

# GEOMETRICAL INVERSION IN THE ACIDS DERIVED FROM THE COUMARINS.

Part III. *Trans* to *Cis*.

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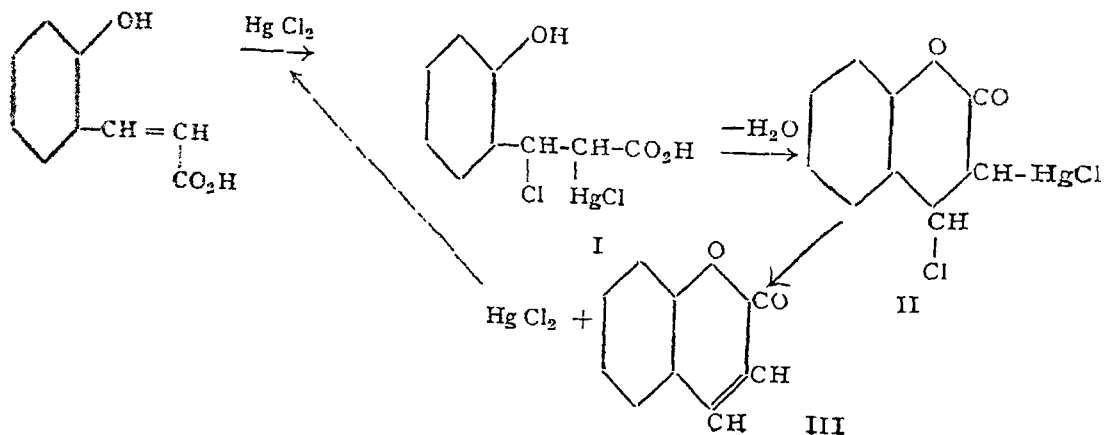
IN Part I<sup>1</sup> it was shown that coumaric acids (*trans*) as a rule decompose when heated above their melting points into carbon-dioxide and hydroxy-styrenes whereas the corresponding esters undergo conversion into the coumarins with the evolution of alcohols.

In the course of our investigation of certain mercurated coumaric acids we noticed that their decomposition was rather abnormal since only a fraction of the expected quantity of carbon-dioxide was evolved. We were consequently led to examine the decomposition of coumaric acids in the presence of added mercury compounds and we found that in the presence of mercuric oxide the decomposition of the acids took place much below their melting points and from the products over 50% yield of the pure coumarins could be isolated. The conditions of the decomposition seem to indicate that due to the influence of the mercury compound on the double bond inversion of the *trans* acid to the *cis* form first takes place with the subsequent ready elimination of water at a comparatively low temperature.

Amongst the methods of producing *trans* to *cis* inversion concentrated sulphuric acid at 100° has been sometimes used. But no details about the scope of this method are available in the literature. On careful examination it is now found that this method gives only a poor yield of coumarin and 7-methylcoumarin (10–15%) from coumaric and 4-methylcoumaric acids respectively. About 5% only of the original acids could be recovered after the reaction. The loss of the remaining portion may be due to simultaneous nuclear sulphonation taking place resulting in the formation of soluble sulphonic acids. From 5-nitrocoumaric acid, however, an almost theoretical yield of 6-nitrocoumarin was produced. This could be attributed to the influence of the nitro group on one or both of the following factors, (1) the facility with which inversion takes place and (2) the hindrance to nuclear sulphonation.

When boiled with an alcoholic solution of 2% hydrogen chloride, coumaric acid gives a good yield of the ester whereas with a higher concentration of hydrogen chloride coumarin formation takes place.<sup>1</sup> It is now found that if alcohol saturated with hydrogen chloride is employed about 75% yield of coumarin is obtained from coumaric acid and about 30% yield of 7-methylcoumarin from 4-methylcoumaric acid. Obviously, this reagent is superior to sulphuric acid for these two cases. No ester could be isolated probably due to its immediate conversion into coumarin. On the other hand, 5-nitrocoumaric acid gave about 20% yield of the ester and no nitrocoumarin could be obtained. For this case sulphuric acid is the better reagent.

