CCCXXXII.—*Stereochemical Influences on Aromatic Substitution. Substitution Derivatives of* 5-*Hydroxyhydrindene.*

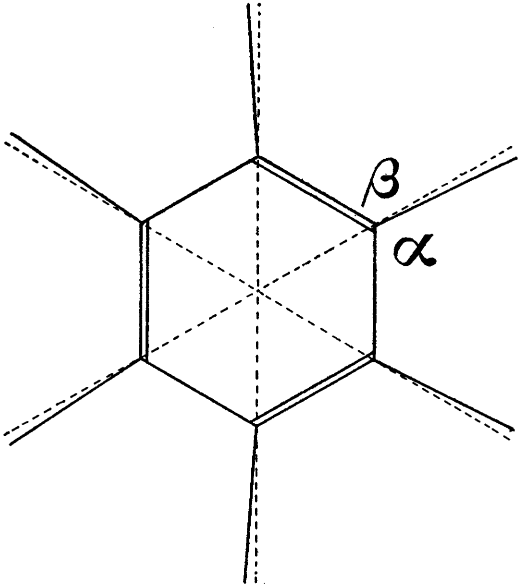
By William Hobson Mills and Ivor Gray Nixon.

The application of the tetrahedral theory of the distribution of the carbon valencies to the Kekulé formula for benzene would indicate that the external valencies of a benzene nucleus thus constituted are not directed as from the centre of the hexagon, as shown by the dotted lines in Fig. 1, but lie as indicated in the figure in directions inclined alternately to either side of these.

This follows from the probable configuration of the valencies of the doubly bound carbon atom. If, in a doubly bound carbon atom, the angle α between the two single bonds is the same as that between the valencies of the carbon atom in methane (according to the tetrahedral theory, 109·5°), then the angle β which the single bonds make with the plane of the double bonds would be one half of 360—109·5°; that is, 125·25°.

It is improbable that the true magnitudes of these angles can be deduced in this way because of the likelihood that the angle between two of the valencies of the carbon atom will be altered when the other two take part in a double bond. The inequality which is thus indicated between the angles α and β is, however, so considerable that it seems reasonable to assume that, although it is probably diminished, it is not removed by such adjustments between the valency angles. We accordingly assume provisionally that in the residue $\dot{:}C<$ the angles β are appreciably greater than the angle α. This inequality being admitted, a further adjustment is involved when six of these residues are united to form a Kekulé benzene nucleus, since this union will require that the internal angle of each residue is reduced to 120°. This reduction of the internal angle must cause correlated increases in the external angles and if, as is likely, the two external angles are increased approximately proportionally, the difference between them will be rendered still greater by this adjustment. We therefore conclude that there is reason to suppose that in the benzene nucleus constituted in accordance with the Kekulé formula the angle α, which each of the external valencies makes with the intranuclear single bond on the one side of

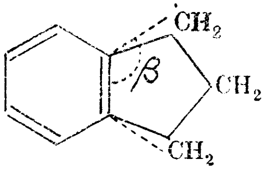
FIG. 1.

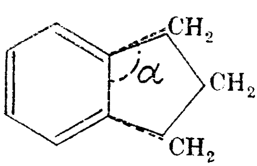


it, is less than that β which it makes with the plane of the double bond on the other side.

It seemed that the simplest way to test these conclusions experimentally would be through the examination of compounds in which the benzene ring is fused with appropriate five- and six-membered rings. If our hypothesis is correct, the stable form of a compound in which the benzene ring is fused with a five-atom ring must clearly be that in which the linking common to the two rings consists of a single bond.

(Ia)





(Ib)

In hydrindene, for example, of the two forms Ia and Ib conditioned by the two possible arrangements of the bonds in the benzene ring, the one with the double bond common to the two rings (Ia) will be under the greater intramolecular strain, since in it two β-intervalency angles are included in the five-ring and considerable distortion of the natural valency directions (indicated by the dotted lines) will be required to approximate these angles to 108°, the intervalency angle of the symmetrical five-carbon-atom ring. In the form (Ib), on the other hand, with the single bond common to the two rings, two α-angles are brought into the five-ring, and since the α-angles do not differ so greatly from the intervalency angle of the five-carbon ring the molecule of this form will be more nearly strain-free.

