

# THE STERIC FACTOR IN ORGANIC CHEMICAL REACTIONS.

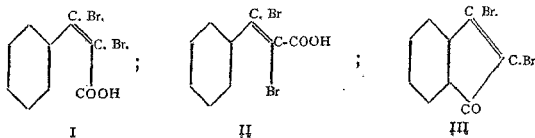
## PART I. INFLUENCE OF ESTERIFICATION ON THE MODE OF ADDITION OF BROMINE TO $\beta$ -PHENYL-PROPIOLIC ACID.

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### INTRODUCTION.

Reactions with organic compounds in which the nature of the resulting products is dependent on their spatial configurations are of exceptional importance from the standpoint of structural organic chemistry. The long known difficulty in the esterification of *diortho*-substituted benzoic acids, for example, has been continuously explained by the hypothesis of a "Steric Hindrance" (*J. Amer. Chem. Soc.*, 1921, 43, 925). Many other types of reactions, however, afford valuable steric evidence if the products are carefully studied with regard to their ease of formation and relative yields. The remarkable ease, for example, with which elimination of hydrogen bromide or of bromine, or of carbon dioxide has been found to occur from  $\alpha\beta$ - and  $\alpha\beta\beta$ -tribromo-,  $\beta$ -phenylpropionic acids and their esters (*J. Indian Inst. Sci.*, 1923, 6, 88) is a clear indication of the sterically crowded position of the respective group facilitating its easy removal. Similar observations in a series of other reactions have yielded most interesting steric evidence about the mono-methyl esters of 3- and 4-nitro-phthalic acids, nitro-derivatives of halogenated cinnamic acids, substitution products of *ortho*-nitro-toluene and *meta*-nitro-phenol, and about 3- and 5-nitro-salicylic acids. These will form the subjects of further communications in this series.

*Bromine addition to phenylpropionic acid.*—The present paper describes a remarkable difference observed in the mode of addition of bromine to  $\beta$ -phenylpropionic acid and its methyl ester. The products of the reaction are the isomeric 'cis' (I) and 'trans' (II)  $\alpha\beta$ -dibromo-cinnamic acids melting at 100° and 136° respectively. This



addition reaction has been studied with phenylpropionic acid by a number of workers since 1887 (Roser and Haselhoff, *Annalen*, 1888, 247, 139; *Ber.*, 1887, 20, 1576) who have all reported formation of a preponderant proportion of the 'cis' isomer. Addition of bromine to ethyl phenyl-propiolate has been studied by Ruhemann and Cunningham (*J. C. S.*, 1899, 75, 961), but the relative yields of the isomers were not noted.

*Bromine addition to phenylpropionic ester.*—The present work originated in an attempt to prepare a quantity of the *cis*-acid by the addition of bromine to methyl phenylpropiolate, hoping that the same preponderant proportion of *cis*-acid would be obtained, as when the free acid was used. The *trans*-acid, however, predominated when the ester was used. Comparative experiments were therefore made adding bromine to the acid as well as to the ester. One such set of experiments was carried out in the diffused day light of the laboratory allowing the product to warm up to room temperature 25°C.; and a second set, in the dark, maintaining 0° throughout. In the former case, the *trans*-acid predominated even more (75 per cent.) than under the latter conditions, when the ester was used.

## DISCUSSION.

Formulæ (I) and (II) make it clear that in the *cis*-acid (I) the carboxyl group is placed close to the benzene nucleus, whereas in the *trans*, the carboxyl is away. The assignment of this structure was made independently on the evidence of the ready conversion of the *cis*-acid into dibromo-indenone (III) by treatment with concentrated sulphuric acid (*Ber.*, 1898, 31, 2096), while the *trans*-acid is unchanged under the same conditions. Hence the formation of a smaller proportion of the *cis*-ester in the addition of bromine to phenylpropionic ester indicates that the volume of the ester group in close proximity to the benzene nucleus hinders the formation of much *cis*, and consequently facilitates the *trans* addition of bromine to the acetylenic bond. Conversely, the *cis* structure of the isomeric acid melting at 100° gets confirmed by this observation.

It is further of interest to note, as shown later in this series, that *cis*-dibromo-cinnamic acid resists not only esterification with methyl alcohol but also nitration in the *ortho*-position, whereas the *trans*-isomer is easily esterified, but resists nitration in the *ortho*-position as well. These facts further confirm the close spatial proximity of the carboxyl group of the *cis*-isomer to the benzene nucleus.

## EXPERIMENTAL.

*Preparation of  $\beta$ -phenylpropionic acid.*—This substance was prepared starting from cinnamic acid through the following stages:—cinnamic acid dibromide,  $\alpha$ -bromo-*allo*-cinnamic acid,  $\alpha$ -bromo-cinnamic acid and  $\beta$ -phenylpropionic acid by methods essentially similar to those adopted by Sudborough and co-workers (*J. C. S.*, 1903, 83, 1155).

