564. *Halogen Derivatives of Phenyl Styryl Ketone. Part I. Bromo- and Chloro-derivatives.*

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Contrary to other records, phenyl styryl ketone and chlorine give two stereoisomeric dichlorides, CHPhCl·CHCl·COPh; their structure is rigidly proved.

The analogous dibromide is used for an improved preparation of dibenzoylmethane.

Some incidental observations are recorded.

Two dibromides may be obtained by addition of hydrogen bromide to β-bromostyryl phenyl ketone. In 1914, at the request of the late Sir Gilbert Morgan one of us (R. D. A.) studied the preparation of dibenzoylmethane from the dibromide of m. p. 158°, by the following series of reactions:

(*a*) CHPhBr·CHBr·COPh + KOAc ⟶ CHPh:CBr·COPh + KBr + AcOH
(*b*) CHPh:CBr·COPh + NaOEt ⟶ EtO·CPh:CH·COPh + NaBr
(*c*) EtO·CPh:CH·COPh + H_2O ⟶ Ph·CO·CH_2·COPh + EtOH

Reaction (*a*) was complete within 30 minutes at the boiling point, and reaction (*b*) within 10 minutes; on the basis of these observations it was possible to prepare dibenzoylmethane from 92-g. batches of the dibromide in an overall yield of 81·4% in a total time of 45 minutes; this is in both respects superior to the claims in *Org. Synth.*, **8**, p. 60 (cf., *inter al.*, Pond, Maxwell, and Norman, *Amer. Chem. J.*, 1899, **21**, 964; Pond, Yorke, and Moore, *ibid.*, 1901, **23**, 798; *Org. Synth.*, **20**, p. 32).

Goldschmidt (*Ber.*, 1895, **28**, 2540) had reported the preparation of a dichloride, m. p. 113°, by addition of chlorine to phenyl styryl ketone. We have resolved this well-defined material by fractional crystallisation into two stereoisomers, m. p. 116° and 99° respectively, in proportions of about 9 : 1. The material of m. p. 113° appears to be a molecular compound, as also do two other sets of crystals, of different forms, which melt sharply at 82—83° and 87°. Jackson and Pasint (*J. Amer. Chem. Soc.*, 1927, **49**, 2071) obtained the materials of m. p. 82—83°, 98—99°, and 113—114°, and von Auwers and Hügel (*J. pr. Chem.*, 1935, **143**, 159) also studied the reaction, but the pure isomers appear not to have been recorded before. Both isomers react with alcoholic potassium acetate to give β-chlorostyryl phenyl ketone and, quantitatively, potassium chloride and acetic acid. The unsaturated ketone and phenylmagnesium bromide give quantitatively α-chloro-ββ-diphenylpropiophenone, which was also obtained from ethyl α-chlorocinnamate and phenylmagnesium bromide, thus proving the structures of the unsaturated chloro-ketone and thence also of the stereoisomeric dichlorides, CHPhCl·CHCl·COPh.

β-Chlorostyryl phenyl ketone does not recombine with hydrogen chloride as β-bromostyryl phenyl ketone does with hydrogen bromide. But it adds bromine, to give αβ-dibromo-α-chloro-β-phenylpropiophenone, CHPhBr·CClBr·COPh. Its addition of hydrogen bromide is discussed in the following paper.

In the Experimental section we record reactions of the mono- and di-bromo-compounds with ketonic reagents, the products from the unsaturated ketones varying according to the conditions.

EXPERIMENTAL

Preparation of Dibenzoylmethane.—According to *Org. Synth.* (*loc. cit.*), dibenzoylmethane is prepared from the dibromide, m. p. 158°, in an overall yield of 59—61% in two stages occupying 5 hr. After a study of the stages (*a*—*c*) above in detail, partly with Miss G. Fell, the following procedure was standardised.

The dibromide (92 g.), potassium acetate (35 g.), and absolute alcohol (300 c.c.) were heated under reflux for 1 hr. To the cooled mixture N-ethanolic sodium ethoxide (500 c.c.) was added and the whole boiled for 10 min., a trace of alkalinity remaining. Acetic acid (10 c.c.) was added and most (700 c.c.) of the alcohol distilled off. Addition of water then precipitated α-ethoxystyryl phenyl ketone. The supernatant liquid was decanted and extracted twice with ether, the ethereal extracts being then used to collect the oily ethoxy-derivative. Removal of the ether gave a residual oil which was heated to boiling with alcohol (30 c.c.) and concentrated hydrochloric acid (10 c.c.), with vigorous shaking, for 5 min. Addition of water (150 c.c.) and cooling, with shaking, gave dibenzoylmethane as a granular mass which was filtered off. The filtrate was extracted with ether and the extract freed from acid and treated with copper acetate solution, to afford 0·5 g. of the copper derivative. The crude dibenzoylmethane, recrystallised from the minimum of alcohol, gave 41·5 g. of the pure product, m. p. 77—78°; the recrystallisation liquors afforded 4·2 g. of the copper compound. The total yield was 81·4%.

