152. *The Interaction of Arylhydrazines with Halogenated Aldehydes.*

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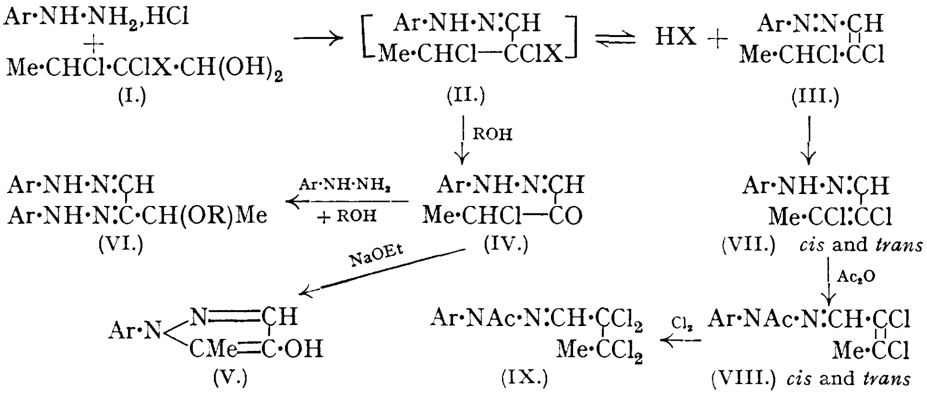
The interaction of arylhydrazines with various ααβ-chloro- and/or -bromo-butaldehydes is profoundly influenced by changes in reaction medium and temperature. The labile crimson *azo-butylene* (III) assumed in previous papers to occur as an intermediate has been isolated, and its transformations in different solvents examined under a variety of conditions. Its isomerisation into *cis-* and *trans*-forms of *αβ-dichlorocrotonaldehyde-*2 : 4-*dichloro* (or *dibromo*)*phenylhydrazone* (VII) is noteworthy.

To complete previous studies of the action of arylhydrazines upon halogenated aldehydes by Chattaway and his collaborators (J., 1927, 2850; 1928, 2756; 1930, 87, 94; 1931, 751, 786, 1088; *J. Amer. Chem. Soc.*, 1932, **54** 263) the behaviour of ααβ-trihalogenated butaldehydes (Chattaway, Irving, and Outhwaite, J., 1933, 993) containing both chlorine and bromine has been examined.

Although the reactions proceed less smoothly as bromine is introduced progressively into the aldehyde, αα-dichloro-β-bromobutaldehyde hydrate, $CH_3\cdot CHBr\cdot CCl_2\cdot CH(OH)_2$, has been condensed in ethyl alcohol with 2 : 4-dichloro(or dibromo)phenylhydrazine hydrochloride to yield β-chloro-α-ketobutaldehyde-2 : 4-dichloro(or dibromo)phenylhydrazone (IV), previously prepared from butylchloral itself (Chattaway and Irving, J., 1930, 92). *β-Bromo-α-ketobutaldehyde-*2 : 4-*dichloro*(or *dibromo*)*phenylhydrazone* (as IV; Cl = Br) results similarly from these hydrazines and alcoholic solutions of either ααβ-tribromobutaldehyde hydrate or α-chloro-αβ-dibromobutaldehyde hydrate. Treated with an alcoholic solution of sodium ethoxide, it yields 4-hydroxy-1-2′ : 4′-dichloro(or dibromo)phenyl-5-methylpyrazole (V) (Chattaway and Irving, J., 1931, 788), and when boiled with one molecular equivalent of 2 : 4-dichloro(or dibromo)phenylhydrazine hydrochloride in methyl (or ethyl)-alcoholic solution it gives α-keto-β-methoxy(or ethoxy)butaldehyde-2 : 4-dichloro(or dibromo)phenylosazone (VI) identical with the product previously obtained from butylchloral.



