907. *Compounds of Curcumin and Boric Acid. Part II.* The Structure of Rubrocurcumin.*

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The red compound formed when curcumin reacts with boric acid in the presence of oxalic acid has been isolated and called rubrocurcumin. This substance is a 1 : 1 : 1 compound of curcumin, boron, and oxalate. Consideration of analytical results, absorption spectra, etc., suggests a structure similar to that of rosocyanin but containing the curcumin molecules joined by a boro-oxalate bridge. The use of rubrocurcumin and rosocyanin in the determination of boron is briefly discussed.

Cassal and Gerrans (*Chem. News*, 1903, **87**, 27) observed that the red colouration when curcumin and boric acid reacted was greatly promoted by oxalic acid, and this acid has been used in most subsequent analytical methods for boron in which curcumin is employed (cf. Naftel, *Ind. Eng. Chem., Anal.*, 1939, **11**, 407). In early unpublished investigations of Naftel's technique we noted that the oxalate reaction gave rise to some rosocyanin (for its structure see Part I *), but that the main product was a compound differing therefrom in being slightly soluble in ether. This substance we propose to call rubrocurcumin. A substance so named was obtained by Clarke and Jackson (*Amer. Chem. J.*, 1908, **39**, 696) when they allowed boric acid to react with curcumin in the absence of added mineral acid, but we failed to repeat this synthesis. The recorded properties of their "rubrocurcumin," however, agree so well with most of those of the red compound formed by the curcumin–boric acid–oxalic acid reaction that we propose to retain the name. Very probably oxalic acid was present in the curcumin used by Clarke and Jackson, as this acid is formed in quantity as an oxidation product of curcumin.

When boric acid is mixed with curcumin in alcoholic solution the reaction is more rapid when oxalic acid is added than when any other acid is used, although the resulting red compound is not precipitated unless the solutions are very concentrated. The reaction in alcohol is complete only on evaporation to dryness and the same product is apparently formed irrespective of which reactants are present in excess. Oxalic acid is not sufficiently soluble in molten phenol for the formation of rubrocurcumin therein to be directly compared with that of rosocyanin (cf. Part I).

If both oxalic acid and a mineral acid are present a mixture of rubrocurcumin and rosocyanin results, although the yield of the former greatly exceeds that of the latter when the two acids are present in equimolar quantities. The presence of water inhibits the formation of both rubrocurcumin and rosocyanin but its effect is most marked on the yield of the former.

Experimental

Rubrocurcumin.—A solution of oxalic acid dihydrate (2 g.), boric acid (0·5 g.), and curcumin (2 g.) in acetone (*ca.* 100 ml.) was evaporated to dryness and the residue was powdered, leached by

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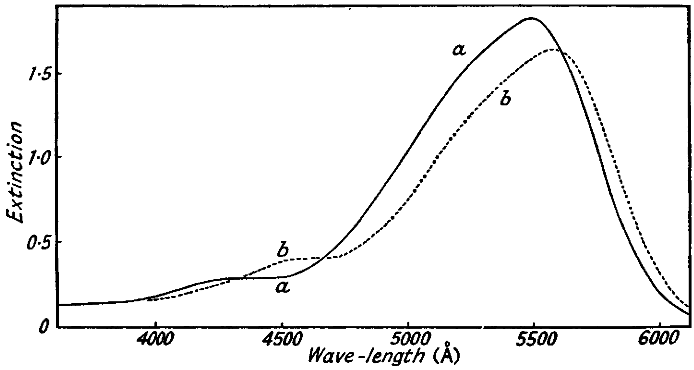
* Part I, preceding paper.

cold water (200 ml.), filtered off, and washed liberally. The crude rubrocurcumin, after being dried in a vacuum-desiccator, was extracted (Soxhlet) for 4 hours with dry ether. This removed a small amount of orange-red material containing combined boron which, however, did not appear to be a distinct form of rubrocurcumin. A saturated solution of the solid left in the extractor was prepared by heating it at 100° with dry phenol and filtering this solution hot into four times its volume of benzene. The precipitated solid, after filtration and washing with benzene, was dried to constant weight (1·6 g.) in a desiccator over anhydrone.

