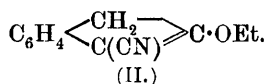
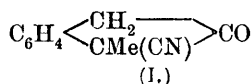


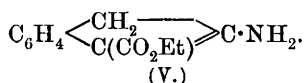
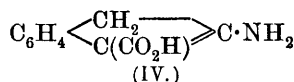
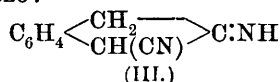
CXLV.—*The Action of Bromine on β -Hydrindone.*

By NORMAN ALLEN CREETH and JOCELYN FIELD THORPE.

IN a communication (Trans., 1908, 93, 165) dealing with the preparation and reactions of β -hydrindone, it was shown that the α -carbon atom of this substance cannot apparently carry a group of more than a certain molecular weight or volume, and that if a group greater than this is introduced the compound exists as a derivative of hydroxyindene. Thus, whereas α -cyano- α -methyl- β -hydrindone (I) exists as a true ketone, the corresponding ethyl derivative cannot be prepared in this form, but always occurs as 3-cyano-2-ethoxyindene (II):



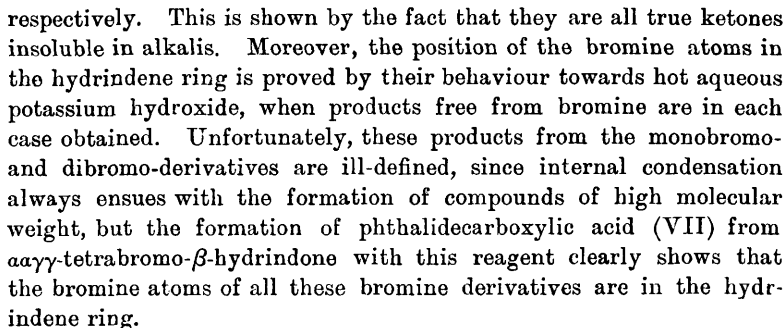
Attention was also drawn to the same phenomenon in the case of β -iminohydrindene and its derivatives, for whereas β -imino- α -cyano-hydrindene (III) is a true imino-compound, the corresponding carboxylic acid (IV) and its ethyl ester (V) are derivatives of 2-aminoindene:



It was suggested at the time that these instances of "steric inhibition" in all probability depended on the molecular weights or a function of the molecular weights of the groups uniting with the α -carbon atom, and in order to ascertain whether the actual weights of the groups as distinct from their volumes were the determining cause of the inhibition, experiments were tried in which the effect of the introduction of a heavy atom such as bromine on the molecule of β -hydrindone was closely studied.

It was found that β -hydrindone is brominated very readily in chloroform solution, and that the bromination proceeds quite normally, yielding ultimately $\alpha\alpha\gamma\gamma$ -tetrabromo- β -hydrindone. The monobromo- and *sym.*-dibromo-derivatives are also easily prepared when the correct quantity of the chloroform solution of bromine is used. It was found, however, that instead of the tribromo-derivative being formed when the calculated quantity of bromine is added, the product always consists of a mixture of the tetrabromo- and *sym.*-dibromo-derivatives. We were unable to isolate the tribromohydrindone from the products

There is no doubt that the monobromo-, dibromo-, and tetrabromo-derivatives of β -hydrindone prepared in this way have the formulæ


$$\begin{array}{c}
 \text{C}_6\text{H}_4 \begin{array}{c} \text{CBr}_2 \\ \text{CBr}_2 \end{array} \text{CO} \rightarrow \text{C}_6\text{H}_4 \begin{array}{c} \text{CO} \\ \text{CO} \end{array} \text{CO} \rightarrow \text{C}_6\text{H}_4 \begin{array}{c} \text{CO}_2\text{H} \\ \text{CO} \cdot \text{CHO} \end{array} \rightarrow \\
 \text{C}_6\text{H}_4 \begin{array}{c} \text{CO}_2\text{H} \\ \text{CH}(\text{OH}) \cdot \text{CO}_2\text{H} \end{array} \rightarrow \text{C}_6\text{H}_4 \begin{array}{c} \text{CO} \\ \text{CH}(\text{CO}_2\text{H}) \end{array} \text{O} \rightarrow \\
 \text{C}_6\text{H}_4 \begin{array}{c} \text{CO} \\ \text{CH}_2 \end{array} \text{O.}
 \end{array}$$
$$\begin{array}{ccc} \text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CHO} & \longrightarrow & \text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{CO}_2\text{H}. \\ (\text{IX.}) & & (\text{X.}) \end{array}$$
$$\alpha\text{-Bromo-}\beta\text{-hydrindone, } \text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{CHBr} \\ \diagdown \text{CH}_2 \end{array} \text{CO.}$$

The preparation of β -hydrindone for the purposes of these experiments was effected by means of the reactions described previously

(Trans., 1908, 93, 186). 1.17 Grams of β -hydrindone were dissolved in well-dried chloroform and the solution mixed as quickly as possible with 3.2 c.c. of a solution of bromine in chloroform (1 c.c. = 0.4255 gram Br). A violent reaction ensued, and the colour of the bromine rapidly disappeared, leaving the solution pale yellow in colour; at the same time large quantities of hydrogen bromide were evolved. When the reaction was complete, the chloroform solution was slowly concentrated on the water-bath until the residue solidified on cooling, when the solid was spread on a porous plate until free from oil. α -Bromo- β -hydrindone may be recrystallised either from methyl alcohol or from light petroleum (b. p. 80—90°), and can be obtained from either solvent in colourless prisms melting at 91°:

0.1931 gave 0.1730 AgBr. Br = 38.1.