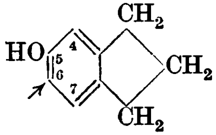
The form Ib should therefore be the more stable, and hydrindene in the liquid or dissolved state should consist of an equilibrium mixture in which this form preponderates.

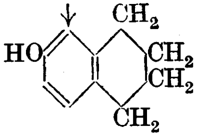
As far as we are aware, there is no method known at the present time by which the distribution of double bonds in hydrindene itself could be determined; there would appear, however, to be a simple means of investigating their arrangement in 5-hydroxyhydrindene.

It is well recognised that the coupling of diazo-compounds with phenols is closely related to the condensation of these compounds with aliphatic enols, the reactions being apparently analogous and brought about by analogous mechanisms; and similarly, that the processes of bromination of phenols and of enolic compounds, which take place with such characteristic readiness, are likewise analogous phenomena. Diazo-compounds and bromine react with enolic compounds in such a way that the substituting group is introduced at the carbon atom which is linked to that bearing the hydroxyl by the double bond. It is therefore to be inferred that in the ortho-substitution of phenols by a diazo-residue or by bromine, of the two ortho-carbon atoms, the substituent will likewise become attached to that which lies on the same side as the double bond.

If, then, in 5-hydroxyhydrindene (IV) the double bonds are arranged as would be expected from the foregoing considerations (*i.e.*, with a single bond common to the two rings), substitution by diazo-residues or by bromine should take place at the 6-position, as indicated by the arrow.

(IV.)

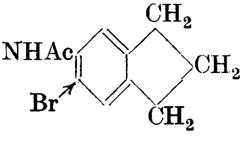


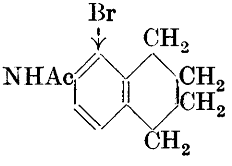


(V.)

We have accordingly examined the action of diazotised *p*-toluidine, diazotised sulphanilic acid, and of bromine on 5-hydroxyhydrindene. In each case there is formed as the main product of the reaction a compound in which on investigation the substituent arylazo-group, or bromine atom, proved to have entered the 6-position. (The methods by which the orientation of the substituent groups was established are described below.) It would therefore appear that the more stable arrangement of the double bonds in 5-hydroxyhydrindene is actually that which we had been led to expect from the foregoing considerations.

The effect on the benzene nucleus of fusion with a six-ring is quite different. The analogue of 5-hydroxyhydrindene in which the alicyclic five-ring is replaced by a six-ring is *ar*-tetrahydro-β-naphthol (V), and a large number of derivatives of this substance have been described by Schroeter (*Annalen*, 1922, **426**, 83). Schroeter found that it yielded, on bromination, 1-bromo-2-hydroxytetrahydronaphthalene and, on coupling with diazotised aniline, 1-benzeneazo-2-hydroxytetrahydronaphthalene. Bromination of the corresponding acetamido-derivatives gives analogous results. Thus 2-acetamidotetrahydronaphthalene yields mainly 1-bromo-2-acetamidotetrahydronaphthalene (Clarence Smith, J., 1904, **85**, 730), whereas 5-acetamidohydrindene yields 6-bromo-5-acetamidohydrindene (Borsche and Bodenstein, *Ber.*, 1926, **59**, 1910).

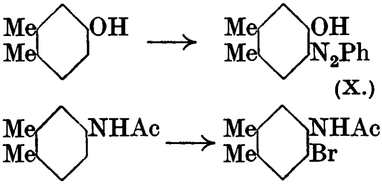




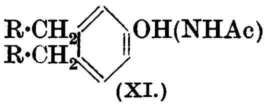
It thus appears that 5-hydroxy (and 5-acetamido) -hydrindene show a marked difference from *ar*-tetrahydro-β-naphthol (and acet-*ar*-tetrahydro-β-naphthalide) with respect to the position in the benzene ring entered by substituents. This difference must arise presumably either (i) from alterations of the reactivity of the hydrogen atoms on either side of the hydroxyl (or acetamido-) group consequent on polarity effects due to the replacement of the trimethylene chain by a tetramethylene chain, or (ii) from differences between the stereochemical effects of the five- and six-membered hydroaromatic rings, or of course a combination of these influences. The trimethylene and tetramethylene groups are, however, so similar chemically that it is difficult to suppose that sufficient polar differences to produce the observed effect could arise from their interchange; on the other hand, the differences in the stereochemical effects of the two types of alicyclic ring produced are evidently likely to be considerable. There is thus an *a priori* probability that the difference in behaviour shown by the two dicyclic systems is mainly due to the different stereochemical influences of the alicyclic rings.

