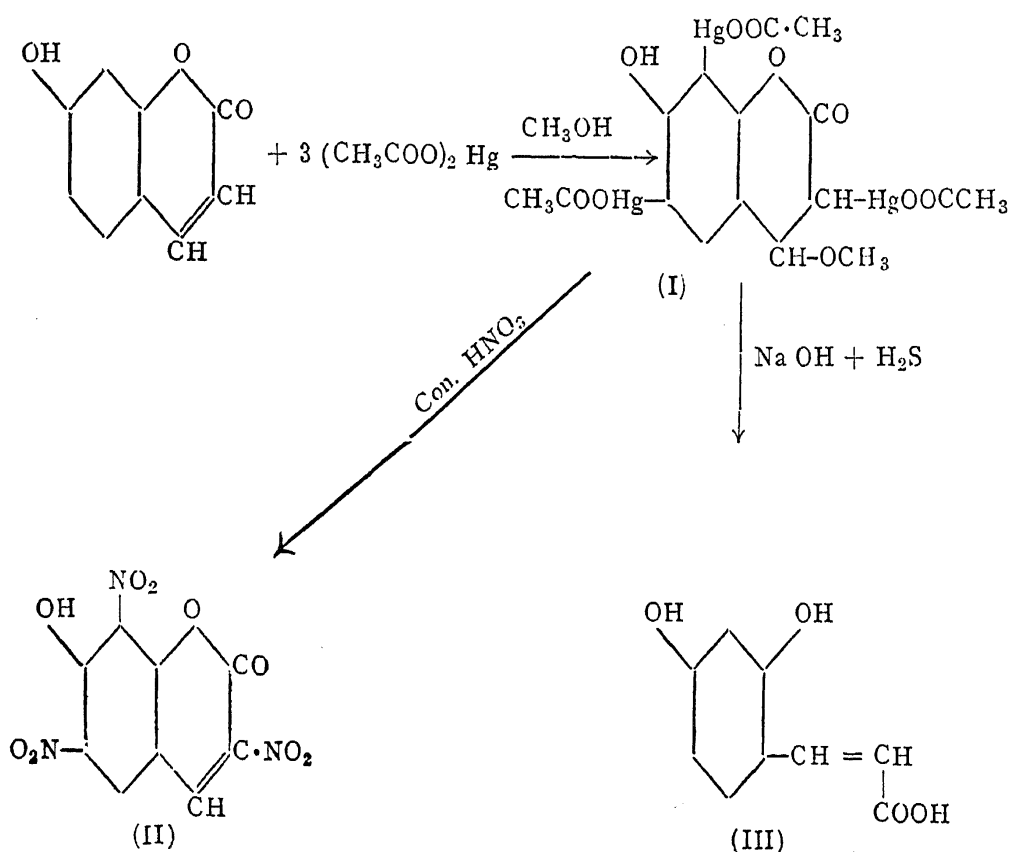
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IN continuation of our study of the action of mercury salts on coumarin and substituted coumarins<sup>1</sup> the action of mercuric acetate in methyl alcoholic solution on 7-hydroxycoumarin, 7-hydroxy-4-methylcoumarin and 4:7-dimethylcoumarin has now been investigated.

The effect of mercury salts on 7-hydroxycoumarin does not seem to have been studied before. In methyl alcoholic solution, this substance reacts with mercuric acetate rather rapidly to produce a mercuri-compound which is found to be 3:6:8-triacetoxymercuri-7-hydroxy-4-methoxy melilotic anhydride (I). The constitution is established not only from the



analysis of the compound but also from its conversion by treatment with concentrated nitric acid into 3:6:8-trinitro-7-hydroxycoumarin (II) identified by comparison with an authentic sample obtained by the direct nitration of umbelliferone.<sup>2</sup> It further gives rise to umbellic acid (III) when hydrogen sulphide is passed into an alkaline solution. The production of a coumaric acid under these conditions clearly indicates that there has been addition at the double bond.<sup>3</sup> Thus umbelliferone behaves like coumarin and 7-methylcoumarin, though its reaction is more vigorous because of the presence of a hydroxyl group in the benzene ring.