Rubrocurcumin is a dark red amorphous powder without the metallic reflex of rosocyanin. It does not melt but decomposes with swelling and sintering at about 300°. Its solutions in acidified alcohol are very similar in colour to those of rosocyanin but noticeably more ruby-red. In general the solubility of the two compounds is similar, although that of rubrocurcumin in alcohol and phenol is much less when the solid is heated at 100—150° than when it is dried at room temperature. The most significant difference is, however, the slight solubility of rubrocurcumin in solvents of low dielectric constant (ether, benzene, etc.) in which rosocyanin is completely insoluble. In these solvents a pink solution with an orange fluorescence is obtained. Alcoholic solutions of rubrocurcumin, like those of rosocyanin, change from red to blue-green on basification, but alkaline solutions of rubrocurcumin are hydrolysed much more rapidly, having decomposed completely within a few minutes. In wet acidic alcohol hydrolysis of rubrocurcumin is also markedly the more rapid.



Absorption spectra of rubrocurcumin, 2·0 × 10^{-5}M *with respect to boron;* 1-*cm. cell. a, Rubrocurcumin. b, Rosocyanin.*

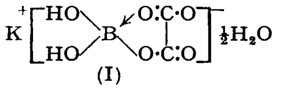
Boron and the curcumin formed on hydrolysis were determined as described in Part I. Oxalate could not be determined after a wet oxidation, because curcumin gave a considerable amount of oxalic acid on such treatment. Gentle alkaline hydrolysis (see Part I) was therefore employed, the curcumin produced suffering little decomposition; acidification of the resulting solutions precipitated the curcumin (which was dissolved in alkali and reprecipitated to free it from occluded oxalate) and the oxalate was determined by titration with permanganate after several precipitations as calcium oxalate. Results for carbon by combustion were not consistent with any likely structures unless water was assumed to be present and this was confirmed by the erratic and apparently low molecular weights obtained by the cryoscopic method. These methods gave, for *rubrocurcumin*: C, 57·8; B, 2·25; curcumin, 76·0; $H_2C_2O_4$, 18·8 ($C_{44}H_{38}O_{16}B_2,C_2O_4,1{\cdot}5H_2O$ requires C, 57·6; B, 2·25; curcumin, 76·8; $H_2C_2O_4$, 18·7%).

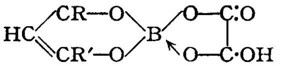
Absorption Spectrum.—Without an instantaneous presentation spectrophotometer it was impossible to record the absorption spectra of the alkaline forms of rubrocurcumin as their solutions began to decompose in a few seconds. However, when very dilute alcoholic potassium hydroxide was rapidly added to dry alcoholic solutions of rubrocurcumin and rosocyanin, visually identical colour changes appeared to take place, *i.e.*, red to purple, purple to ink-blue, ink-blue to blue-green. Only the ruby-red solution of rubrocurcumin was sufficiently stable for an absorption spectrum to be taken with the Uvispek spectrophotometer. This is shown in the Figure for a solution 2 × 10^{-5}M with respect to combined curcumin (and boron), together with the curve for rosocyanin, 2 × 10^{-5}M with respect to combined curcumin and 1 × 10^{-5}M for combined boron.

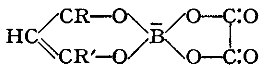
Behaviour on Ion-exchange Resins.—Here again the comparatively slight stability of rubrocurcumin solutions prevented quantitative study. In alkali, decomposition of the compound was so rapid that not even qualitative observations could be made. In dry acidic solutions, however, rubrocurcumin could be observed to enter the resin phase of a cation-exchanger in the hydrogen-ion form. It thus has cationic properties similar to those of rosocyanin under these conditions (cf. Part I) and was leached off the resin when the acid concentration of the alcoholic solution was increased. The rate of decomposition in strongly acidic solutions, such as were required for this leaching, was too great for quantitative measurements to be made. No cationic behaviour was found when rubrocurcumin solutions were equilibrated with an exchanger in other than the H^+ form.

