

REACTIVITY OF THE DOUBLE BOND IN COUMARINS AND RELATED α - β UNSATURATED CARBONYL COMPOUNDS.

Part III. Action of Mercuric Acetate on Coumarinic and Coumaric Acids and Esters.

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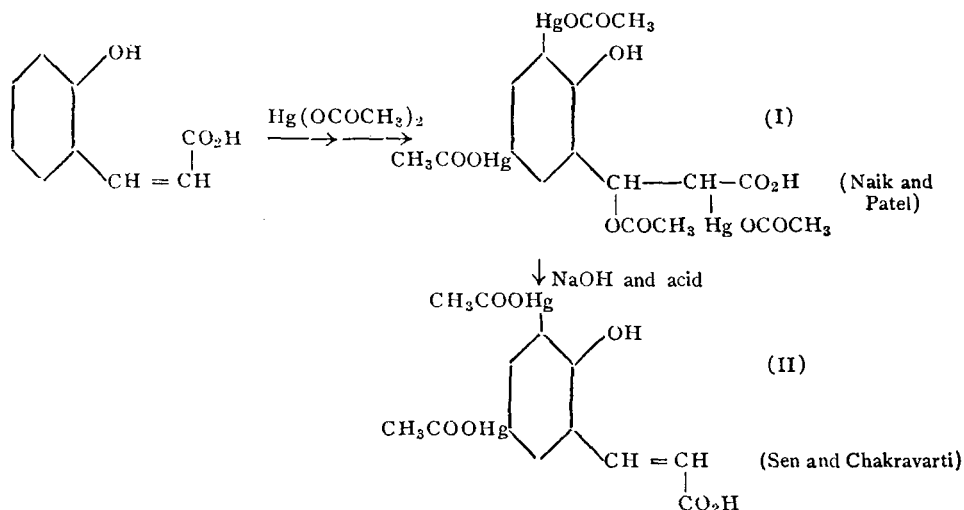
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It was shown in Part II¹ that when mercuric acetate reacts with coumarin, 7-methyl and 6-nitrocoumarins in alcoholic solution addition at the double bond takes place and along with this mercuration is effected in positions 6 and 8 if they should be free. Sen and Chakravarti² and Naik and Patel³ who failed to observe this opened out the pyrone ring by dissolving coumarin in aqueous alkali and after neutralising the excess of alkali added to it mercuric acetate. The product was considered to be diacetoxymercuro-coumaric acid by the former authors whereas the latter thought it was bisacetoxymercuro-coumarin. We⁴ have already shown that it is a coumaric acid derivative and not a coumarin. Although due to the inherent defect of the method and the sparing solubility of the product in ordinary solvents it is not possible to obtain it as pure as desirable, the differences between the analytical figures for mercury of the two groups of authors is more than what can be expected from such considerations. On closer scrutiny we realised that there was a slight difference between the two methods. Sen and Chakravarti purified their product by dissolving it in caustic alkali and reprecipitating it with acetic acid whereas Naik and Patel seem to have omitted this step. By making this distinction we have been able to reproduce the results of both groups of authors and we suggest that the following represents correctly the course of reaction.



The triacetoxymercuri compound (α : 3 : 5-triacetoxymercuri- β -acetoxy melilotic acid) resulting from addition at the double bond and simultaneous mercuration is produced first and this eliminates the addenda on treatment with alkali and goes over into the diacetoxymercuri-coumaric acid on acidification. This satisfactorily explains our results and the results of older investigators as shown below :

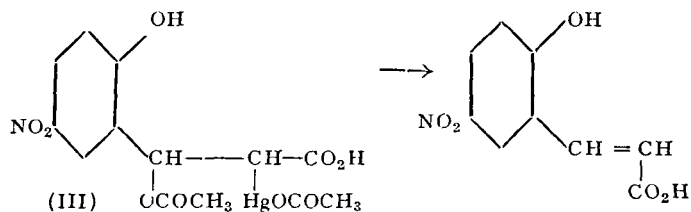
Required for formula I : Hg, 60.2% ; Found : by Naik and Patel, 60.8% ;
by us 60.6%.

Required for formula II : Hg, 58.9% ; Found : by Sen and Chakravarti,
58.4% ; by us, 58.4%.