Sen and Chakravarti<sup>4</sup> and Naik and Patel<sup>5</sup> studied the action of mercuric acetate on 4-methyl-7-hydroxycoumarin in neutral aqueous medium. Their method involved the opening out of the pyrone ring by dissolving the compound in dilute alkali, neutralising the solution with acetic acid and immediately treating it with an aqueous solution of mercuric acetate. Both the sets of authors noticed that there was dimercuration and the two acetoxymercuri groups were assumed by them to occupy 6 and 8 positions. The reaction has now been carried out in methyl alcoholic solutions. It proceeds very rapidly, producing a monomercuri-compound, the acetoxymercuri group entering position 8. When treated with concentrated nitric acid, this is replaced by a nitro-group and the nitro-compound is found to be identical with 8-nitro-7-hydroxy-4-methylcoumarin obtained by the direct nitration of 4-methyl-umbelliferone.<sup>6</sup> By the action of sodium hydroxide and hydrogen sulphide the original coumarin is obtained and not a coumaric acid, thereby indicating that there has been no addition at the double bond.<sup>3</sup> It is difficult to explain why the reagent has not attacked the double bond because in 4:7-dimethylcoumarin with a methyl group in position 4 addition at the double bond is not prevented. The readiness with which position 8 is mercurated is easily understood from analogy with other reactions of 4-methyl-7-hydroxycoumarin which takes up an aldehyde group<sup>7</sup> and a nitro group<sup>6</sup> into position 8 alone under ordinary conditions. A plausible explanation for the entry of only one acetoxymercuri group would be that the high reactivity of position 8 controls the situation. It is substituted first and the resulting compound rapidly gets precipitated owing to its sparing solubility so that no addition at the double bond or further mercuration in position 6 takes place.

Clayton<sup>8</sup> observed that 4:7-dimethylcoumarin combined readily with one molecule of mercuric chloride in ether solution. Later Sen and Chakravarti (*loc. cit.*) noticed that when this substance was boiled with mercuric oxide in alkaline solution, a compound containing two mercury atoms was produced. Naik and Patel (*loc. cit.*) studied the action of mercuric acetate

in aqueous medium and reported the occurrence of mono-mercuration which they believed to take place in position 6. In methyl alcoholic solution the reaction proceeds rather slowly and the product obtained is a dimercuri-compound, whose constitution is established as 3 : 6-diacetoxymercuri-4 : 7-dimethyl-4-methoxymelilotic anhydride. It yields 3 : 6-dibromo-4 : 7-dimethylcoumarin when treated with bromine in glacial acetic acid medium. The identity of the bromo-compound is established by comparison with the one obtained by direct bromination of 4 : 7-dimethylcoumarin<sup>9</sup> and by its conversion into 2 : 5-dimethyl-4-bromo-coumarilic acid.<sup>9</sup>

In coumarin and 7-methylcoumarin, besides addition on the double bond, 6- and 8-positions undergo easy mercuration. The introduction of a methyl group in position 4 has a marked influence on the course of the reaction. The double bond still continues to be reactive and addition takes place. Position 6 is obviously more reactive than 8 in 4 : 7-dimethylcoumarin as could be easily realised from the results of direct bromination<sup>9</sup> and nitration.<sup>10</sup> Only after position 6 has been substituted can position 8 come under the influence of mercuric acetate. Obviously at this stage, that is, as soon as addition at the double bond and mercuration at position 6 are over, the sparingly soluble product separates out and the eighth position escapes mercuration.

With regard to the action of mercuric acetate there are three centres of reactivity in the coumarin molecule:—(1) the pyrone double bond, (2) the position 6, and (3) the position 8. From the results recorded in this series of papers it could be concluded that their relative activity is considerably affected by substituents already present. A hydroxyl group in position 7 seems to enhance markedly the reactivity of (3) as compared with the others and a methyl group in position 4 seems to decrease to some extent the reactivity of (1).

#### *Experimental*

##### *Action of Mercuric Acetate.—*

(1) *On 7-hydroxycoumarin (umbelliferone) : Preparation of 3 : 6 : 8-triacetoxymercuri-7-hydroxy-4-methoxy-melilotic anhydride.* Umbelliferone (2 g.) and mercuric acetate (12 g.) were dissolved in 10 and 200 c.c. respectively of pure methyl alcohol containing a little acetic acid. The solutions which were quite clear in the cold were mixed together and then raised to the boiling point under reflux. Almost immediately, a brown coloured solid separated out. It was filtered off and discarded and the mother liquor boiled under reflux on a water-bath. Now an almost colourless substance was precipitated gradually and it was collected at intervals. The reaction was practically complete after heating for ten hours. The condensation

product was purified by repeated washing with a cold dilute solution of acetic acid and subsequently with hot methyl alcohol. It was first dried in air and then in a vacuum desiccator. The yield of the pure product which decomposed at  $232^{\circ}$  was about 7 g. It was almost insoluble in all the ordinary organic solvents and under the microscope it exhibited no definite crystalline structure. (Found : Hg, 61.5;  $C_{16}H_{16}O_{10}Hg_3$  requires Hg, 62.1 %.) Even when less quantities of mercuric acetate were used (4 or 8 g. of mercuric acetate for every 2 g. of the hydroxycoumarin) the same condensation product was obtained but in diminished yields. In all the cases better yields were obtained by mixing hot saturated solutions of the reactants; but the purity of the product suffered a good deal.