It is accordingly suggested that the position assumed by the substituent group in the coupling and bromination of these hydrindene and tetralin derivatives is determined by the disposition of the system of alternate single and double bonds in the benzenoid ring; that in 5-hydroxyhydrindene the more stable modification is that in which a single bond, in 2-hydroxytetralin that in which a double bond, is common to the two rings; and it is further suggested that this difference in the disposition of the bonds is due to the difference in the position of minimum strain according as the tri- or the tetra-methylene chain is attached to the benzene nucleus.

A point of evident importance in this connexion is the behaviour of *as*-*o*-xylenol (4-hydroxy-1 : 2-dimethylbenzene). Diepolder found (*Ber.*, 1909, **42**, 2918) that when this phenol is coupled with diazotised aniline the benzeneazo-residue enters mainly into the 5-position, the product containing 83% of the 5-derivative (X) and 17% of the 3-derivative. We have also examined, with the assistance of Mr. R. R. T. Young, the bromination of acet-*as*-*o*-xylidide (4-acetamido-1 : 2-dimethylbenzene) and find that in this compound also substitution takes place in the 5-position.



(X.)



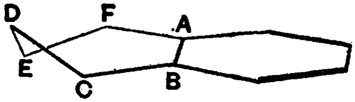
(XI.)

It may hence be inferred that in a 1 : 2-dialkyl-4-phenol the more stable arrangement of the intranuclear bonds is that represented in (XI). It would accordingly appear that the arrangement of the bond-system in 5-hydroxyhydrindene is the normal arrangement, whereas that in 2-hydroxytetralin is an abnormal arrangement brought about through the attachment to the benzene nucleus of the tetramethylene chain.

When the 5-ring is fused with the benzene ring the relations seem clear; the chemical effect of the substituents and the stereochemical effect of the ring combine to bring the system of bonds into the position in which a single bond is common to the two rings.

The effect of the six-ring presents greater difficulty. Here the chemical influence of the substituents and the stereochemical influence of the ring appear to be opposed, and the experimental evidence indicates that the latter is predominant, the stable arrangement of the bonds in 2-hydroxytetralin being that in which a double bond is common to the two rings.

The tetrahedral theory might at first sight seem to indicate that both arrangements of the double bonds would give strainless systems, the approximate configurations of which are represented in perspective by (XII) and (XIII). In (XIII), in which the bonds are arranged so that the dicyclic bond is single, the alicyclic ring has the configuration of the *C*-form of *cyclo*hexane in the phase in which the methylene groups in the 1 : 4-position are at closest approximation. In (XII), where the dicyclic link is double, it has a configuration similar to that of the *Z*-form of *cyclo*hexane.



(XII.)

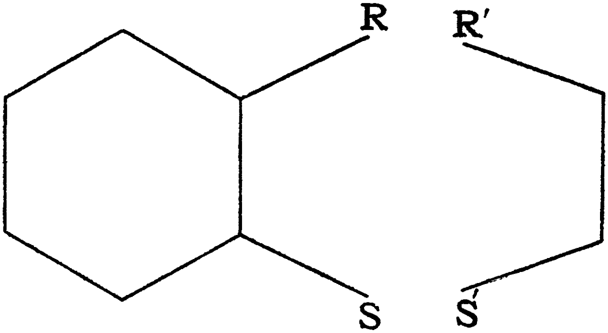
(XIII.)

In examining the question more closely it is, however, to be remembered that (i) the carbon atoms of the benzene nucleus probably have a smaller diameter than those of the aliphatic chain, and that (ii) if we assume that the benzene nucleus is composed of six similar co-planar ⁚CH· groups, the internal angle will be 120°, the α and β angles will therefore together amount to 240°, and any probable partition of this between them must make the α angle considerably greater than 109·5°.

On the basis of *X*-ray measurements we may take 1·42 Å.U. as the diameter of the carbon atoms of the benzene nucleus and 1·54 Å.U. as that of those of the tetramethylene chain. We should then have, in the tridimensional hexagon ABCDEF (XII), AB = 1·42, BC = AF = 1·48, and CD = DE = EF = 1·54 Å.U.