By a slight change in the conditions the reactions between arylhydrazines and halogenated butaldehydes can be made to give an entirely different series of products. When, for example, 2 : 4-dibromophenylhydrazine hydrochloride in suspension in a highly concentrated alcoholic solution of butylchloral hydrate (I, X = Cl) is kept at room temperature, it dissolves to give a deep crimson solution, from which a compound, $C_{10}H_8N_2Cl_2Br_2$, separates whose brilliant colour suggests that it must be 2 : 4-*dibromobenzeneazo-βγ-dichloro-*Δ^{α}*-butylene* (III), formed by the elimination of a molecule of hydrogen chloride from the intermediate butylchloral-2 : 4-dibromophenylhydrazone (II). It is certain that the halogen atom eliminated is one of those attached to the α-carbon atom, since the interaction of 2 : 4-dibromophenylhydrazine hydrochloride with αβ-dichloro-α-bromobutaldehyde hydrate (as I; X = Br) takes place with the evolution of hydrogen bromide and the same azo-butylene (III) is produced.

If the original alcoholic solution containing the azo-compound (III) and liberated hydrogen halide is kept at room temperature for some days, the crimson colour fades and yellow β-chloro-α-ketobutaldehyde-2 : 4-dibromophenylhydrazone (IV) separates. The same reaction takes place quantitatively and almost instantaneously when dry hydrogen chloride is passed into a solution of the pure azo-butylene (III) in alcohol. Evidently the equilibrium postulated (J., 1930, 89) between this azo-compound and the parent butylchloral-2 : 4-dibromophenylhydrazone (as II; X = Cl) is here progressively disturbed by the addition of hydrogen chloride to the former and by the irreversible hydrolysis of the latter to the keto-hydrazone (IV).

When, however, the azo-compound (III) is refluxed with absolute alcohol in the absence of acid, rearrangement of the double bonds takes place with the formation of *αβ-dichlorocrotonaldehyde-2 : 4-dibromophenylhydrazone* (VII), m. p. 150°, which forms a colourless N-*acetyl* derivative (VIII), m. p. 166°. The mobility of the pentad system in the labile crimson azo-butylene (III) is such that even on keeping at room temperature for some weeks, or more rapidly in contact with an indifferent solvent (benzene, light petroleum), a similar rearrangement ensues: the αβ-dichlorocrotonaldehyde-2 : 4-dibromophenylhydrazone described above is not, however, obtained, but an *isomer*, m. p. 119°, which gives an N-*acetyl* derivative, m. p. 141°.

These two forms of αβ-dichlorocrotonaldehyde-2 : 4-dibromophenylhydrazone (VII) and the corresponding pair of *N*-acetyl derivatives (VIII) are doubtless to be regarded as the theoretically possible *cis*- and *trans*-isomers, since each of the *N*-acetyl derivatives combines readily with two atoms of chlorine to give one and the same product, *ααββ-tetrachlorobutaldehyde-*N*-acetyl-2 : 4-dibromophenylhydrazone* (IX). Alternative explanations for the above cases of isomerism are excluded on the basis of evidence provided by analogous 2 : 4-dichlorophenylhydrazones and detailed below.

The azo-butylene formed when butylchloral hydrate is condensed with 2 : 4-dichlorophenylhydrazine hydrochloride has not yet been obtained analytically pure, and only one of the two isomeric forms of αβ-dichlorocrotonaldehyde-2 : 4-dichlorophenylhydrazone (as VII) has been isolated (Chattaway and Irving, J., 1930, 90). *N*-Acetyl derivatives of both the possible isomers can nevertheless be obtained, for the above hydrazone yields an *N*-acetyl derivative, m. p. 122° (*loc. cit.*), and the red viscous mass which separates during the early stages of the reaction between dichlorophenylhydrazine hydrochloride and butylchloral hydrate in water yields on acetylation an isomeric *αβ-dichlorocrotonaldehyde-*N*-acetyl-2 : 4-dichlorophenylhydrazone* (as VIII), m. p. 154°. These two isomeric *N*-acetyl derivatives have normal molecular weights in benzene. Furthermore, since addition of one isomer depressed the freezing point of a saturated solution of the other isomer in benzene, the relationship of the two substances is proved to be one of isomerism and not of polymorphism (cf. Sidgwick, J., 1915, **107**, 672). That the isomerism is due to differences in arrangements about the ethylenic rather than about the -N=CH (hydrazone) linkage is shown by the fact that both acetyl derivatives yield the same product, *ααββ-tetrachlorobutaldehyde-*N*-acetyl-2 : 4-dichlorophenylhydrazone* (as IX), on the addition of two atoms of chlorine.