The mercuri-compound was dissolved in cold 10% sodium hydroxide solution, cooled to  $0^{\circ}$  with ice and saturated with hydrogen sulphide. The precipitated mercuric sulphide was filtered off and the clear filtrate acidified with dilute hydrochloric acid keeping the temperature at  $0^{\circ}$  throughout. A slightly brown solid separated out during the acidification. It was filtered, washed with a small quantity of water and crystallised from alcohol. It was completely soluble in sodium bicarbonate solution and was found to be identical with 4-hydroxycoumaric acid (umbellic acid) decomposing at  $260^{\circ}$  with a little previous sintering.

The condensation product (5 g.) was suspended in concentrated sulphuric acid (20 c.c.) and cooled to  $-10^{\circ}$ . A mixture of fuming nitric acid (15 c.c.) and concentrated sulphuric acid (22 c.c.) was added drop by drop to the suspension keeping the temperature below  $-5^{\circ}$  and stirring well with an electric stirrer. The addition took about an hour. As the nitric-sulphuric acid mixture was added, the suspension gradually disappeared, and subsequently a yellow substance began to separate out. After stirring for another hour, the contents were poured on to crushed ice. Not much ice could be used, as the nitrocompound was soluble in water to some extent. The yellow solid which separated was filtered and crystallised from benzene as needles melting at  $219^{\circ}$ – $20^{\circ}$ . It was identified as 3 : 6 : 8-trinitro-7-hydroxycoumarin by a comparison with an authentic sample prepared by the direct nitration of umbelliferone.

(2) *On 4-methyl-7-hydroxycoumarin: Preparation of 8-acetoxy-mercuri-7-hydroxy-4-methylcoumarin.*—The reaction was carried out under the same conditions as with umbelliferone. The condensation took place extraordinarily rapidly and the product separated out within two or three minutes, giving rise to violent bumping. From 2 g. of 4-methyl-7-hydroxycoumarin in 8 c.c. of methyl alcohol and 4 g. of mercuric acetate in 60 c.c. of the same solvent, 4 g. of the condensation product were obtained. It

was purified as in the case of the condensation product from umbelliferone. After drying in the vacuum desiccator, it was found to decompose at  $246^{\circ}$ . It had no definite crystalline structure and was insoluble in all the ordinary organic solvents, though it easily dissolved in sodium hydroxide without showing any fluorescence (compare 4-methyl-7-hydroxycoumarin which exhibits a beautiful violet fluorescence in alkaline solutions). The same product was obtained even when larger amounts of mercuric acetate were employed. (Found : Hg, 45.5 ; C, 32.7 ;  $C_{12}H_{10}O_5Hg$  requires Hg, 46.1 ; C, 33.1%.)

When hydrogen sulphide was passed into an alkaline solution (10% NaOH) of the substance, mercuric sulphide was precipitated along with 4-methyl-7-hydroxycoumarin. The hydroxymethylcoumarin was separated from the mercuric sulphide by extraction with hot alcohol. The alkaline filtrate on acidification gave some more of the 4-methyl-7-hydroxycoumarin melting at  $185^{\circ}$ .

The condensation product was subjected to the action of nitric acid as in the case of umbelliferone. For 20 g. of the mercuri-compound suspended in 100 c.c. of con. sulphuric acid, a mixture of 12 c.c. of fuming nitric acid and 24 c.c. of concentrated sulphuric acid was used in the first instance and another 18 c.c. of the acid mixture added after stirring for 4 hours. Stirring was continued for one hour more. The yellow solid that separated out on the dilution of the contents with ice-cold water was filtered and crystallised from alcohol. It came down as yellow rhombic plates and was identified as 4-methyl-7-hydroxy-8-nitrocoumarin by comparison with an authentic specimen melting at  $256^{\circ}$ .

(3) *On 4 : 7-dimethylcoumarin : Preparation of 3 : 6-diacetoxymercuri-4 : 7-dimethyl-4-methoxy-melilotic anhydride.*—The procedure was just the same as in the previous cases. However, the condensation product did not immediately separate out and the reaction was very slow. From 8 g. of mercuric acetate in 12 c.c. of pure methyl alcohol containing a little acetic acid and 2 g. of 4 : 7-dimethylcoumarin in 100 c.c. of the same solvent, only 0.5 g. of a colourless solid separated out after boiling for 40 hours. The mother-liquor on further refluxing gave more and more of the product. The condensation was incomplete even after 100 hours, 3 g. being the amount produced at the end of this period. Purification and drying of the mercuri-compound were effected as already described. It was sparingly soluble in all the ordinary organic solvents and did not possess any definite crystalline structure. It sintered at  $233^{\circ}$  and decomposed at  $242^{\circ}$ . (Found : Hg, 55.9 ;  $C_{16}H_{18}O_7Hg_2$  requires Hg, 55.5%.) Even when three times the molecular proportion of mercuric acetate were employed, the same product

containing two mercury atoms was obtained. By starting with saturated boiling solutions of the reactants and mixing them, the speed of the reaction and the yield improved but the product was then rather impure.

