

A NEW EFFECT OF HYDROGEN BOND FORMATION (CHELATION)

Part III. Isomerization of Rottlerone Analogous to Rottlerin-Iso- Allorottlerin (Isorottlerin) Change

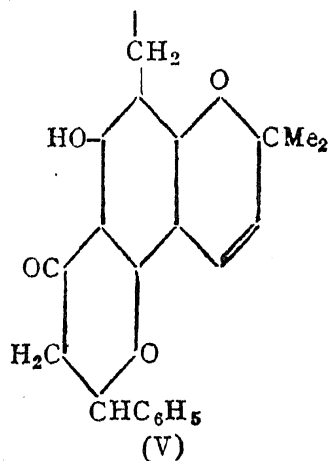
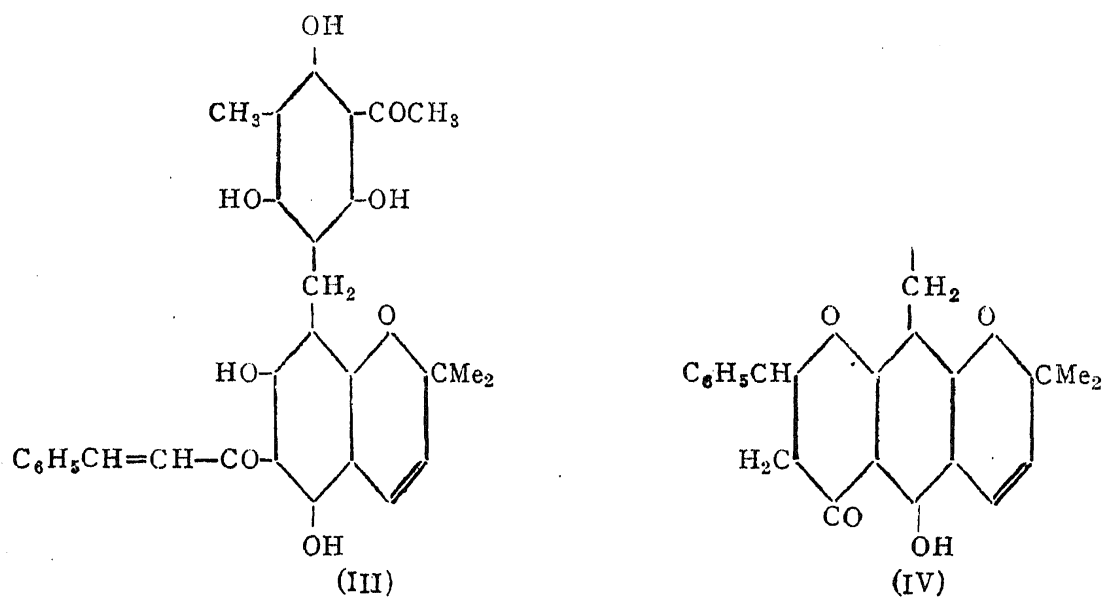
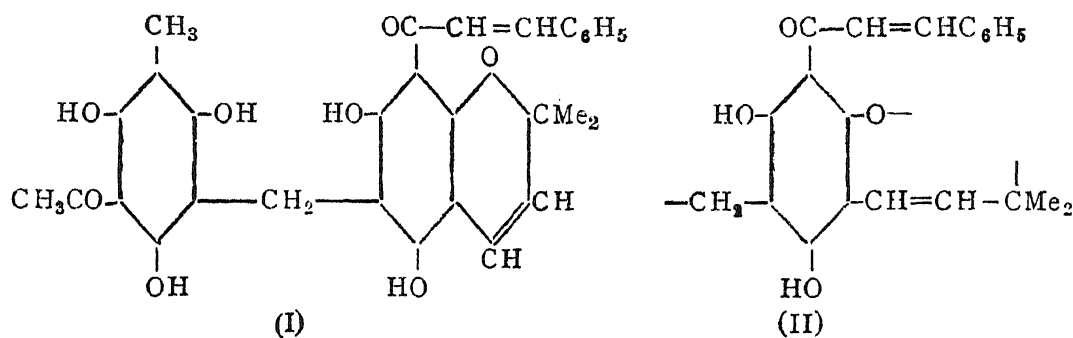
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THE isomerization of rottlerin into iso-allorottlerin (isorottlerin) was observed by a number of workers.^{1,2,3} Brockmann and Maier¹ considered it to consist of the cyclisation of the chalkone form into the flavanone. McGookin, Robertson and Tittensor³ later showed that it was not a simple chalkone-flavanone change but involved further an interchange of the cinnamoyl and the substituted phloroglucinol residues. In their extremely careful and clear study of this interesting isomeric change, they expressed the opinion that it can best be explained on the view that the first stage of the reaction is the conversion of rottlerin (I) into the intermediate (II) by the opening of the chromene ring system and that this is followed by the reformation of the latter to produce (III) which is strictly analogous to rottlerin and termed allorottlerin. At the same time, the chalkone is cyclised to dihydro-*r*-pyrone system with the production of type (IV) which they regarded as representing Brockmann and Maier's isorottlerin and which they appropriately designated iso-allo-rottlerin. From the intermediate allorottlerin, two formulæ for the cyclisation product (IV and V) are possible but owing to lack of evidence a decision between the two orientations could not be made by them.