When heated with acetyl chloride in a sealed tube, the acetyl derivative of m. p. 122° appears to be converted slowly into the higher-melting isomer.

EXPERIMENTAL.

β-Bromo-α-ketobutaldehyde-2 : 4-dichlorophenylhydrazone (IV; Cl = Br).—20 C.c. of ethyl alcohol were added to 12 g. (1 mol.) of α-chloro-αβ-dibromobutaldehyde (Chattaway, Irving, and Outhwaite, J., 1933, 994), heat being evolved owing to alcoholate formation. When the mixture was cold, 50 c.c. of alcohol and 9·7 g. (1 mol.) of finely powdered 2 : 4-dichlorophenylhydrazine hydrochloride were added, and the whole warmed cautiously. As the hydrazine dissolved, a deep red colour developed and a vigorous reaction set in. Hydrogen chloride was evolved and the alcohol continued to boil for some time without further heating. From the pale yellow solution *β-bromo-α-ketobutaldehyde-2 : 4-dichlorophenylhydrazone* separated on standing. It crystallised from boiling alcohol, in which it was readily soluble, in slender, pale yellow prisms, m. p. 135° (Found: C, 36·9; H, 2·4; Cl, 22·2; Br, 24·8. $C_{10}H_9ON_2Cl_2Br$ requires C, 37·0; H, 2·8; Cl, 21·9; Br, 24·7).

The same compound was obtained by the interaction in alcohol of 2 : 4-dichlorophenylhydrazine hydrochloride and ααβ-tribromobutaldehyde (Chattaway, Irving, and Outhwaite, *loc. cit.*), but greater care was needed in starting the reaction to avoid overheating, which gave rise to profound decomposition.

β-*Bromo*-α-*ketobutaldehyde*-2 : 4-*dibromophenylhydrazone* (as IV), obtained similarly by the interaction of 2 : 4-dibromophenylhydrazine hydrochloride (1 mol.) and α-chloro-αβ-dibromobutaldehyde hydrate or ααβ-tribromobutaldehyde hydrate (1 mol.) in ethyl alcohol, crystallised from boiling alcohol, in which it was readily soluble, in golden-yellow, stout prisms, m.p. 146° (decomp.) (Found : C, 28·9; H, 2·0; Br, 58·3. $C_{10}H_9ON_2Br_3$ requires C, 29·0; H, 2·2; Br, 58·1%).

When 1 mol. of halogenated aldehyde (4·7 g. of α-chloro-αβ-dibromobutaldehyde hydrate, 3·9 g. of αβ-dichloro-α-bromobutaldehyde hydrate, or 5·4 g. of ααβ-tribromobutaldehyde hydrate) was warmed with 7·5 g. (2 mols.) of 2 : 4-dichlorophenylhydrazine hydrochloride in 50 c.c. of methyl alcohol, the hydrazine slowly dissolved, a red colour being developed. When the liquid was raised to the b. p., α-keto-β-methoxybutaldehyde-2 : 4-dichlorophenylosazone (as VI) gradually separated, m. p. 193°. After crystallisation from boiling pyridine, in which it was readily soluble and from which it separated in fine, bright yellow, compact prisms, it had m. p. 201°, not depressed by an authentic specimen prepared from butylchloral hydrate (Chattaway and Irving, *loc. cit.*).

