565. *Halogen Derivatives of Phenyl Styryl Ketone. Part II.* Bromo-chloro-derivatives. Two Cases of " Extra " Isomers.*

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The ketones, CHPhBr·CHCl·COPh and CHPhCl·CHBr·COPh, are each obtained in three optically inactive isomeric forms though only two are to be expected on the basis of two asymmetric atoms. The structure of each of the triads appears to be rigidly established and there is no evidence of polymorphism. The " extra " isomers may owe their existence to restricted rotation about the single α–β carbon–carbon bond.

ADDITION of hydrogen bromide to β-chlorostyryl phenyl ketone occurs readily in carbon disulphide solution :

$$\text{CHPh:CCl·COPh} + \text{HBr} \longrightarrow \text{CHPhBr·CHCl·COPh} \quad \text{(I)}$$

Three isomers, m. p. 106°, 124°, and 134°, respectively, were separated by fractional crystallisation. When heated with potassium acetate in alcohol, each isomer gave β-chlorostyryl phenyl ketone and, quantitatively, bromide ion with no trace of chloride :

$$\text{CHPhBr·CHCl·COPh} + \text{KOAc} \longrightarrow \text{CHPh:CCl·COPh} + \text{KBr} + \text{AcOH}$$

Each isomer therefore appears unequivocally to have the structure (I).

Hydrogen chloride does not add to β-bromostyryl phenyl ketone. However, bromine chloride added to phenyl stryyl ketone, to give three isomers (II), m. p. 93°, 135—136°, and 144—145°, respectively :

$$\text{CHPh:CH·COPh} + \text{BrCl} \longrightarrow \text{CHPhCl·CHBr·COPh} \quad \text{(II)}$$

Potassium acetate in boiling alcohol yielded from each isomer β-bromostyryl phenyl ketone with, quantitatively, chloride ion and no trace of bromide :

$$\text{CHPhCl·CHBr·COPh} + \text{KOAc} \longrightarrow \text{CHPh:CBr·COPh} + \text{KCl} + \text{AcOH}$$

Structure (II) thus seems firmly established for each of these isomers.

The isomers gave depressions of the melting point when mixed in pairs. During an extremely extensive series of crystallisations no transformation of one form into another was observed. The melting points have remained unchanged after storage for many years, those of (I) for more than 40 years and those of (II) for more than 10 years. There is thus no evidence of polymorphism.

When boiled with hydroxylamine hydrochloride and a drop of hydrochloric acid the isomers slowly lose hydrogen halide (the same halide as with potassium acetate); in one case of such slightly incomplete hydrolysis of the chlorobromo-compound (I), m. p. 106°,

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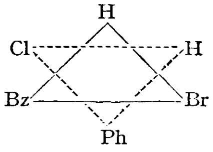
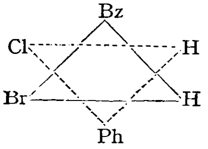
* Part I, preceding paper.

the small amount of recovered (I) had m. p. 134°. This was the sole transformation achieved. In all similar experiments with this or the other isomers, of (I) or of (II), the recovered material was unchanged in melting point.

Since the compounds (I) and (II) have each two different asymmetric carbon atoms, two optically inactive forms of each are to be expected. In each case, however, three forms have been obtained. The extra form may owe its existence to restricted rotation about the single α–β carbon–carbon bond, cf. (III)—(IV) which represent the same diastereoisomer.



(III)



(IV)

(III) Could lose HCl to give the *cis*-form of PhCH=CBr·Bz—m.p. 44°.
(IV) Could not be expected to lose either HCl or HBr.

It must be noted however that modern methods of separating similar substances were not available when this work was done. It should be noted that the ketone group appears to be sterically hindered, insofar as no oxime could be obtained.

EXPERIMENTAL

Analytical values for bromine and chlorine in the same compound are based on determination of total halogen by Stepanow's method and calculation therefrom on the assumption of equimolar content of the two halogens.