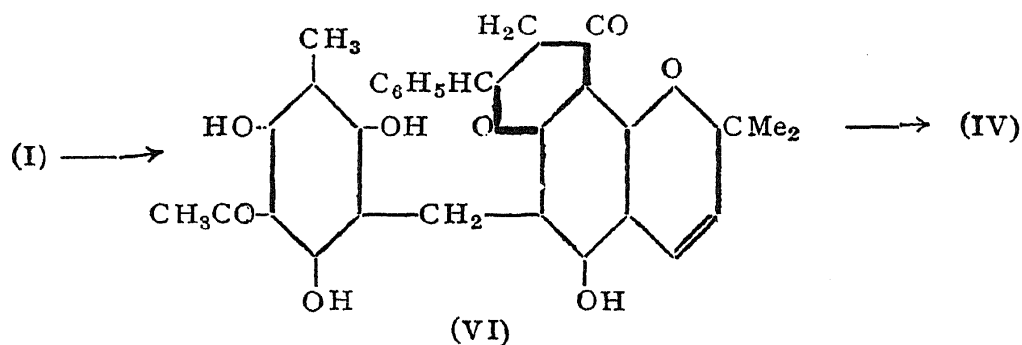
The most important and valuable point which the above authors have definitely made out is the shift of the chromene ring. The reason as to why this takes place has not so far been clear. Some light seems to be thrown on this question by the recent work of Narasimhachari and Seshadri⁴ on a new effect of hydrogen bond formation. In their paper, the importance of a 5-hydroxyl for the stability of a flavanone structure has been brought out. It arises from the formation of a chelate ring involving the carbonyl group and the 5-hydroxyl. If there were no shift of the chromene ring and only the flavanone ring closure took place, a 7-hydroxyflavanone derivative (VI) would have resulted. But on account of the rearrangement of the chromene ring a 5-hydroxyflavanone derivative (IV or V) is obtained and this represents a more stable structure. The reason for the iso-allorottlerin change



would therefore appear to be that thereby the molecule reaches greater stability.

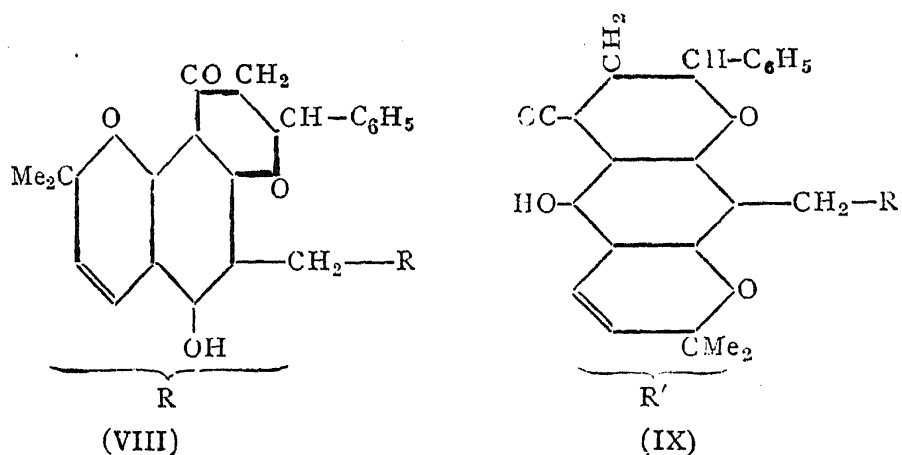
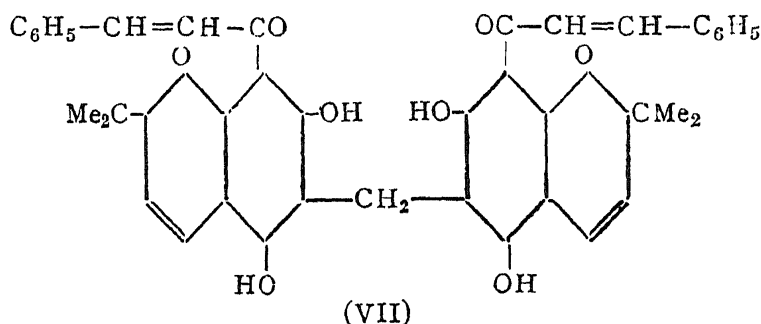
Based on the above considerations it would be simplest to picture that the flavanone ring closure which generally proceeds readily in acid solutions, takes place first yielding the 7-hydroxy flavanone derivative (VI) and then the rearrangement of the chromene ring follows producing the stabler 5-hydroxy flavanone derivative. The constitution of isoallorottlerin then becomes reasonably certain as in (IV). But Robertson and his coworkers who recognised this possibility were not inclined to accept it because they felt that the closing of the dihydro- γ -pyrone ring involving the protection of a free hydroxyl