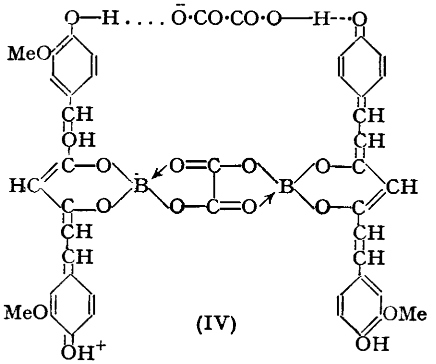
DISCUSSION

The structure of rubrocurcumin is clearly related to that of rosocyanin, but the compound cannot simply be an oxalate of the rosocyanin cation. The simple mode of preparation and the hydrolysis, however, indicate that the components are not radically altered during combination. The more rapid formation of rubrocurcumin must be due to formation of a boro-oxalate complex. Werner (*J.*, 1904, **85**, 1449) wrote potassium boro-oxalate as $2[K{\cdot}BO(C_2O_4)],3H_2O$, which should now be formulated as (I). Analysis indicates rubrocurcumin as containing a 1 : 1 : 1 ratio of boron, oxalate, and curcumin. From the similarity of absorption spectra, it is apparent that the curcumin portion of rubrocurcumin has the same basic type of electronic configuration as in rosocyanin and the only reasonable formulæ, assuming the combination of one curcumin molecule with one of boron and one of oxalate, are (II) and (III). (II) might exist in solution as a neutral zwitter-ion but would require an equivalent of anion to be present in the solid state. Structure (III) overcomes this difficulty but this compound would not then behave as a cation in solution. The most decisive evidence against these two formulæ, however, is the fact that, in neither case, would one expect an identical series of colour changes to be observed when solutions of rubrocurcumin and rosocyanin are made progressively more alkaline.

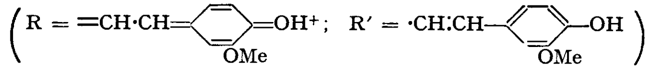

(I)


(II)


(III)



(IV)



We consider it more likely, therefore, that rubrocurcumin contains two atoms of boron combined with two molecules of curcumin and two oxalate groups. There would then be more possibility of a basic resemblance between the rubrocurcumin and rosocyanin molecules with similar colour changes on addition of alkali, etc., and an oxalate molecule could act as an anion for the main cationic complex. The greater susceptibility of the rubrocurcumin molecule to hydrolysis, compared with rosocyanin, must arise from a marked difference in the stability of the centre grouping of these two compounds. It is logical to suppose that the centre grouping in rubrocurcumin is weakened by the presence of one of the two oxalate molecules as boro-oxalate. This grouping, when combined by condensation with two curcumin molecules and two hydrogen ions, would give rise to the rosocyanin analogue (IV), the *two* positive charges left on this molecule, as a result of the condensation, being neutralised in the solid state by the remaining molecule of oxalate acting as a bivalent anion (cf. the rôle of the sulphate group in rosocyanin sulphate). Furthermore, this oxalate ion can join on to the terminal hydroxyl groups of the curcumin chains by hydrogen bonding.

Unlike the curcumin groups in rosocyanin, those in (IV) would be roughly coplanar and spatially such that an oxalate ion could bridge the two ends without strain. Such a bridged coplanar molecule would be expected to be more soluble in solvents of low dielectric constant than the ionic rosocyanin molecule and a slight shift of the absorption spectrum to shorter wave-lengths would be expected from the nature of the centre grouping, which has two boron–oxygen bonds somewhat allied in nature to the carbonyl-donated bonds in the beryllium–curcumin complex (cf. Part I).

Structure (IV) for rubrocurcumin represents one of the very few ways in which the groups known to be present can be combined to give a molecule having properties in agreement with those found experimentally. It is only proposed tentatively, however, although further evidence is difficult to obtain except by *X*-ray studies.

The structures suggested for rosocyanin and rubrocurcumin have implications for the determination of traces of boron. As the boron in rosocyanin is displaying its maximum co-ordination valency and each of the two co-ordinating curcumin groups in this substance has oscillator strengths approaching unity, the quantitative formation of rosocyanin must give rise to about the most sensitive absorptiometric test for boron which is theoretically possible. It is doubtful whether this sensitivity could be substantially increased by using more complicated derivatives of curcumin.

The formation of rubrocurcumin has found favour in analytical methods for boron because of the great increase in yield and speed of formation of the red colour. However, it will be seen from the present work, that for a given weight of boron only half the maximum possible extinction is obtained when this element is combined as rubrocurcumin, because this molecule, with an oscillator strength comparable with that of rosocyanin, nevertheless contains two atoms of combined boron instead of only one. This fact, and the relatively poor stability of rubrocurcumin, suggests that the formation of rosocyanin should be attempted in analytical methods if it can be brought about in high yield and at a reasonable speed. This is possible at 50—70° in acidified phenols, although the exact reaction conditions must be carefully determined.

Of other likely elements germanium is the only one we have found able to form compounds analogous to rosocyanin and rubrocurcumin.

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