C_9H_7OBr requires Br = 37.9 per cent.

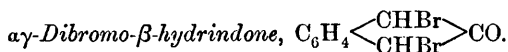
α -Bromo- β -hydrindone is soluble in all the usual organic solvents, and is characterised by possessing greater solubility in methyl alcohol and in light petroleum than either the dibromo- or tetrabromo-derivatives. It is insoluble in cold aqueous alkali hydroxides or carbonates, but rapidly darkens on boiling with these reagents, leaving ultimately a black solid free from bromine from which, however, no definite products could be isolated. When boiled with water, the hydrindone loses hydrogen bromide, and slowly passes into solution, from which, on cooling, a viscid oil separates not containing bromine. Up to the present, we have not succeeded in obtaining this oil in a solid condition.

Conversion of α -Bromo- β -hydrindone into α -Cyano- β -hydrindone.—This conversion was carried out in order to prove that the bromine atom of α -bromo- β -hydrindone is in the hydrindene ring and not in the benzene nucleus. Five grams of the bromo-derivative were dissolved in alcohol and mixed with a concentrated aqueous solution of excess of potassium cyanide, the operation being carried out in a flask fitted with a reflux condenser, so arranged that a current of hydrogen could be passed by means of a narrow tube down the condenser and thus replace all the air in the flask throughout the reaction. This precaution was found to be necessary since both α -bromo- β -hydrindone and α -cyano- β -hydrindone rapidly oxidise in the presence of alkali. After the contents of the flask had been heated on the water-bath for two hours, they were filtered as rapidly as possible, and the filtrate acidified with dilute hydrochloric acid. The solid which then separated was collected and recrystallised from dilute alcohol, when the characteristic plates of α -cyano- β -hydrindone, melting and decomposing at 172°, were obtained (compare Trans., 1908, 93, 179):

0.2213 gave 17.1 c.c. N_2 at 18° and 764 mm. $N = 9.0$.

$C_{10}H_7ON$ requires $N = 8.9$ per cent.

From this experiment it is therefore evident that the bromine atom in α -bromo- β -hydrindone is in the α -position of the hydrindene ring.



This substance was prepared in the same manner as the monobromo-derivative, 1.85 grams of β -hydrindone being dissolved in dry chloroform and mixed as rapidly as possible with 10.5 c.c. of a solution of bromine in chloroform (1 c.c. = 0.4255 gram Br). A vigorous reaction took place, and just as in the former case the whole of the bromine was quickly absorbed, considerable quantities of hydrogen bromide being at the same time eliminated. The pale yellow chloroform solution was then concentrated on the water-bath to a small bulk, when the residue solidified on cooling. The solid was spread on a porous plate and recrystallised, first from methyl alcohol and finally from light petroleum (b. p. $80-90^\circ$), being obtained in large, colourless needles melting at 111° . The compound becomes red on exposure to the air:

0.1963 gave 0.2555 AgBr. Br = 55.4.

$C_9H_6OBr_2$ requires Br = 55.2 per cent.

$\alpha\gamma$ -Dibromo- β -hydrindone is much less soluble in hot methyl alcohol and in hot light petroleum than α -bromo- β -hydrindone, and these two substances can be readily separated from one another by means of these solvents. It is insoluble in cold aqueous alkali hydroxides and in alkali carbonates, but when boiled with these reagents becomes first red and finally dark green. We were unable to isolate any definite products from this reaction, the dark green substance formed in the manner described above being insoluble in all the usual organic solvents, and therefore impossible to purify. It does not contain bromine.

$\alpha\alpha\gamma$ -Tribromo- β -hydrindone.

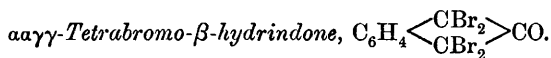
It has already been mentioned that in the experiment which should have yielded this tribromo-derivative a mixture of the dibromo- and tetrabromo-derivatives was obtained, but although the experiment in this respect was unsuccessful, yet it is worthy of recording because the mixture of the two bromo-compounds behaves in many respects as a homogeneous substance having the composition of the tribromo-derivative, and for some time we did not recognise that it was in reality a mixture. The bromination was effected in the usual way, the exact quantity of the chloroform solution of bromine (for 6 atoms)

being added all at once to a weighed quantity of β -hydrindone dissolved in chloroform. The colour of the bromine did not immediately disappear, and it was found necessary to warm the chloroform solution in a flask fitted with a reflux condenser for some time before the whole of the halogen had been absorbed. It is evident, therefore, that the formation of the bromo-derivatives of β -hydrindone at the ordinary temperature ceases with the dibromide, and that beyond this the aid of heat is required. After all the bromine had been absorbed, the chloroform solution was evaporated, the solid residue spread on a plate and finally recrystallised from methyl alcohol. In this way colourless prisms were obtained which appeared to be quite homogeneous and which melted fairly sharply at 153° :

0.2135 gave 0.3274 AgBr. Br = 65.25.