In support of the above explanation may be stated the following points: (1) mercury salts have been shown to add on to the double bond in coumarins and acids derived from them (see Part II¹ and this paper also) ; (2) the elimination of the addenda takes place in alkaline solution in the case of coumarin-mercuri-chloride, β -methoxymelilotic acid (see Part II) and melilotic acid- β -sulphonate (Dey and Row⁵).

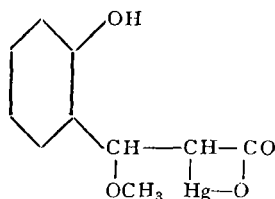
The position is slightly different in the case of 6-nitrocoumarin. Under the above conditions the nitrocoumarinic acid forms a mono-mercuri compound which eliminates the mercury completely on simple solution in aqueous alkali so that subsequent acidification with acetic acid or hydrochloric acid yields free nitrocoumaric acid (see Sen and Chakravarti² also). Mercury analysis of the mercury compound shows that it is an addition product of 5-nitrocoumarinic acid and mercuric acetate and the constitution III (α -acetoxymercuri- β -acetoxy-5-nitro-melilotic acid) explains the ready

elimination of mercury since compounds mercurated in the benzene nucleus do not eliminate mercury under such conditions.

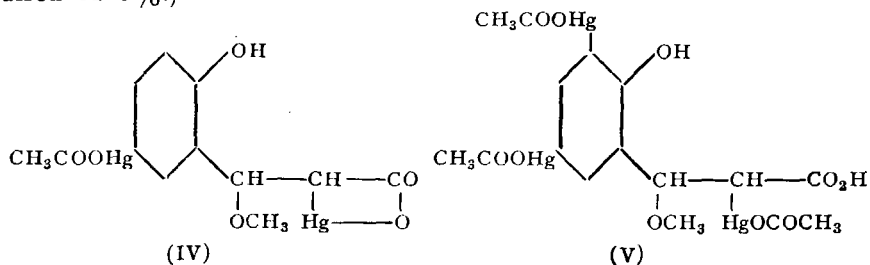


Obviously in the reaction of mercuric acetate under mild conditions the nitro group is able effectively to prevent the mercuration of the benzene ring so that addition at the double bond alone takes place. It may therefore be stated that the addition reaction takes place with great facility in the case of these acids.

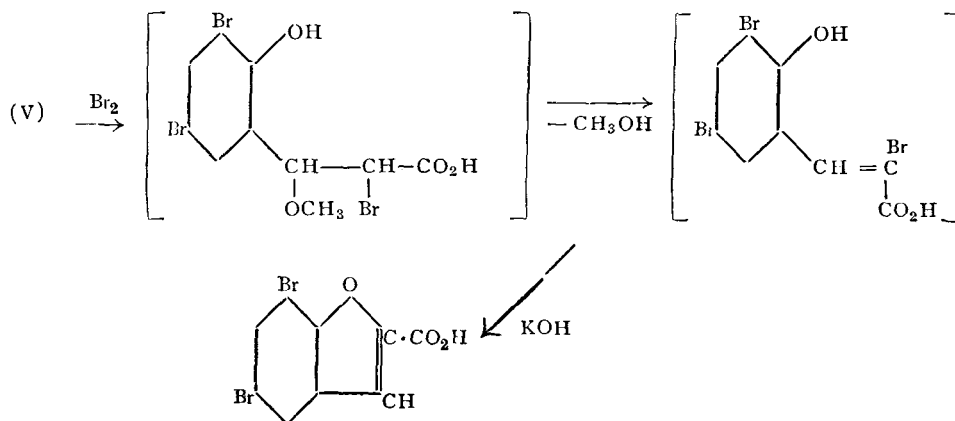
The action of mercuric acetate on coumaric acid in cold methyl alcoholic solution was first studied by Biilmann⁶ who assigned the following constitution to the product as an inner anhydride.



At the temperature of our laboratories (30° C.) we could not reproduce the result since the product contained a higher percentage of mercury and did not seem to have a definite composition. At the boiling point of methyl alcohol, however, a definite product was obtained with very great ease. On the basis of the inner anhydride formulation of Biilmann the mercury analysis indicated that this product had the constitution (IV). (Found: Hg, 61.5%. Required for formula IV 61.4%.) But it was easily soluble in aqueous sodium bicarbonate thereby showing that it had a free carboxyl group. The mercury percentage is also compatible with the alternative formula (V). (Required 61.9%.)