This methoxy-osazone (VI) was also obtained when β-bromo-α-ketobutaldehyde-2 : 4-dichlorophenylhydrazone (IV) was heated in methyl alcohol with 2 : 4-dichlorophenylhydrazine hydrochloride (1 mol.).

Elimination of Hydrogen Bromide from β-*Bromo*-α-*ketobutaldehyde*-2 : 4-*dichloro*(or *dibromo*)-*phenylhydrazone*.—3 G. (1 mol.) of the dichlorophenylhydrazone were added to a solution of 1 g. of sodium (2 mols. + excess) in 50 c.c. of ethyl alcohol. The deep orange solution was gradually heated to its b. p. and kept at this temperature for 2 hours; it was then poured with vigorous stirring into 1 l. of boiling water and boiled with charcoal (5 g.), and the filtered solution acidified. A solution of the precipitate in 100 c.c. of 10% caustic soda solution was boiled (charcoal), filtered, cooled, and made faintly acid. Several repetitions of this process gave a sandy microcrystalline product, which was recrystallised from benzene–light petroleum (charcoal); 4-hydroxy-1-(2′ : 4′-dichlorophenyl)-5-methylpyrazole (V) separated in colourless prisms, m. p. 183°, identical with an authentic specimen (Chattaway and Irving, J., 1931, 786).

Interaction of Butylchloral Hydrate and 2 : 4-*Dibromophenylhydrazine in Cold Alcohol : Formation of* 2 : 4-*Dibromobenzeneazo*-βγ-*dichloro*-Δ^{α}-*butylene* (III).—When 2 : 4-dibromophenylhydrazine hydrochloride (3·7 g.; 1 mol.) was added to a solution of 2·5 g. of butylchloral hydrate (1 mol.) in 12 c.c. of cold ethyl alcohol, it slowly dissolved, giving a bright red solution. The temperature was kept below 15°, since any marked heating initiated profound decomposition leading to a large variety of products. After ½ hour, a crimson solid began to separate and fill the whole bulk of the solution : the process was accelerated by seeding and by vigorous scratching. The solid was collected, pressed, and extracted with light petroleum. After filtration from any arylhydrazine hydrochloride, the deep red extract slowly deposited 2 : 4-*dibromobenzeneazo*-βγ-*dichloro*-Δ^{α}-*butylene* (III), which on repeated crystallisation from the same solvent afforded bright red, flattened prisms, m. p. 83° (Found : C, 31·2; H, 2·0; N, 7·1; Cl, 18·2; Br, 41·3. $C_{10}H_8N_2Cl_2Br_2$ requires C, 31·0; H, 2·1; N, 7·2; Cl, 18·3; Br, 41·3%).

On vigorous reduction with tin and hydrochloric acid an acetic acid solution of the azobutylene (III) was decolourised and by steam-distillation a 95% yield of 2 : 4-dibromoaniline (identified as its *N*-acetyl derivative) was obtained.

The Reversible Addition of Hydrogen Chloride to 2 : 4-*Dibromobenzeneazo*-βγ-*dichloro*-Δ^{α}-*butylene* (III).—When dry hydrogen chloride was passed into a solution of the azo-butylene (III) in dry benzene, the colour faded from red to pale yellow owing to the formation of butylchloral-2 : 4-dibromophenylhydrazone (II; X = Cl). If the excess of hydrogen chloride was removed by washing with dilute sodium bicarbonate solution and water, the neutral yellow solution obtained by separating the benzene and drying thoroughly over anhydrous sodium sulphate slowly lost hydrogen chloride on keeping or warming, the original azo-butylene being recovered unchanged.