$C_9H_5OBr_3$ requires Br = 65.0 per cent.

The analysis therefore agrees closely with $\alpha\alpha\gamma$ -tribromo- β -hydrindone, and we saw no reason to doubt the homogeneous character of this substance until while recrystallising a quantity of it from light petroleum (b. p. $80-90^\circ$) we noticed that a portion appeared to be much less soluble in this solvent than the remainder. Ultimately it was found that by repeated fractional recrystallisation from light petroleum two substances could be isolated, one of which melted at 111° and the other at 173° . Direct comparison proved the former to be $\alpha\gamma$ -dibromo- β -hydrindone and the latter to be $\alpha\alpha\gamma\gamma$ -tetrabromo- β -hydrindone. It is probable, although we have not experimentally investigated the point, that $\alpha\gamma$ -dibromo- β -hydrindone and $\alpha\alpha\gamma\gamma$ -tetrabromo- β -hydrindone are isomorphous, and that the substance melting at 153° is an isomorphous mixture of molecular proportions of the two. It is unusual, however, for an isomorphous mixture to possess so definite a melting point, but any further doubts on this point were set at rest by recrystallising a prepared mixture of the two constituents from methyl alcohol, when the substance melting at 153° was again obtained.



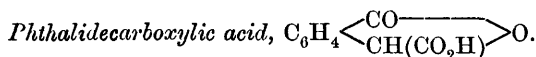
In order to prepare this substance, 3 grams of β -hydrindone were dissolved in dry chloroform and mixed with 34.4 c.c. of a solution of bromine in chloroform (1 c.c. = 0.4255 gram Br), the whole being subsequently placed in a flask fitted with a reflux condenser and heated on the water-bath for two hours. At the end of this time the colour of the halogen had completely disappeared, but in order to replace any possible loss of bromine which might have occurred during the process of heating, a further quantity (1.5 c.c.) of the chloroform solution of bromine was added and the heating continued

for half an hour longer. At the end of this time the chloroform solution, still slightly coloured by excess of bromine, was evaporated, and the solid which remained, after being spread on a porous plate, recrystallised from chloroform, or, better, from a mixture of chloroform and light petroleum (b. p. 80—90°). In this way the compound was obtained in large, colourless, rhombic prisms melting at 173°:

0.2009 gave 0.3370 AgBr. Br = 71.54.

$C_9H_4OBr_4$ requires Br = 71.4 per cent.

alpha-gamma-Tetrabromo-beta-hydrindone is very sparingly soluble in methyl alcohol and in light petroleum (b. p. 80—90°), and it can readily be separated from lower brominated products by means of either of these solvents. It is quite unacted on by cold alkali hydroxides, but gradually passes into solution on boiling, yielding ultimately phthalidecarboxylic acid.



This substance can be readily and quantitatively prepared from *alpha-gamma-tetrabromo-beta-hydrindone* by the action of hot potassium hydroxide solution. The finely-ground bromo-derivative is mixed with excess of a 20 per cent. solution of potassium hydroxide and boiled until all has passed into solution. During this process the bromide gradually dissolves, and when five grams are used the operation is usually finished at the end of one hour. The alkaline solution is then acidified with hydrochloric acid and extracted thoroughly with ether, the ethereal extract being subsequently shaken with dilute sodium carbonate solution. The sodium carbonate extract, after being acidified, is again extracted with ether, the ethereal extract being dried and evaporated. The residue, which solidifies on cooling, is then recrystallised from water, when colourless needles are obtained melting at 152°, and evolving carbon dioxide at about 180°:

0.1864 gave 0.4142 CO_2 and 0.0572 H_2O . C = 60.61; H = 3.41.

$C_9H_6O_4$ requires C = 60.7; H = 3.3 per cent.

The *silver* salt is precipitated as a white crystalline powder on adding a solution containing the calculated quantity of silver nitrate to a neutral solution of the ammonium salt:

0.3185 gave 0.1205 Ag. Ag = 37.83.

$C_9H_5O_4Ag$ requires Ag = 37.9 per cent.

The acid when distilled yielded an oily distillate, which solidified on cooling. On recrystallising the distillate from water, colourless needles were obtained melting at 73°:

0.1795 gave 0.4701 CO_2 and 0.0746 H_2O . $\text{C} = 71.42$; $\text{H} = 4.61$.

$\text{C}_8\text{H}_6\text{O}_2$ requires $\text{C} = 71.6$; $\text{H} = 4.5$ per cent.

The compound is therefore phthalide, and the acid, phthalide carboxylic acid.

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