group would tend to stabilise the chromene system and would thus hinder rearrangement. Some unequivocal evidence is therefore required to settle this point and it does not seem to be available at present. But at the same time it should be borne in mind that even in chalcones the ortho-hydroxyl is not entirely free and it is involved in a chelate ring.



No other example of this type of rearrangement seems to have been described in the literature. A closely analogous substance suitable for this study is rottlerone (VII), the main degradation product of rottlerin. Its constitution has been definitely established by Robertson and his co-workers⁵ and it has all the structural features required for this test. In the past, Brockmann and Maier¹ reported that they did not get any definite reaction product by refluxing rottlerone with acetic acid. McGookin *et al.*⁵ noticed that a yellow amorphous substance was formed under these conditions but stated that they had been so far unable to determine conditions required for cyclisation of rottlerone and the isolation of the resulting pure dihydro- γ -pyrone derivative. We have again examined this reaction. Rottlerone undergoes change almost completely by boiling its acetic acid solution for one hour. The deep red colour of rottlerone disappears and a pale yellow product is obtained in good yield. For it the name iso-allorottlerone is suggested. It could not be crystallised satisfactorily from any solvent, but could be obtained as an almost colourless (very pale yellow) crystalline powder from glacial acetic acid solution, by the addition of water. Though its melting point too is not very definite, it is clear that the isomeric change has taken place. The very pale yellow colour of iso-allorottlerone as contrasted with the highly coloured rottlerone is in agreement with the flavanone structure and the colour reaction with ferric chloride (immediate deep green colour) supports the presence of a hydroxyl group in the 5-position of each of the flavanone units. A hydroxyl in the 7-position does not give rise to any colour with ferric chloride. There is no possibility of attributing this ferric chloride colour to contamination with rottlerone because it gives an entirely different colour (brown). Iso-allorottlerone can therefore be considered to have a 5:5'-dihydroxy-diflavanone structure (IX). The isomeric change

taking place is very similar to the change of rottlerin into iso-allorottlerin, the possible intermediate 7-hydroxy flavanone stage being represented by (VIII).



Simpler and typical examples are further being investigated in order to test the validity of the above explanation of the isomeric changes.

EXPERIMENTAL

Rottlerone required for the following experiments was prepared from rottlerin using saturated barium hydroxide according to the method described by Mcgookin, Reed and Robertson.⁶ It was obtained from chloroform-alcohol mixture in the form of garnet red prisms melting at 234–35°. It was very sparingly soluble in alcohol and insoluble in aqueous sodium carbonate solution. It was also insoluble in cold aqueous sodium hydroxide and on heating it decomposed forming a red coloured semi-solid, the solution turning yellow. With alcoholic ferric chloride, rottlerone gave first a very feeble brown colour which deepened on standing.

Iso-allorottlerone

Rottlerone (2 g.) and glacial acetic acid (50 c.c.) were heated on an oil-bath kept at 120–30° for one hour. By this time the initial bright red colour of the solution had completely changed to yellow. The solution was cooled and added to cold water and allowed to stand over night. The very pale yellow (almost colourless) substance that separated out was filtered and

dried. Attempts to crystallize the product from acetone-alcohol, ethyl acetate-petroleum ether and ether-petroleum ether mixtures were not successful. But in the course of these treatments, particularly the last, some amount of sparingly soluble impurity could be removed. It was then taken up in glacial acetic acid, the solution treated with animal charcoal, filtered and diluted with water. This process was repeated several times. A very pale yellow (almost colourless) crystalline looking powder was thus obtained. It was insoluble in aqueous alkali even on heating and did not show any signs of decomposition. It gave an immediate deep green colour with alcoholic ferric chloride which was entirely different from the colour given by rottlerone. On heating it sintered at 98° and melted down to a liquid at 140° . (Found: C, 75.0; H, 5.8; $C_{41}H_{39}O_8$ requires C, 75.0; H, 5.8%.)

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Backhouse, *et al.* .. *Ibid.*, 1948, 113.
6. McGookin, Reed and Robertson .. *Ibid.*, 1937, 748.