Recovery from the copper derivative. Wislicenus (*Annalen*, 1899, **308**, 345) recovered dibenzoylmethane from its copper derivative by heating the latter with hydrochloric acid but this involves loss by hydrolysis to benzoic acid and acetophenone. 33% Sulphuric acid is slower in action but causes more hydrolysis.

A rapid method is to shake the derivative with ether and concentrated hydrochloric acid, wash and evaporate the ethereal solution, and recrystallise the residue from alcohol. The product is, however, always a deep pink.

Passage of hydrogen sulphide into a hot alcoholic suspension of the copper derivative, storage to permit coagulation of copper sulphide, filtration, and washing of the solid with hot alcohol gave, from the cooled filtrate, pale yellow crystals, m. p. 77—78°. The mother-liquors yielded, on concentration, a further small quantity.

αβ-*Dichlorostyryl Phenyl Ketone*.—Saturation of a cold solution of phenyl styryl ketone in chloroform, ether, carbon disulphide, or acetic acid with chlorine, and working up in the usual way, gave crystals melting sharply at 113° (cf. Goldschmidt, *loc. cit.*). Crystallisation of a not too concentrated alcoholic solution of these gave the *dichloride* as short needles, m. p. 116° unaltered by recrystallisation from the same or other solvents (Found: Cl, 25·4. $C_{15}H_{12}OCl_2$ requires Cl, 25·45%). Further concentration gave, first, material of the same m. p. (116°), and then crystals which melted at 82—83°, 87°, or 113° (cf. Jackson and Pasint, *loc. cit.*). The crystals and liquor were then united and evaporated to dryness in a vacuum-desiccator over sulphuric acid. A warm, not too concentrated methyl-alcoholic solution of the residue yielded, on cooling, the *isomer* as prisms, m. p. 99° (Found: Cl, 25·4%). Concentration of the methyl-alcoholic mother-liquors yielded further crops of m. p. 99°, but later crystals of m. p. 82—83 or 87°. Alternation of crystallisation from ethyl and methyl alcohol permitted separation of all the material into the isomers of m. p. 116° (9 parts) and 99° (1 part), almost without loss; but solvents must be anhydrous and the evaporations conducted without heat, in order to prevent hydrolysis which is even more rapid than with the corresponding dibromides (Abell, *loc. cit.*).

Conversion of the Dichloride into β-*Chlorostyryl Phenyl Ketone*.—Each of the dichlorides, when heated under reflux with potassium acetate (1·25 mols.) in ethyl alcohol for 0·5 hr., gave (i) quantitatively, potassium bromide and acetic acid (for determination see above) and (ii) β-chlorostyryl phenyl ketone, b. p. 214°/13 mm., m. p. 40° (from light petroleum) (Found: Cl, 14·5. Calc. for $C_{15}H_{11}OCl$: Cl, 14·6%); von Auwers and Hügel (*loc. cit.*) obtained the ketone only as an oil, b. p. 204—205°/10 mm. The chlorostyryl phenyl ketone and phenylmagnesium bromide gave α-chloro-ββ-diphenylpropiophenone, m. p. 144°.

During analysis of α-chloro-ββ-diphenylpropiophenone by Stephanow's method an unidentified acid was obtained as pale yellow plates, m. p. 246° (decomp.), almost insoluble in water; this acid is obtained in approx. 20% yield when this chloro-ketone or its bromo-analogue is heated with alcoholic sodium ethoxide or hydroxide or potassium hydroxide.

αβ-*Dibromo*-α-*chloro*-β-*phenylpropiophenone*.—β-Chlorostyryl phenyl ketone and bromine in carbon disulphide give the *trihalogeno-ketone*, m. p. 102° (Found: Br, 39·65; Cl, 8·8. $C_{15}H_{11}OClBr_2$ requires Br, 39·75; Cl, 8·8%).