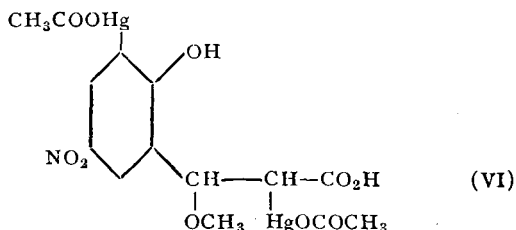
That the latter formula is the correct one is shown by the following facts : (1) the compound is easily soluble in cold aqueous sodium bicarbonate ; (2) the percentage of carbon in it agrees with this formula. (Found : C, 20.3% ; Formula IV required 22.0% and Formula V required 19.8%) ; (3) in the presence of glacial acetic acid it reacts rapidly with bromine producing mercuric bromide and a bromocompound which on treatment with alcoholic potash gives 4 : 6-dibromocoumarilic acid (Simonis and Wenzel⁷).



Hence it has to be concluded that in boiling methyl alcoholic solution mercuric acetate not only adds on to the double bond in coumaric acid but also mercu- rates positions *para* and *ortho* to the hydroxyl group and that the product does not possess the anhydride formula. When dissolved in sodium hydroxide and decomposed with hydrogen sulphide it forms β -methoxy-melilotic acid.

The methyl ester of coumaric acid reacts with mercuric acetate in methyl alcoholic solution giving the methyl ester of compound (V) containing three atoms of mercury. It is insoluble in aqueous sodium carbonate. It reacts rather more easily than the acid with bromine giving a bromocompound which eventually gives 4 : 6-dibromocoumarilic acid when treated with alcoholic potash.

5-nitrocoumaric acid forms a dimercury compound which is obviously α : 3-diacetoxymercuri-5-nitro- β -methoxy-melilotic acid.



With aqueous potash and hydrogen sulphide it formed 5-nitro-coumaric acid owing to the instability of the corresponding nitro-methoxy-melilotic acid. With bromine it formed a bromocompound which with boiling aqueous potash gave 6-bromo-4-nitrocoumarilic acid identified by comparison with a specimen obtained from 3 : 8-dibromo-6-nitro-coumarin (Dey and Row⁶).

The methyl ester of the nitro-coumaric acid behaved quite similarly giving rise to products which eventually gave the above bromo-nitrocoumarilic acid.

The series of reactions outlined above have again been achieved with 4-methyl-coumaric acid and its methyl ester. They form 3 : 5 : α -triacetoxy-mercuri-4-methyl- β -methoxy melilotic acid and its methyl ester respectively. The bromocompounds obtained from these give with alcoholic potash 4 : 6-dibromo-5-methyl-coumarilic acid identical with the one obtained from 7-methyl-3 : 6 : 8-tribromocoumarin (see Part II¹).

Experimental.

Action of Mercuric Acetate in Aqueous Solution.

(i) *On coumaric acid : 3 : 5 : α -triacetoxymercuri- β -acetoxy melilotic acid.*—Coumarin (2 g.) was dissolved in 1% aqueous sodium hydroxide (220 c.c.), the cold solution was neutralised with acetic acid (litmus) and immediately treated with a cold aqueous solution of mercuric acetate containing a little acetic acid (13 g. of mercuric acetate in 100 c.c. of water). On shaking the mixture a bulky flocculent precipitate separated out. It was filtered and washed thoroughly with very dilute cold acetic acid till the wash liquid gave no test for mercury and finally with about 200 c.c. of hot alcohol. The substance was dried first in air and finally in a vacuum desiccator. The yield was 6 g. The compound did not exhibit any definite crystalline structure and was sparingly soluble in all the ordinary organic solvents. It was, however, easily soluble in aqueous sodium carbonate and bicarbonate and decomposed on heating at 245°. (Found: Hg, 60.6; C₁₇H₁₈O₁₁Hg₃ required Hg, 60.2%.) (Compare Naik and Patel³.)

3 : 5-diacetoxymercuri-coumaric acid.—The above compound was treated with aqueous sodium hydroxide, filtered and the clear filtrate acidified with acetic acid. The white precipitate that was produced was filtered and washed thoroughly first with cold water containing acetic acid and finally with alcohol. It exhibits no definite crystalline structure, is sparingly soluble in ordinary organic solvents, dissolves easily in aqueous sodium bicarbonate and decomposes at 215° C. (Found: Hg, 58.4; C₁₃H₁₂O₇Hg₂ required Hg, 58.9%.) (Compare Sen and Chakravarti².) The two compounds

described above yielded coumaric acid on being decomposed with hydrogen sulphide in alkaline solution.

