

A CONVENIENT METHOD OF PREPARATION OF CYANIDIN CHLORIDE FROM (+) CATECHIN AND (–) EPICATECHIN

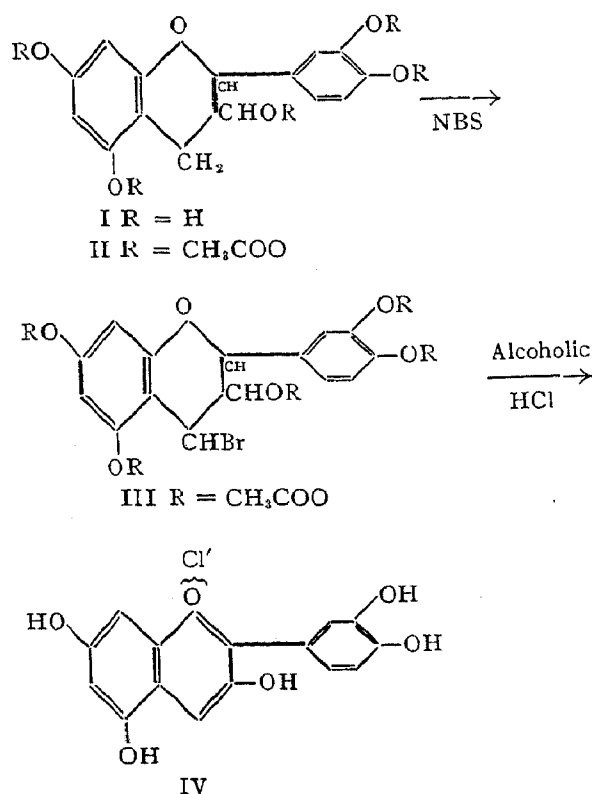
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THE conversion of cyanidin (IV) to (+) epicatechin (I) by reduction¹ played an important part in establishing the constitution of catechins. The reverse change of (+) catechin (I) to cyanidin chloride (IV) was effected by Appel and Robinson.² They employed (+) catechin tetramethyl ether and treated it with excess of bromine in technical dioxan solution. The crude bromocyanidin tetramethyl ether bromide which contained bromine in the 8-position also, was subjected to treatment with hydriodic acid in presence of red phosphorus. The resulting cyanidin iodide was converted into the chloride through the colour base as intermediate. We have repeated this process using pure samples of the naturally occurring stereoisomer (–) epicatechin (I) prepared from the heartwood of *Acacia catechu*. The same results are obtained, the yield being almost the same as from (+) catechin. When the penta-acetates of the catechins are used instead, only a trace of cyanidin is produced, the major product appearing to be a red-coloured polymer.

Though the method involving the bromination of the methyl ether works, it is rather time-consuming and gives poor yields. The conversion becomes far more convenient when N-bromosuccinimide and the acetate of (–) epicatechin (II) are used in carbon tetrachloride solution. A monobromo compound (III) is produced and it can be readily converted into cyanidin chloride (IV) by boiling with excess of alcoholic hydrochloric acid; the yield was poor in this method (18%). In her preparation of cyanidin chloride from butea gum Lady Robinson³ used an ingenious method employing an aqueous solution of sodium acetate, zinc chloride and picric acid for extraction and simultaneous conversion of leucoanthocyanidin into cyanidin picrate. This method has also been employed in the present case on the assumption that the bromo compound (III) is similar to leucoanthocyanidin, and thereby a considerably enhanced yield of cyanidin picrate has been obtained and this could be converted into the chloride (IV). There is some loss involved in the conversion of picrate into the chloride. In later experiments it was found that purification through the picrate is not necessary in the present case and the chloride (IV) can be obtained directly in higher

yield (25%). Using (+) catechin (I) the yield of the bromo compound was the same though somewhat better yields of cyanidin (30%) have been obtained in repeated experiments. The difference however may not be significant for the stereochemistry of the 2 and 3 positions of the catechins.