*Preparation of the methyl ester of  $\beta$ -phenylpropionic acid.*— $\beta$ -phenylpropionic acid (50 g.) was esterified with absolute methyl alcohol (200 c.c.) and conc. sulphuric acid (7 c.c.), boiling the mixture overnight; most of the alcohol was distilled and the residue poured on ice and extracted with benzene. After washing the benzene solution with aqueous sodium carbonate and water it was finally dried with calcium chloride. The benzene was distilled and the residual crude ester distilled under reduced pressure; yield of pure methyl ester was 42 g., b.p. 110°/5 mm. Another 50 g. was similarly esterified and yielded 42 g. of pure ester b.p. 104°/4 mm.

*Addition of bromine to  $\beta$ -phenylpropionic acid at 0–25°C. in diffused day light.*— $\beta$ -phenylpropionic acid (14.5 g.) in chloroform solution was mixed in the cold with bromine (16 g.) in chloroform solution. Decolourisation of bromine was pretty rapid with the first quantities added but the complete absorption of the theoretical quantity of bromine required several hours overnight. From the reaction product chloroform was distilled and 30.1 g. of yellowish red mixed acids were obtained. The mixture of the *cis* and *trans* isomeric acids was separated by the sodium salt–sodium chloride method described in a previous communication (*J. Indian Inst. Sci.*, 1923, 6, 73). In all about 60 g. of the mixed acids were separated and they yielded nearly 40 g. of the *cis*-acid melting at 88–90° and 20 g. of *trans*-acid melting at 134–36°. The proportions, therefore, work up to 66 per cent. *cis* and 34 per cent. *trans*, the variations in the individual separations being from 75 to 55 per cent. of *cis*-acid, giving a *cis* to *trans* ratio of 2: 1 on an average.

*Addition of bromine to the methyl ester of  $\beta$ -phenylpropionic acid at 0–25°C. in diffused day light.*—The ester (25 g.) dissolved in carbon tetrachloride (220 c.c.) was treated at 0° with bromine (30 g.) added slowly during half-an-hour. The decolourisation of bromine was quite rapid, but, however, the mixture was left overnight for the completion of the reaction. After distillation of the solvent, the residual yellowish brown ester was hydrolysed by alcoholic caustic soda solution (12 g. in about 100 c.c. of 90 per cent. alcohol) boiling the

mixture overnight. The saponified solution after neutralisation with hydrochloric acid and evaporation of the alcohol is diluted to 500 c.c. with water mixed with 100 g. of powdered sodium chloride and heated again to a clear solution. The precipitated sodium salts are filtered after cooling and the acids recovered from the insoluble sodium salt as well as from the filtrate. The *cis*-acid recovered from the soluble sodium salts after one crystallisation from a mixture of chloroform and (60–80°) petrol melted at 97–99°. The yield of *trans*-acid m.p. 133–136° was equal to 32 g. The yield of *cis*-acid isolated was 11 g. The above results show that the esterification of the carboxyl group in  $\beta$ -phenylpropionic acid favours the *trans* addition of bromine much more than the free acid, *cis* to *trans* ratio working up to 1:3 approximately.

*Addition of bromine to  $\beta$ -phenylpropionic acid at 0° in the dark.*—The ice-cooled solution of the acid (20 g.) in chloroform (150 c.c.) was added to a similarly cooled solution of bromine (1 mol.) in chloroform in the dark. The mixture was left in ice-bath in the dark for 8 hours. The solvent was then distilled, the residue neutralised by aqueous caustic soda, and enough common salt added to make a 10 per cent. solution. The precipitated sodium salt was filtered and on decomposition with hydrochloric acid gave the *trans*-acid melting at 134–135°, yield 15 g. The soluble sodium salt on acidification and extraction with ether gave a thick yellow oil (23.0 g.) which solidified to pale yellow crystals melting at 86–94°, corresponding to 95 per cent. of *cis* (cf. melting point data of the author, *J. Indian Inst. Sci.*, 1923, 6, 74). On repeated crystallisation from a mixture of chloroform and petrol the *cis*-acid was obtained in pale yellow needles melting at 97–99°. The ratio of *cis* to *trans* here works up to 3 :2 approximately.

*Addition of bromine to methyl-  $\beta$ -phenylpropionate at 0° in the dark.*—The ester (12.5 g.) was dissolved in chloroform (100 c.c.) and bromine (4 c.c.) in chloroform was added at 0° in the dark and the product worked up as in the previous experiment. The ester product was saponified by alcoholic soda and the resulting sodium salts gave by separation with sodium chloride 11.6 g. of *trans*-acid and 10 g. of a crude *cis* melting at 75–90° corresponding to a 75 per cent. content of pure *cis*-acid melting at 97–99° after recrystallisation of the crude *cis*-acid from a mixture of chloroform and petrol. In this case, the *cis* to *trans* ratio works up to 1 : 2 approximately.

**SUMMARY.**

A larger (more than thrice) proportion of *trans*- $\alpha\beta$ -dibromocinnamic acid is formed by addition of bromine to the methyl ester of  $\beta$ -phenylpropionic acid than in the case of the free acid itself. This observation indicates the existence of steric hindrance to the formation of the *cis*-ester, in which the carbo-methoxy group is close to the benzene nucleus.

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