(ii) *On 5-nitrocoumarinic acid: 5-nitro- α -acetoxymercuri- β -acetoxymelilotic acid.*—Starting with 6-nitrocoumarin (2 g.) and mercuric acetate (4 g.) the reaction was carried out under the same conditions as with coumarin. The purified dry product decomposed at 170° and weighed 4.5 g. (Found : Hg, 38.2 ; $C_{13}H_{13}O_9NHg$ required Hg, 38.0%.) When the compound was treated with aqueous sodium hydroxide, filtered and the clear filtrate acidified with hydrochloric acid (see Sen and Chakravarti²) or even with acetic acid pure 5-nitrocoumaric acid was obtained.

Action of Mercuric Acetate in Methyl Alcoholic Solution.

(i) *On coumaric acid: 3 : 5 : α -triacetoxymercuri- β -methoxymelilotic acid.*—Mercuric acetate (12 g.) was dissolved in pure methyl alcohol (240 c.c.) containing a little acetic acid and a solution of coumaric acid (2 g.) in the same solvent (5 c.c.) added. The mixture which was quite clear in the cold was boiled under reflux. In about 15 minutes a heavy colourless precipitate separated out giving rise to violent bumping. It was filtered off in the hot and washed well with cold dilute acetic acid and subsequently with hot methyl alcohol. Further boiling of the alcoholic solution gave more solid which was however less pure. The yield of the pure dry solid was about 6 g. A better yield could be obtained by using more concentrated solutions but the product was not so pure. It cannot be crystallised from any of the ordinary organic solvents. It is easily soluble in aqueous sodium bicarbonate. The pure substance melts at 234° (decomp.). (Found : Hg, 61.5, C, 20.3 ; $C_{16}H_{18}O_{10}Hg_3$ required Hg, 61.9, C, 19.8%.)

The mercury compound was dissolved in normal sodium hydroxide and was saturated with hydrogen sulphide at 0° C. It was then allowed to stand overnight in the cold chamber, the precipitated mercuric sulphide filtered off and the filtrate kept cooled and acidified with a normal solution of sulphuric acid. Hydrogen sulphide was removed by passing a current of air through the solution. β -methoxy-melilotic acid was thereby obtained as a white solid which was filtered, washed with a small quantity of water and crystallised from hot water, m.p. 125° C. (Compare Part II¹.)

The substance in a fine state of division 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 more bromine was added in small quantities at a time till the colour just persisted after shaking. After filtering off mercuric bromide the acetic acid solution was poured into a large volume of water. The precipitated bromo-compound was crystallised from

ethyl alcohol. The purified product (2 g.) was boiled with alcoholic potash (4 g. in 50 c.c.) for about 3 hours, the solution diluted with water and acidified when a white crystalline solid separated out. It could be recrystallised from glacial acetic acid as colourless long narrow plates melting at 274° and was found to be identical with 4 : 6-dibromo-coumarilic acid prepared directly from 3 : 6 : 8-tribromocoumarin (Simonis and Wenzel⁷).

(ii) *On methyl coumarate.*—The methyl ester of 3 : 5 : α -triacetoxy-mercuri- β -methoxymelilotic acid was obtained from mercuric acetate and the ester of coumaric acid by the procedure described above. The precipitate was formed after an hour and a half of boiling and the yield of the pure product was 7 g. from 2 g. of coumaric ester and 12 g. of mercuric acetate.⁷ It decomposes at 265° . (Found : Hg, 61.5 ; C, 20.1 ; $C_{17}H_{20}O_{10}Hg_3$ required Hg, 61.0, C, 20.6%.) It was insoluble in aqueous sodium bicarbonate. By the action of bromine in glacial acetic acid a bromocompound was obtained which yielded 4 : 6-dibromo-coumarilic acid on treatment with boiling alcoholic potash.

(iii) *On 5-nitrocoumaric acid.*—3 : α -diacetoxymercuri-5-nitro- β -methoxy melilotic acid was obtained from 5-nitrocoumaric acid (2 g.) which was dissolved in methyl alcohol (10 c.c.) and mixed with mercuric acetate (8 g.) in the same solvent (150 c.c.) containing a little acetic acid. The product separated out after boiling for about 5 minutes. It was yellow and was so fine that it could not be filtered under suction. It was therefore centrifuged and was subsequently purified in the usual way. It was very sparingly soluble in all the ordinary organic solvents, but dissolved easily in aqueous sodium bicarbonate. On heating it turns grey at 258° and does not decompose below 300° . (Found : Hg, 53.4 ; $C_{14}H_{15}O_{10}Hg_2N$ required Hg, 52.9%.)