When a solution of the mercuri-compound in aqueous sodium hydroxide was decomposed with hydrogen sulphide and the clear alkaline filtrate obtained after the removal of the mercuric sulphide was acidified, a colourless crystalline precipitate soluble in sodium bicarbonate solution was obtained. It melted at about  $150^{\circ}$  with decomposition and was evidently  $\beta$ :4-dimethylcoumaric acid. It underwent change slowly into 4:7-dimethylcoumarin when allowed to remain in contact with mineral acids and very rapidly when boiled with alcohol for purposes of crystallisation. This peculiar rapid ring closure is evidently due to the presence of a methyl group in the  $\beta$ -position in the coumaric acid.<sup>11</sup>

The mercuri-compound was suspended in glacial acetic acid and treated with a solution of bromine in the same solvent with vigorous shaking. The colour was rapidly discharged and the suspension disappeared. More bromine was added in small quantities at a time till the colour just persisted after shaking. Gradually the bromo-compound separated out, along with a little mercuric bromide. The precipitation was completed by adding excess of water and the solid was collected. The bromo-compound could be freed from the accompanying mercuric bromide by repeated crystallisations from glacial acetic acid. Another method of effecting the separation was to treat the mixture with 20% sodium hydroxide when the bromo-compound went into solution, leaving behind mercury in the form of the oxide. Acidification of the clear filtrate reprecipitated the bromo-compound in a pure condition. It crystallised from alcohol as long rods with rectangular sides and melted at  $220^{\circ}$ . Its identity with 3:6-dibromo-4:7-dimethylcoumarin was established by a comparison with an authentic sample.<sup>9</sup> (Found: Br, 47.8;  $C_{11}H_8O_2Br_2$  requires Br, 48.2%.)

The identity of the bromo-compound was further confirmed by its conversion into 2:5-dimethyl-4-bromocoumarilic acid. 2 g. were refluxed for 3 hours with 50 c.c. of alcohol containing 4 g. of potassium hydroxide. On dilution of the clear solution with water and subsequent acidification, a colourless precipitate was obtained. It was completely soluble in sodium bicarbonate. A very dilute solution of the bicarbonate should be used, as otherwise the sparingly soluble sodium salt of the coumarilic acid gets precipitated. The substance could be easily crystallised from glacial acetic acid or alcohol in the form of rectangular plates melting at  $273^{\circ}$ . The silver salt was obtained as a colourless solid. (Found: Ag, 28.8;  $C_{11}H_8BrO_3$  Ag requires Ag, 28.7%.) This bromocoumarilic acid was compared and found

to be identical with 2:5-dimethyl-4-bromocoumarilic acid obtained from 3:6-dibromo-4:7-dimethyl coumarin.<sup>9</sup> It should be noted that the above coumarilic acid melts at 273° and not at 225° as stated by previous workers.

### Summary

The action of mercuric acetate in methyl alcoholic solution on (1) umbelliferone, (2) 4-methylumbelliferone and (3) 4:7-dimethylcoumarin has been investigated. With umbelliferone addition at the double bond and substitution in positions 6 and 8 take place whereas in the case of its 4-methyl derivative position 8 alone is mercurated to yield a monoacetoxymercuri-compound. In regard to the last compound the reaction stops with addition at the double bond and mercuration of the 6th position, the position 8 escaping the attack of the reagent. It is concluded that owing to the influence of the substituent groups the reactivity of the three active centres of the coumarin molecule are differently affected.

### REFERENCES

1. Seshadri and Suryaprakasa Rao *Proc. Ind. Acad. Sci.*, (A), 1936, **4**, 162.
2. Posen .. *Ber.*, 1881, **14**, 2747.
3. Seshadri and Suryaprakasa Rao *Proc. Ind. Acad. Sci.*, (A), 1936, **3**, 293.
4. Sen and Chakravarti .. *J.I.C.S.*, 1929, 847.
5. Naik and Patel .. *J.C.S.*, 1934, 1043.
6. Pechmann and Obermiller *Ber.*, 1901, **34**, 660.
7. Rangaswami and Seshadri *Proc. Ind. Acad. Sci.*, (A), 1937, **6**, 112.
8. Clayton .. *J.C.S.*, 1908, 528.
9. Simmonis, H. .. *Die Cumarine*, p. 155.
10. Clayton .. *J.C.S.*, 1910, **97**, 1391.
11. Murty, Rao and Seshadri *Proc. Ind. Acad. Sci.*, (A), 1937, **6**, 316.