Hydrolysis of Butylchloral-2 : 4-*dibromophenylhydrazone*.—Attempts to isolate this hydrazone from the above benzene solution proved fruitless. Slow crystallisation gave ultimately the original azo-butylene, and the effect of heat was to cause profound decomposition. When dry hydrogen chloride was passed into a solution of the azo-butylene (III) in dry alcohol, the red colour faded at once and from the solution β-chloro-α-ketobutaldehyde-2 : 4-dibromophenylhydrazone separated, m. p. (from alcohol) 143·5° alone or admixed with an authentic specimen.

The Isomerisation of 2 : 4-*Dibromobenzeneazo-βγ-dichloro-Δ^{α}-butylene*.—(a) *On standing.* When kept at room temperature for 6 weeks in a sealed tube, the azo-butylene lost its red colour and the brown residue on crystallisation from boiling alcohol gave αβ-dichlorocrotonaldehyde-2 : 4-dibromophenylhydrazone (as VII), m. p. 119°, identical with an authentic specimen (Chattaway and Irving, *loc. cit.*). The same change took place in the course of a few days if the azo-butylene (III) was dissolved in, or was in contact with light petroleum, benzene or chloroform.

(b) *On boiling with alcohol.* A solution of the azo-butylene (III) in dry ethyl alcohol was refluxed for ½ hour. On cooling, the isomeric *αβ-dichlorocrotonaldehyde-*2 : 4-*dibromophenylhydrazone* (as VII) separated (m. p. 145°); after several recrystallisations from boiling alcohol it gave almost colourless, slender prisms, m. p. 150° (Found : C, 30·7; H, 2·2; N, 7·4; Cl, 18·2; Br, 41·0. $C_{10}H_8N_2Cl_2Br_2$ requires C, 31·0; H, 2·1; N, 7·2; Cl, 18·3; Br, 41·3%).

On warming with acetic anhydride to which a drop of concentrated sulphuric acid had been added, the (isomeric) *αβ-dichlorocrotonaldehyde-*N*-acetyl-*2 : 4-*dibromophenylhydrazone* (as VIII) was obtained. It separated from boiling alcohol, in which it was readily soluble, in colourless prisms, m. p. 166° (Found: Cl, 16·5; Br, 37·2. $C_{12}H_{10}ON_2Cl_2Br_2$ requires Cl, 16·5; Br, 37·2%).

*Formation of ααββ-Tetrachlorobutaldehyde-*N*-acetyl-*2 : 4-*dibromophenylhydrazone* (as IX).—A slow stream of dry chlorine was passed through a solution of (either) *N*-acetyl derivative in acetic acid. After ½ hour, the excess of chlorine was removed in a rapid stream of air and on addition of water *ααββ-tetrachlorobutaldehyde-*N*-acetyl-*2 : 4-*dibromophenylhydrazone* separated. It formed colourless, compact prisms, m. p. 108°, from aqueous acetic acid (Found : Cl, 28·8; Br, 32·5. $C_{12}H_{10}ON_2Cl_4Br_2$ requires Cl, 28·4; Br, 32·0%).

*Preparation of the Isomeric αβ-Dichlorocrotonaldehyde-*N*-acetyl-*2 : 4-*dichlorophenylhydrazones* (as VIII), *m. p.* 154°.—To 20 g. (1 mol.) of 2 : 4-dichlorophenylhydrazine hydrochloride dissolved in 1000 c.c. of water at 75° acidified with 5 c.c. of concentrated hydrochloric acid, was added a solution of 18 g. of butylchloral hydrate (1 mol.) and 13 g. of sodium acetate in 250 c.c. of water also at 75°. The liquid became turbid and a red viscous oil separated. After 5 minutes the mixture was cooled, the oil extracted in chloroform and dried with calcium chloride, and the solvent blown off in a rapid current of hot air. Acetic anhydride and a drop of concentrated sulphuric acid were then added; on warming, a vigorous reaction commenced : the viscous red mass dissolved, hydrogen chloride was copiously evolved, and the colour faded to a dull brown. On cooling, the (isomeric) *αβ-dichlorocrotonaldehyde-*N*-acetyl-*2 : 4-*dichlorophenylhydrazone* separated; on crystallisation from boiling alcohol, or acetic acid, in which it was rather less soluble than the isomeric *N*-acetyl derivative of m. p. 122·5°, it formed slender six-sided prisms, m. p. 153·5° (Found : C, 43·0; H, 3·0; N, 8·3; Cl, 41·9; *M*, cryoscopic in benzene, 330, 335. $C_{12}H_{10}ON_2Cl_4$ requires C, 42·3; H, 3·0; N, 8·2; Cl, 41·7%; *M*, 340).