There is at present no precise knowledge of the magnitude of the intervalency angle θ of the methylene group at C, D, E and F, but if we provisionally assume that the molecule in the configuration (XII) is strainless we can calculate the value of β corresponding with different values of θ. Thus, if θ is taken as 109° 28′ and the sides of the figure have the lengths given above, β will be 124° 2′. The corresponding value of α obtained by subtracting β from 240° is 115° 58′. Assuming these values of α and θ, we can then get a measure of the strain in the form (XIII) by comparing the distance RS between the centres of two carbon atoms attached to two singly linked carbon atoms of the benzene nucleus (Fig. 2) with the distance R′S′ between the centres of the terminal carbon atoms of the tetramethylene chain in its unstrained *cis*-uniplanar arrangement. Calculated from the above data, RS is 2·57 and R′S′ is 2·72 Å.U. Strain must therefore be set up when R and R′ and S and S′ are made to coincide so as to form the alicyclic ring in the configuration (XIII); thus on the above values of the intervalency angles and atomic diameters the configuration (XIII) would be strained and (XII) would be strainless.

Fig. 2.



In this manner the values of β, RS and R′S′ corresponding with a series of arbitrarily assumed values of θ can be calculated. In view of the different linkings of the two pairs of valencies of the carbon atom in the methylene group it is probable that θ will be somewhat greater than the interaxial angle of the regular tetrahedron; we may accordingly take it as lying between the limits 109·5° and 115·3°, the latter value being that suggested by Ingold (J., 1921, **119**, 307). To see how the related dimensions vary over this range we have made the calculation for θ = 109° 28′, 112°, and 115° and the results are given in the following table:—

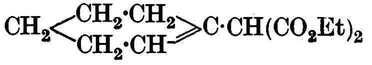
θ (assumed).	β.	RS.	R′S′.
109° 28′	124° 2′	2·57 Å. U.	2·72 Å. U.
112	123 46	2·69	2·73
115	123 20	2·84	2·75

As θ increases, RS and R′S′ increase also, but RS much more rapidly than R′S′, that so whilst at θ = 109° 28′ RS is 6% less than R′S′, at θ = 115° RS has become 3·3% greater than R′S′. At θ = 112° 48′ RS and R′S′ are equal and both configurations would be strainless. β decreases slowly as θ increases; the values indicated for α and β are approximately 116° and 124° and are thus such as would be expected on the basis of the considerations we have put forward regarding the benzene intervalency angles.

Provided, therefore, that the value of θ is not too near to 112·8°, the tetralin molecule should be under less intra-annular strain in configuration (XXII) than in (XIII) and the former configuration should be the more stable.

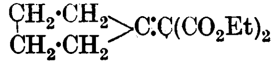
This enquiry into the relationship between the two forms thus indicates the possibility of their having different intra-annular strains, and to this extent it supports the view we have put forward to explain the effect of the attached six-ring on the benzene nucleus. At the same time it would seem to show that any difference in stability thus produced would be small, too small possibly to overcome what has been referred to above as the chemical effect of the substituents on the arrangement of the double bonds, which from the behaviour of *o*-xylenol would appear to favour the form (XIII). It may therefore be that the data employed for the atomic diameters may differ appreciably from the values applicable to the present case; it is possible, moreover, that the interaction of the hydrogen atoms may also have an appreciable effect on the relative stability of the two configurations, and if so, this would presumably favour the alicyclic ring in (XII) in comparison with that in (XIII), which, as has been remarked, corresponds with an extreme phase of the *C*-form of *cyclo*hexane.

The inequality of the α and β angles of the doubly linked carbon atom indicated by the foregoing consideration seems to be confirmed by the observations of Kon and Speight (J., 1926, 2728) on certain cyclic derivatives of malonic ester. The *cyclo*hexenyl derivative (XIV) was found to be stable in the βγ-unsaturated form, whilst the corresponding *cyclo*pentenyl derivative was stable in the αβ-unsaturated form (XV).



$$CH_2<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH\end{matrix}>C\cdot CH(CO_2Et)_2$$

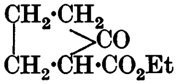
(XIV.)



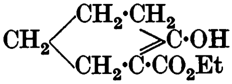
$$\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>C:C(CO_2Et)_2$$

(XV.)