By the action of hydrogen sulphide in the presence of alkali 5-nitrocoumaric acid was regenerated. Bromine in glacial acetic acid gave a bromocompound which on boiling with 10% aqueous potash for two hours produced an acid identified as 6-bromo-4-nitrocoumarilic acid by comparison with a sample obtained from 3 : 8-dibromo-6-nitrocoumarin (Dey and Row⁶). It should be noted that the use of alcoholic potash in this case results in the production of an impure unworkable product and 10% aqueous potash was found to be the most suitable for the purpose. The coumarilic acid melted at 252 – 53° .

(iv) *On the methyl ester of 5-nitrocoumaric acid.*—The methyl ester of the above mercurated acid (5 g.) was obtained easily from methyl-5-nitrocoumarate (2 g.) and mercuric acetate (7 g.). It shrinks at about 215° and decomposes at 238° . (Found : Hg, 52.5 ; $C_{15}H_{17}O_{10}Hg_2N$ required Hg, 51.9%.)

The bromocompound produced from this yielded 6-bromo-4-nitrocoumarilic acid on treatment with hot aqueous potash.

(v) *On 4-methyl coumaric acid.*—This acid (2 g.) and mercuric acetate (12 g.) produced 3 : 5 : α -triacetoxy-mercuri-4-methyl- β -methoxymelilotic acid (4 g.) melting at 228° (decomp.). (Found : Hg, 61.4 ; $C_{17}H_{20}O_{10}Hg_3$ required Hg, 61.1%.) No methoxy-melilotic acid derivative could be obtained in this case also by the action of alkali and hydrogen sulphide. The bromocompound obtained by the action of bromine on treatment with 25% aqueous potash gave 4 : 6-dibromo-5-methyl coumarilic acid melting at 270° found to be identical with a sample of the acid obtained from 3 : 6 : 8-tribromo-7-methyl coumarin (see Part II). It crystallised from glacial acetic acid in flat needles. (Found : in silver salt Ag, 25.0% ; $C_{10}H_5Br_2O_3Ag$ required Ag, 24.5%.)

(vi) *On the methyl ester of 4-methylcoumaric acid.*—This ester (2 g.) and mercuric acetate (11 g.) in methyl alcohol (200 c.c.) gave 6 g. of the pure product. It turned black at about 255° and melted down to a dark liquid at about 284°. (Found : Hg, 60.7 ; $C_{18}H_{22}O_{10}Hg_3$ required Hg, 60.2%.) The bromocompound produced from this gave the same dibromo-methyl-coumarilic acid on treatment with potash as described above.

Summary.

When mercuric acetate reacts with coumarinic acid in cold aqueous solution it adds on to the double bond and mercurates the benzene ring in positions 3 and 5. When the product is dissolved in sodium hydroxide the addenda get eliminated so that 3 : 5-diacetoxymercuri-coumaric acid is produced on acidification. These compounds yield pure coumaric acid on being decomposed with hydrogen sulphide in alkaline solution. 5-Nitrocoumarinic acid adds only at the double bond and does not get mercurated. The product therefore yields the nitrocoumaric acid easily on dissolving in aqueous alkali and subsequently acidifying the solution.

In methyl alcoholic solution mercuric acetate adds on to the double bond in coumaric acids and their esters and mercurates positions 3 and 5 if they should be free. The constitution of these compounds has been established by treatment with bromine in glacial acetic acid and by examination of the action of caustic alkali on the bromocompounds. They give rise to brominated coumarilic acids.

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3. Naik and Patel, *J. C. S.*, 1934, 1043.
4. Seshadri and Suryaprakasa Rao, *Proc. Ind. Acad. Sci.*, 1936, **3**, 293.
5. Dey and Row, *J. C. S.*, 1924, 554.
6. Biilmann, *Ann.*, 1912, **388**, 262.
7. Simonis and Wenzel, *Ann.*, 1900, **33**, 421 and 1964.

Note.—The numbering of the positions in the Coumarone ring is that adopted in Richter's Lexicon.