A solution of this *N*-acetyl derivative (3 g.) in 25 c.c. of acetic acid was boiled with excess of granulated tin and 20 c.c. of concentrated hydrochloric acid for 1 hour. The hot solution was then strongly basified and steam-distilled; 2 : 4-dichloroaniline (1·34 g.; calc., 1·5 g.) separated in the distillate and was identified by conversion into its acetyl derivative, m. p. 145·5° alone or mixed with an authentic specimen.

When αβ-dichlorocrotonaldehyde-*N*-acetyl-2 : 4-dichlorophenylhydrazone of m. p. 122·5° was prepared in quantity by the method previously described (J., 1930, 91), the crystals did not appear to be homogeneous, since compact rhombs often accompanied the slender six-sided prisms. Rapid cooling from moderately concentrated solutions appeared to favour the formation of the prismatic form and it was at first thought that a case of polymorphism was involved. However, measurements of representative crystals of each type established their identity and indicated that the observed differences were due to habit only.

The crystals belong to the digonal equatorial class of the monoclinic system. The axial elements are $a : b : c = 2{\cdot}2268 : 1 : 1{\cdot}8456$; $\beta = 126° 28'$. The forms observed were *a* {100}, *m* {110}, *q* {011}, and less frequently *R* {$\bar{1}01$}. The interfacial angles are given below :

Angle.	No.	Limits.	Mean.	Calc.
100 : 110	8	60° 2′— 60° 55′	60° 49′	*
100 : 011	6	70° 23′— 70° 48′	70° 36′	*
011 : $0\bar{1}1$	2	112° 2′—112° 4′	112° 3′	*
011 : $\bar{1}01$	2	70° 38′— 70° 42′	70° 40′	70° 47′
$\bar{1}00$: $\bar{1}01$	2	73° 32′— 73° 45′	73° 38′	73° 45′

The crystals showed strong negative double refraction with a fairly wide axial angle : there is strong inclined dispersion. No good cleavage was found. In the compact, rhomb-like tablets the form *m* {110} is almost suppressed. In the slender prism form the prism zone of six faces is well and fairly equally developed, the form *R* $\{\bar{1}01\}$ is absent, and *q* {011} is represented by a pinakoid only.

That the isomerism of the two *N*-acetyl derivatives of αβ-dichlorocrotonaldehyde-2 : 4-dichlorophenylhydrazone, m. p. 122·5° and 153·5°, is not simply a case of polymorphism was established as follows (cf. Sidgwick, J., 1915, **107**, 672). Cryoscopic measurements in benzene established that the two isomers were unimolecular. Further, the freezing point of benzene saturated with the acetyl derivative, m. p. 122·5° (excess solute present) was lowered from 4·005° to 3·991° and 3·882° by successive additions of the acetyl derivative, m. p. 153·5°. Finally, when chlorine was passed through a solution of the isomer of higher m. p. in acetic acid, there resulted ααββ-tetrachlorobutaldehyde-*N*-acetyl-2 : 4-dichlorophenylhydrazone, m. p. 97—98° (after crystallisation from boiling alcohol), alone or admixed with the specimen previously prepared (J., 1930, 92) by the addition of two atoms of chlorine to the isomer of m. p. 122·5° (Found : Cl, 51·9. Calc. for $C_{12}H_{10}ON_2Cl_6$: Cl, 51·8%).

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