Reactions with Hydroxylamine.—(a) αβ-*Dibromo*-β-*phenylpropiophenone*. The dibromide, m. p. 158° (3·65 g.), and hydroxylamine hydrochloride (0·7 g.) in alcohol (100 c.c.) were boiled for 2 hr., yielding the oxime, m. p. 156° (Found: N, 3·65. Calc. for $C_{15}H_{13}ONBr_2$: N, 3·7%); this was also obtained by addition of bromine to phenyl styryl ketoxime (Rupe and Schneider, *Ber.*, 1895, **28**, 965). At slightly above the m. p. the oxime yields 3 : 5-diphenyl*iso*oxazole, m. p. and mixed m. p. 140°, and 2 mols. of hydrogen bromide.

The dibromide, m. p. 122°, similarly gave an *oxime*, m. p. 113° (Found: N, 3·6%), which decomposes above the m. p. into hydrogen bromide and 3 : 5-diphenyl*iso*oxazole.

(*b*) αβ-*Dichloro*-β-*phenylpropiophenone*. The dichlorides, m. p. 116° and 99°, similarly gave their *oximes*, m. p. 157° (Found: N, 4·7. $C_{15}H_{13}ONCl_2$ requires N, 4·7%), and 83° (Found:

N, 4·6%), respectively. Both oximes gave, above the m. p., hydrogen chloride and 3 : 5-diphenyl*iso*oxazole, m. p. and mixed m. p. 140°.

(c) β-*Bromostyryl phenyl ketone.* When β-bromostyryl phenyl ketone similarly (4 hr. at the b. p.) gave the oxime, m. p. 151° (cf. von Auwers, *Ber.*, 1929, **62**, 1320); which with hot alcoholic alkali gave 3 : 5-diphenyl*iso*oxazole, m. p. and mixed m. p. 140°.

When the solution was made just alkaline to phenolphthalein (pH 9) before being heated, only 3 : 5-diphenyl*iso*oxazole was produced.

When an alcoholic solution of hydroxylamine hydrochloride was neutralised to methyl-orange (pH 4), treated with less than 1 mol. of β-bromostyryl phenyl ketone, and set aside at room temperature for several days (preliminary warming is permissible but the solution must not be boiled), crystals were deposited which yielded, from alcohol or light petroleum, *α-bromo-β-hydroxyamino-β-phenylpropiophenone* as rhombs, m. p. 199°, which slowly reduce warm Fehling's solution (Found : N, 4·25. $C_{15}H_{14}O_2NBr$ requires N, 4·4%).

(d) β-*Chlorostyryl phenyl ketone.* This ketone, at pH 1 (2 hr.), gave the *oxime* as prisms, m. p. 156° (Found : N, 5·4; Cl, 13·7. $C_{15}H_{12}ONCl$ requires N, 5·4; Cl, 13·8%).

Neutralisation, as in (c) above, to phenolphthalein gave 3 : 5-diphenyl*iso*oxazole, m. p. and mixed m. p. 140°.

Reaction in solution neutral to methyl-orange at room temperature, as in (c) above, gave *α-chloro-β-hydroxyamino-β-phenylpropiophenone*, m. p. 133—134° (Found : N, 5·1. $C_{15}H_{14}O_2NCl$ requires N, 5·1%), soluble in 2N-sodium hydroxide or warm dilute hydrochloric acid. The compound reduces warm Fehling's solution but is unaffected by warm formic acid.

Reactions with Hydrazine.—Mixing β-bromostyryl phenyl ketone and hydrazine hydrate in alcohol caused an exothermic reaction. The solution deposited 3 : 5-diphenylpyrazole as prisms, m. p. and mixed m. p. 199° (Found : N, 12·8. Calc. for $C_{15}H_{12}N_2$: N, 12·7%) (cf. Wislicenus, *Annalen*, 1899, **308**, 219; Knorr and Duden, *Ber.*, 1883, **16**, 115).

Similar treatment of β-chlorostyryl phenyl ketone caused transitory appearance of needles (? the hydrazone) and then the above pyrazole, m. p. and mixed m. p. 199° (Found : N, 12·8%), as sole final product.

Reactions with Phenylhydrazine.—(a) β-*Bromostyryl phenyl ketone.* The bromo-ketone and phenylhydrazine in acetic acid on the water-bath for 1 hour, gave only 1 : 3 : 5-triphenylpyrazole, m. p. and mixed m. p. 136—137°. Heating for only 1 min. afforded a mixture, m. p. 110—126°, whereas treatment with hot alcohol separated a small amount of the sparingly soluble, orange-yellow *phenylhydrazone*, m. p. 114—115° (Found: N, 7·5; Br, 21·0. $C_{21}H_{17}N_2Br$ requires N, 7·4; Br, 21·2%). The soluble material from the mother-liquors yielded 1 : 3 : 5-triphenylpyrazole, m. p. and mixed m. p. 136°, when warmed with potassium hydroxide solution.