The most satisfactory method of producing this *trans* to *cis* inversion is by the use of mercuric chloride. When this substance is mixed with coumaric acid and the mixture is very carefully heated to the melting point of the acid coumarin is produced and can be isolated. But the conditions are very difficult to control and further change to a dark tarry mass takes place rapidly. No enhanced yield is produced when it is employed in conjunction with concentrated sulphuric acid or alcohol saturated with hydrogen chloride. When the *trans* acids are boiled with dilute aqueous hydrochloric acid containing mercuric chloride the conversion into the coumarins was not satisfactory. The easiest method is to boil the *trans* acids with water containing mercuric chloride. Coumaric acid gave a theoretical yield of coumarin mercuric chloride addition product on boiling equimolecular quantities of the two with water.<sup>2</sup> This addition product is easily decomposed with very dilute hydrochloric acid to yield coumarin. As shown in the experimental section a small quantity of mercuric chloride is enough to effect transformation of large quantities of the *trans* acids and almost theoretical yields of coumarin, 7-methyl and 6-nitrocoumarins are obtained. Mercuric chloride seems to function in virtue of its capacity to add on to the double bond. The following mechanism is suggested as the most probable.



Coumarin mercuric chloride (II) which could be isolated as an intermediate product is obviously capable of undergoing sufficient dissociation in solution to make the transformation complete (*compare Clayton,<sup>2</sup> loc. cit.*).

The use of sun light as a convenient method for effecting *trans* to *cis* inversion has been described in Part I. Regarding the use of sodium sulphite for this purpose reference should be made to the work of Dodge<sup>3</sup> and Dey and Row.<sup>4</sup> Its addition to the *trans* acid seems to be slow though the subsequent conversion into coumarin may be easy.

#### *Experimental.*

*Action of heat and mercuric oxide.*—Coumaric acid (5 g.) was intimately mixed with mercuric oxide (1 g.) and heated in a tall pyrex test-tube of large capacity by means of an oil bath. Decomposition set in even at 170° and was completed by gradually raising the temperature to 210° which is the melting point of free coumaric acid. The mixture was occasionally stirred with a glass rod in order to facilitate the decomposition. Some coumarin sublimed on to the upper portions of the boiling tube. After cooling, the mixture was ether extracted, the extract shaken with 1% sodium hydroxide in order to remove impurities, washed again with water and finally evaporated. Pure coumarin was produced melting at 68–69°, the yield being about 50%.

4-Methylcoumaric acid behaved quite similar to coumaric acid and gave about the same yield of 7-methylcoumarin melting at 126–127°. The decomposition began even at about 150° and was completed by raising the temperature to 200°. In the case of 5-nitrocoumaric acid a similar yield of 6-nitrocoumarin was obtained. After completing the decomposition, the product was extracted with alcohol, the solution distilled to remove alcohol, the resulting solid triturated with cold aqueous sodium bicarbonate and filtered. The residue was pure 6-nitrocoumarin melting at 187–188°.

*Action of concentrated sulphuric acid.*—Coumaric acid (2 g.) was treated with concentrated sulphuric acid (15 c.c.) and the solution heated at 100° (water-bath) for 2 hours. After cooling it was poured into water, the mixture ether extracted, the ether extract shaken with aqueous sodium carbonate in order to remove unchanged acid and after drying evaporated in a tared flask. The product was pure coumarin, the yield being about 10%. On acidifying the sodium carbonate extract and extracting with ether, about 5% of the coumaric acid that was taken was recovered. The yield of coumarin was less when the duration of heating was altered.

4-Methylcoumaric acid was studied in an identical manner and it gave a similar yield of 7-methylcoumarin. In the case of 5-nitrocoumaric acid,

after heating the mixture with sulphuric acid it was poured into water, the precipitate filtered, washed with water, triturated with aqueous sodium bicarbonate, filtered and washed. The residue was found to be pure 6-nitrocoumarin. The yield was 95% in 4 hours, 80% in 2 hours and 60% in 1 hour.

*Action of alcoholic hydrogen chloride.*—Coumaric acid (2 g.) was dissolved in absolute alcohol (25 c.c.) and the solution saturated with hydrogen chloride in the cold. It was left overnight and next morning boiled under reflux for 2 hours. It was then distilled to remove most of the alcohol, water was then added, the whole extracted with ether and the ether solution shaken up with aqueous sodium carbonate. After drying over calcium chloride the ether solution was evaporated in a tared flask. The residue was pure coumarin, yield being 75%. Balance of the unchanged acid was recovered from the sodium carbonate solution.