The mechanism of the conversion of the catechins into cyanidin could be visualised as follows:

(a) The first stage is the entry of a bromine atom in the 4-position of the catechin penta-acetate (II) to form the monobromo derivative (III). In support of this may be mentioned the following points. The presence of acetoxy groups has been known to diminish the possibility of substitution in the benzene ring. Of the other possible positions for the substitution by N-bromosuccinimide the 2 and 4 positions should be considered because they are activated by the neighbouring benzene rings. Since the hydrogen atoms of a CH_2 group are known to be far more reactive as compared with the tertiary hydrogen atom the above conclusion seems to be valid.

(b) When the monobromo compound (III) is boiled with alcoholic hydrochloric acid, the deacetylated compound behaves like a leucoanthocyanidin of the flavan-diol type undergoing dismutation and yielding the flavylum salt along with the simultaneous production of phlobaphenes.

The product, after purification, is found to be pure flavylum chloride having practically no bromide in it. This should be attributed to the predominantly large excess of chloride ions present in the acid solution.

EXPERIMENTAL

Bromination

To a solution of (-) epicatechin penta-acetate (1 gm.) in dry carbon tetrachloride (130 c.c.) were added N-bromosuccinimide (0.35 g.) and benzoyl peroxide (0.02 g.) and the mixture refluxed on a water-bath for seven hours. Initially the reaction mixture was slightly yellow which gradually changed to orange red as the reaction proceeded. It was then allowed to stand overnight when succinimide floated at the top. It was filtered and the solvent was removed from the filtrate by distillation under reduced pressure. The viscous mass thus obtained turned into a definite solid under vacuum. It could not be crystallised and it melted at about 80°. Yield 0.65 g. (Found: Br, 14.9; $C_{25}H_{23}O_{11}$ Br requires Br, 13.8%). (+) Catechin gave the same yield of the bromo compound.

Cyanidin chloride

(a) The above bromo compound (0.25 g.) was refluxed with ethanol (50 c.c.) and concentrated hydrochloric acid (10 c.c.) for three hours. A deep red colour developed. Water was added and the insoluble phlobaphene was filtered off. The filtrate was extracted with isoamyl alcohol. By the addition of petroleum ether the cyanidin chloride was taken in 1% hydrochloric acid solution which was slowly concentrated at the ordinary temperature in the presence of potash when cyanidin chloride separated as small chocolate-coloured crystals (70 mg.). From the colour reactions, paper chromatography (circular Rf., 0.72) and absorption maximum at 545 m μ it was characterised as cyanidin chloride.

(b) By Lady Robinson's method³ the yield of cyanidin picrate was 0.45 g. from 0.65 g. of the bromo compound.

(c) The suspension of the bromo compound (0.65 g.) in water (30 c.c.) containing crystallised sodium acetate (2.5 g.) was boiled for 10 minutes. The boiling was continued for another minute after the addition of powdered fused zinc chloride (3 g.). The sticky mass which gradually solidified on cooling was filtered. The aqueous filtrate gave no appreciable amount of anthocyanidin when treated separately. The solid was then heated with aqueous saturated picric acid (18 c.c.) for 8 minutes. Alcoholic hydrochloric acid (125 c.c.; 8%) was then added and the refluxing continued for 45

minutes. Water was added to the reaction mixture which was then extracted with isoamyl alcohol. The colouring matter was then transferred to 1% hydrochloric acid solution by the addition of petroleum ether. The acid solution, after washing thoroughly with benzene, was slowly concentrated at ordinary temperature in presence of potash when cyanidin chloride (250 mg.) separated out. It was characterised as in the previous case. (+) Catechin bromide gave a better yield (300 mg.).

SUMMARY

Cyanidin has been prepared in satisfactory yields from the acetates of (+) catechin and (–) epicatechin by monobromination with N.B.S. and subsequent treatment.

REFERENCES

1. Freudenberg, Fikentocher and Schmidt *Annalen*, 1925, 444, 135.
2. Appel and Robinson .. *J.C.S.*, 1935, 426.
3. Robinson (Mrs.) .. *Ibid.*, 1937, 1157.