The larger β-angles would clearly fit more easily into the six- than into the five-ring. Dieckmann's observations (*Ber.*, 1922, **55**, 2473) that *cyclo*pentanonecarboxylic ester (XVI) contains only 4·5% of the enolic form whilst *cyclo*hexanonecarboxylic ester (XVII) contains 76% of enol may be similarly interpreted.

(XVI.) 

$$\begin{array}{l}CH_2\cdot CH_2 \\ | \qquad > CO \\ CH_2\cdot CH\cdot CO_2Et\end{array}$$

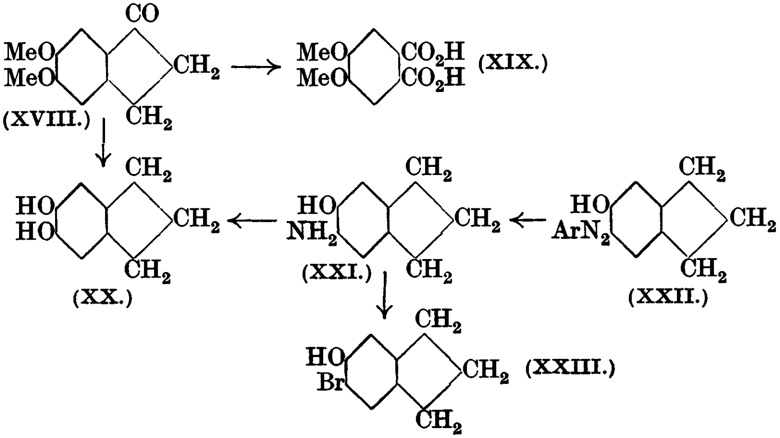
 (XVII.)

$$CH_2 \begin{array}{l} \diagup CH_2\cdot CH_2 \\ \qquad\qquad \geqslant C\cdot OH \\ \diagdown CH_2\cdot C\cdot CO_2Et\end{array}$$

However, in certain similar cases the relationships are not so clear; the stereochemical effects of the double bonds may apparently be obscured by other influences; thus Linstead observed (J., 1929, 2143) that the αβ-unsaturated *cyclo*hexylideneacetonitrile was, if anything, more stable than its *cyclo*pentylidene analogue.

The orientation of the substitution derivatives of 5-hydroxyhydrindene was carried out in the following manner. To determine the point of entry of the arylazo-group, 5-hydroxyhydrindene was coupled with diazotised *p*-toluidine and, as had already been done by Borsche and John (*Ber.*, 1924, **57**, 656), with diazotised sulphanilic acid, and the resulting azo-compounds (XXII) were reduced, giving an aminohydroxyhydrindene (XXI), also obtained by Borsche and John, though regarded by them (*loc. cit.*, p. 657) as being probably a 4-amino-compound on the ground that the ring homologue of 5-hydroxyhydrindene, 6-hydroxytetralin, coupled, according to Schroeter, in the α-position.

We converted this aminohydroxy-compound (XXI) by diazotisation into the corresponding dihydroxy-compound and, for comparison, prepared 5 : 6-dihydroxyhydrindene from the dimethoxyhydrindone synthesised by Perkin and Robinson (J., 1907, **91**, 1079) from 3 : 4-dimethoxyphenylpropionic acid and proved by them to have the constitution (XVIII), since they showed that it gave *m*-hemipinic acid (XIX) on oxidation.



We reduced this dimethoxyhydrindone to the corresponding 5 : 6-*dimethoxyhydrindene* and eliminated the methyl groups by hydrolysis and thus obtained 5 : 6-*dihydroxyhydrindene* (XX) as a reference substance of established constitution.

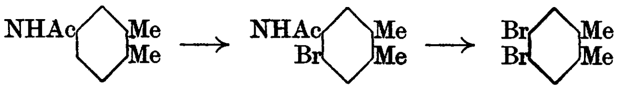
On comparison of this dihydroxyhydrindene with that obtained from the arylazo-5-hydroxyhydrindenes we found the two substances to be identical. Hence the aminohydroxyhydrindene of Borsche and John is the 5 : 6-derivative (XXI) and therefore in the coupling of 5-hydroxyhydrindene with diazo-compounds the arylazo-residue enters the 6-position.