4-Methylcoumaric acid gave 30% yield of 7-methylcoumarin under the same conditions. In the case of 5-nitrocoumaric acid instead of ether extracting the product, it was filtered, washed with water, triturated with sodium bicarbonate solution, filtered and washed with water. The residue (yield 25%) was almost completely soluble in 1% sodium hydroxide and after one crystallisation from alcohol was found to melt at 171°. Mixed melting point with ethyl 5-nitrocoumarate was the same. From the sodium bicarbonate extract almost all the unreacted acid was recovered.

*Action of mercuric chloride.*—(1) Coumaric acid (1 g.) was intimately mixed with mercuric chloride (2 g.) in a test-tube and slowly heated up in an oil bath. At about 190° decomposition started. The temperature was kept steady at this and the mixture stirred. With further rise of temperature it turned brown and underwent complicated changes. About two minutes were found to be the optimum for heating. The product was repeatedly extracted with small quantities of boiling water. The residue was a resin insoluble in water, alcohol and ether. The aqueous solution deposited a colourless crystalline solid on cooling. The whole was shaken up with a fairly large volume of ether, ether solution extracted with aqueous sodium bicarbonate in order to remove a small quantity of unchanged coumaric acid and ether evaporated. A colourless crystalline solid melting at 165° and identical with coumarin mercuric chloride was obtained (yield 0.5 g.). When boiled with 3% hydrochloric acid for 5 minutes it gave coumarin.

(2) Finely powdered coumaric acid (1 g.) and mercuric chloride (2 g.) were boiled with water (100 c.c.) for two hours. On cooling the clear solution, colourless needles of coumarin mercuric chloride, melting at 165°,

were formed. The solid was filtered and the mother-liquor extracted with ether when some more of it was obtained. The yield was theoretical.

(3) Coumaric acid (1 g.) was treated with water (25 c.c.) and a small quantity of mercuric chloride (0.1 g.) and boiled under reflux for 2 hours. At first the mixture was turbid and in about 15 minutes the solution became clear with some viscous liquid (coumarin) floating about. At the end of 2 hours concentrated hydrochloric acid (1 c.c.) was added to the boiling liquid and then allowed to cool. The viscous liquid solidified to a crystalline solid and more crystals were deposited on cooling the solution. After filtering, an almost theoretical yield of pure coumarin (m.p. 68°) was obtained. A very small quantity of it was recovered from the aqueous solution by ether extracting. It should be noted that if hydrochloric acid was added at the beginning of the heating, very little coumarin was produced.

(4) 4-Methylcoumaric acid under exactly the same conditions as above gave an almost theoretical yield of 7-methylcoumarin. 5-Nitrocoumaric acid required longer heating and more mercuric chloride for producing a good yield of 6-nitrocoumarin. The acid (1 g.) was mixed with mercuric chloride (0.5 g.) and water (50 c.c.) and boiled for 6 hours. Concentrated hydrochloric acid (2 c.c.) was then added and allowed to cool. The crystalline product melted at 185–187° with a little previous sintering. When triturated with a little cold sodium bicarbonate solution, filtered and washed, a very small quantity of unchanged acid was removed and the product melted sharp (187–188°), and was found to be identical with 6-nitrocoumarin, yield being over 90%.

#### *Summary.*

Coumaric acids which ordinarily form hydroxystyrenes on heating yield the corresponding coumarins when heated in the presence of mercuric oxide or chloride. The scope of the use of concentrated sulphuric acid and alcohol saturated with hydrogen chloride for producing *trans* to *cis* inversion has been examined. The former is useful for nitrocoumaric acid whereas the latter is suitable for coumaric and methylcoumaric acids. Mercuric chloride in neutral aqueous solution has been found to be very satisfactory for both types of acids.

#### REFERENCES.

1. Dey, Rao and Seshadri, *J.I.C.S.*, 1934, 743.
2. A. Clayton, *J.C.S.*, 1908, 524.
3. F. D. Dodge, *J.A.C.S.*, 1916, 448.
4. Dey and Row, *J.C.S.*, 1924, 554.