β-Bromo-α-chloro-β-phenylpropiophenone.—A solution of β-chlorostyryl phenyl ketone (20 g.) in carbon disulphide (100 c.c.) was saturated with dry hydrogen bromide. After 12 hr. the solvent and excess of acid were removed in a stream of dry air, leaving a colourless crystalline mixture (26·5 g.) which was separated by means of methyl and ethyl alcohols into the following isomers of *β-bromo-α-chloro-β-phenylpropiophenone* : A, prisms (19·0 g.), m. p. 124°, moderately soluble in hot ethyl alcohol, sparingly soluble in cold ethyl alcohol (much less so than isomers B and C) (Found : Cl, 11·0; Br, 24·7. $C_{15}H_{14}OClBr$ requires Cl, 11·0; Br, 24·7%); B, prisms (1·5 g.), m. p. 134°, less readily soluble than C in warm methyl alcohol (Found : Cl, 10·9; Br, 24·65%); and C, fine needles (3·0 g.), m. p. 106° (Found : Cl, 10·9; Br, 24·7%). A residual, more soluble yellow oil (2·5 g.) gradually crystallised, then having m. p. 40° and being identified (mixed m. p.) as β-chlorostyryl phenyl ketone. It is impossible to prescribe a simple scheme of separation, very many operations being required to achieve the yields given above, but the general method will be apparent from the relative solubilities noted above; it is essential that the alcohols be anhydrous and that anhydrous conditions be maintained throughout, in order to minimise hydrolysis—it is hydrolysis, rather than incomplete reaction, which accounts for the " recovered " β-chlorostyryl phenyl ketone.

After treatment of each isomer with an excess of potassium acetate in boiling alcohol for 0·5 hr., Volhard determination demonstrated quantitative liberation of bromide ion, and chloride ion was absent. The β-chlorostyryl phenyl ketone produced had m. p. and mixed m. p. 40°, and its identity was confirmed by quantitative formation of α-chloro-ββ-diphenylpropiophenone, m. p. and mixed m. p. 144°, on reaction with phenylmagnesium bromide.

α-Bromo-β-chloro-β-phenylpropiophenone.—A (standardised) solution of bromine chloride in carbon disulphide or glacial acetic acid was decolorised instantly and exothermally on admixture with an excess of phenyl styryl ketone in the same solvent. On cooling, the solution deposited a large quantity of a crystalline mixture which, when washed with alcohol, melted sharply at 128° (Found : Cl, 11·05; Br, 24·7%). Many crystallisations from various solvents separated the following isomers of *α-bromo-β-chloro-β-phenylpropiophenone* : A, m. p. 144—145° (from alcohol) (Found: Cl, 11·0; Br, 24·7%); B, m. p. 135—136° (from alcohol or light petroleum) (Found : Cl, 11·0; Br, 24·7%); and C, m. p. 93° (Found : Cl, 10·9; Br, 24·6%). It is impossible to prescribe a solvent technique for this separation : only partial separation was achieved in 2 years of experimentation. These isomers are notably less easily hydrolysed by aqueous alcohol than are the β-bromo-α-chloro-compounds.

Each isomer, when dehydrohalogenated as above, gave halide ion quantitatively, which was only chloride; the β-bromostyryl phenyl ketone produced had m. p. and mixed m. p. 44° and with phenylmagnesium bromide gave quantitatively α-bromo-ββ-diphenylpropiophenone, m. p. and mixed m. p. 163°.

Isomerisation.—β-Bromo-α-chloro-β-phenylpropiophenone, m. p. 106° (2 g.), hydroxylamine hydrochloride (1 g.), and concentrated hydrochloric acid (1 drop) in alcohol (25—30 c.c.) were heated under reflux for 4 hr. and then set aside overnight. Next morning a considerable crop of unchanged isomer, m. p. and mixed m. p. 106°, had crystallised and was collected. A second similar treatment of the recovered material gave a reduced amount of the same recovered isomer. A third similar treatment reduced the amount still further, but the melting point remained the same. A fourth similar treatment gave only a few crystals and these had m. p. 134°, alone or mixed with the isomer of that m. p.

Similar experiments with the other five isomers gave only unchanged material until all had been decomposed.

No oximes could be obtained.

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