The coupling does not take place, however, exclusively in this position. It was observed in the interaction with diazotised *p*-toluidine that, along with the 6-*p*-tolueneazo-5-hydroxyhydrindene, a small quantity of an isomeric compound, presumably the 4-tolueneazo-derivative, was produced.

In order to obtain information as to the actual proportion of the 6-derivative formed, we examined the coupling with diazotised *p*-chloroaniline, since with this diazo-compound coupling proceeds exceptionally cleanly and without the formation of tarry by-products. It was found that the proportion of the 6-*p*-chlorobenzeneazo-derivative was 90% of the total azo-dye produced.

To determine the position entered by bromine, 5-hydroxyhydrindene was brominated in acetic acid solution. The reaction proceeded smoothly and a monobromo-derivative was readily obtained. That the bromine had entered the 6-position was established by showing the identity of the product with the 6-*bromo*-5-*hydroxyhydrindene* (XXIII) formed by replacement of the amino-group in 6-amino-5-hydroxyhydrindene (XXII) by bromine through the diazo-reaction.

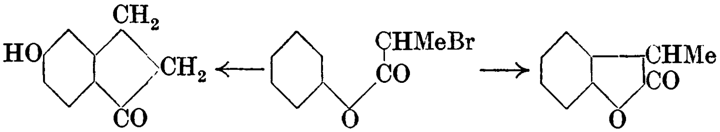
The position of the bromine in the product of monobromination of 4-acetamido-*o*-xylene was determined by converting the bromoacetamido-compound (XXV) into the corresponding dibromo-*o*-xylene. This melted at 88° and was therefore 4 : 5-dibromo-*o*-xylene (XXVI) (Jacobsen, *Ber.*, 1884, **17**, 2377); the isomeric 5 : 6-dibromo-compound melts at 8°.



(XXIV.) (XXV.) (XXVI.)

EXPERIMENTAL.

Preparation of 5-*Hydroxyhydrindene*.—This substance was first prepared by Moschner (*Ber.*, 1900, **33**, 737) by fusion of sodium hydrindenesulphonate with potash, and was afterwards obtained by Borsche and John (*Ber.*, 1924, **57**, 656) by the action of nitrous acid on 5-aminohydrindene. We obtained the substance by reducing 5-hydroxyhydrindone, which we prepared by a method, due to Auwers and Hilliger (*Ber.*, 1916, **49**, 2410), dependent on the transformation of phenyl α-bromopropionate under the influence of aluminium chloride.



We proceeded as follows : propionic acid (55 g.) was mixed with the equivalent weight of thionyl chloride and kept at room temperature till no more hydrogen chloride was evolved ; the reaction was strongly endothermic. The crude propionyl chloride obtained was heated on a boiling water-bath and bromine (120 g.) was added in quantities of about 10 c.c. ; bromination then proceeded smoothly (it is strongly catalysed by sunlight).

The product of the reaction was a mixture of α-bromopropionyl chloride and α-bromopropionyl bromide and boiled at 140—155°. After distillation its composition was determined by decomposing a weighed sample with *N*-sodium hydroxide solution and back-titration. The mixed chloride and bromide were then heated with the calculated quantity of phenol (1—2% excess) for 4 hours at 140° and the resultant phenyl ester was distilled and then treated with aluminium chloride in the manner described by Auwers and Hilliger, 50 g. of ester being used for each experiment. The yield obtained of 5-hydroxyhydrindone (m. p. 183°) was 16% of the theoretical. The hydroxyhydrindone was reduced to hydroxyhydrindene by Clemmensen's method. Amalgamated zinc (170 g.) was covered with dilute hydrochloric acid (1 vol. of conc. acid to 2 vols. of water), the hydroxyhydrindone (17 g.) added, and the mixture warmed to start the reaction. After the vigorous reaction had subsided, the mixture was heated for 1 hour with occasional addition of the dilute hydrochloric acid and then for 2 hours with similar addition of concentrated hydrochloric acid. The mixture was then steam-distilled, the distillate was extracted with ether, and the residue left on evaporation of this ether was crystallised from light petroleum (b. p. 40—60°). Yield, 13·8 g. (90% of the theoretical) ; m. p. 56°.