Heating the bromo-ketone and phenylhydrazine in ether under reflux for 15 min. gave a mixture of 1 : 3 : 5-triphenylpyrazole, prisms, m. p. and mixed m. p. 136°, and the less soluble *α-bromo-β-phenyl-β-phenylhydrazinopropiophenone phenylhydrazone*, plates, m. p. 210—211°, which darken in air (Found : N, 11·6; Br, 16·4. $C_{27}H_{25}N_4Br$ requires N, 11·55; Br, 16·5%).

(b) β-*Chlorostyryl phenyl ketone.* When heated with phenylhydrazine in alcohol and acetic acid for 2 hr., the chloro-ketone gave 1 : 3 : 5-triphenylpyrazole, m. p. and mixed m. p. 137°.

Boiling the chloro-ketone with phenylhydrazine in ether under reflux for 1 hr. gave the yellow *phenylhydrazone*, m. p. 152° (decomp. at 165°) (Found: N, 8·5; Cl, 10·7. $C_{21}H_{17}N_2Cl$ requires N, 8·4; Cl, 10·7%), which with alcoholic alkali gave 1 : 3 : 5-triphenylpyrazole. There was no evidence of formation of the phenylhydrazino-phenylhydrazone [cf. (a) above].

Reactions with 2 : 4-Dinitrophenylhydrazine.—By Brady's method (*J.*, 1931, 757; 2 min.' warming), β-*bromostyryl phenyl ketone* 2 : 4-*dinitrophenylhydrazone* was obtained as yellowish-red rhombs, m. p. 181°, in rather poor yield (Found : N, 11·8%. $C_{21}H_{15}O_4N_4Br$ requires N, 12·0%).

The β-*chloro-ketone* 2 : 4-*dinitrophenylhydrazone*, similarly prepared, had m. p. 242° (Found : N, 13·3; Cl, 8·3. $C_{21}H_{15}O_4N_4Cl$ requires N, 13·2; Cl, 8·4%), which is stable to boiling acetic acid as the nitro-groups prevent ring-closure (cf. von Auwers and Voss, *loc. cit.*, 1929).

Reactions with Semicarbazide.—(a) β-*Bromostyryl phenyl ketones.* The ketone and semicarbazide hydrochloride in alcohol, made just alkaline to phenolphthalein (pH 9), afforded only 3 : 5-diphenylpyrazole, m. p. and mixed m. p. 199°. Reaction at pH 1, alone or with an excess of potassium acetate (1 hr. at the b. p.), gave a mixture, separated by means of alcohol into (i) a small quantity of sparingly soluble crystals which softened and decomposed above 300° (possibly the semicarbazidosemicarbazone), (ii) 3 : 5-diphenylpyrazole, m. p. and mixed m. p. 199°, and (iii) the *semicarbazone*, yellow needles, m. p. 176—177° (Found : N, 12·1; Br, 22·8. $C_{16}H_{14}ON_3Br$ requires N, 12·2; Br, 23·3%). With warm alcoholic potassium hydroxide, the semicarbazone gave 3 : 5-diphenylpyrazole, potassium bromide, and ammonia, and with boiling aqueous-alcoholic hydrochloric acid gave the pyrazole, carbon dioxide, and ammonium chloride and bromide.

(b) β-*Chlorostyryl phenyl ketone*. The chloro-ketone and semicarbazide hydrochloride in boiling alcohol gave, in 3 hr., 3 : 5-diphenylpyrazole, m. p. and mixed m. p. 199°, as sole product. Reaction at pH 4 gave the *semicarbazone* as rhombs (from alcohol), m. p. 179—180° (Found : N, 14·25; Cl, 11·6. $C_{16}H_{14}ON_3Cl$ requires N, 14·0; Cl, 11·85%) (behaviour with alkali and acid as for the bromo-analogue), and from the mother-liquors a small amount of needles, m. p. 237—246° (possibly the semicarbazidosemicarbazone). The latter product, m. p. 246°, was also obtained in small yield when the ketone, hydrochloride, and potassium acetate were boiled in 70% alcohol (100 c.c.) for 1 hr.

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