6-p-*Tolueneazo-5-hydroxyhydrindene.*—5-Hydroxyhydrindene (6·7 g.), dissolved in ice-cold alkaline solution, was coupled in the usual way with diazotised *p*-toluidine (5·35 g.). The product was collected after standing over-night and was separated into two fractions by crystallisation from alcohol. The less soluble fraction (8·3 g.), m. p. 132·5°, consisted of 6-p-*tolueneazo-5-hydroxyhydrindene* (Found: C, 76·5; H, 6·4. $C_{16}H_{16}ON_2$ requires C, 76·2; H, 6·4%). The more soluble fraction, crystallised from light petroleum (b. p. 60—80°), gave a red substance (0·9 g.), m. p. 99—101°, which was probably a mixture of the 6-*p*-tolueneazo- with the 4-*p*-tolueneazo-derivative in the proportion approximating to the eutectic, as it had the composition of a pure tolueneazohydroxyhydrindene (Found: C, 76·1; H, 6·5; N, 11·2. Calc.: C, 76·2; H, 6·4; N, 11·1%) and its m. p. was raised, not depressed, by addition of a small quantity of the 6-*p*-tolueneazo-derivative.

6-p-*Chlorobenzeneazo-5-hydroxyhydrindene.*—*p*-Chloroaniline (1 g.) was diazotised and the diazo-solution, after having been carefully neutralised with sodium carbonate, was added to an ice-cold alkaline solution of 5-hydroxyhydrindene (1 g.). The orange-yellow product was collected after a few minutes and when dried had nearly the theoretical weight. By crystallisation of 1·7 g. of this product from alcohol it was separated into two fractions: *A*, 1·36 g., m. p. 155—156° (Found: Cl, 12·84), and *B*, 0·28 g., m. p. 109—110° (Found: Cl, 12·83. $C_{15}H_{13}ON_2Cl$ requires Cl, 13·0%). *A* was evidently 6-p-*chlorobenzeneazo-5-hydroxyhydrindene* and *B* appeared to be a mixture of *A* with the isomeric 4-derivative. From solubility experiments it was estimated that this mixture contained about 40% of *A*. Thus the coupled product contained 90% of the 6-derivative, the remaining 10% being presumably the 4-derivative.

6-*Amino-5-hydroxyhydrindene.*—6-*p*-Tolueneazo-5-hydroxyhydrindene was dissolved in boiling alcohol (50 c.c.) and reduced by the gradual addition of a solution of stannous chloride prepared from crystallised stannous chloride (168 g.), concentrated hydrochloric acid (160 c.c.), and alcohol (200 c.c.), about 54 c.c. of this solution being required. When reduction was complete the mixture was diluted with water, the tin removed with hydrogen sulphide, the filtrate concentrated and made alkaline, and the *p*-toluidine removed by a current of steam. The aminohydroxyhydrindene was then precipitated by the cautious addition of acetic acid, extracted with ether, and crystallised from benzene. It melted at 185—186°. The compound is also conveniently prepared by the reduction of benzeneazohydroxyhydrindenesulphonic acid by sodium hydrosulphite as described by Borsche and John.

5 : 6-*Dihydroxyhydrindene.*—(a) *From* 5 : 6-*dimethoxy*-1-*hydrindone.* 3 : 4-Dimethoxyphenylpropionic acid was prepared, with slight modifications, by the method described by Perkin and Robinson (J., 1907, **91**, 1079). Veratraldehyde (50 g.) was added to a mixture of sodium wire (10 g.) and ice-cold ethyl acetate (100 g.),

the temperature being maintained between 30° and 40° after the commencement of the reaction. When the reaction had subsided, the mixture was kept over-night, and the ester then hydrolysed by the addition of a solution of potassium hydroxide (45 g.) in methyl alcohol. After the completion of the reaction water was added, the mixture steam-distilled to remove alcohol and the excess of veratraldehyde, and the 3 : 4-dimethoxycinnamic acid precipitated with hydrochloric acid. The dimethoxycinnamic acid was dissolved in a slight excess of dilute aqueous ammonia, and the cold solution of ammonium salt reduced by 3% sodium amalgam, acetic acid being added from time to time to neutralise the liberated ammonia. The acid was purified by crystallisation from benzene; it melted at 97° and the yield was 46 g. It was converted into 5 : 6-dimethoxy-1-hydrindone exactly as described by Perkin and Robinson.

5 : 6-*Dimethoxyhydrindene* was obtained by reducing the hydrindone by Clemmensen's method, the conditions employed being the same as those described above for the reduction of 5-hydroxy-1-hydrindone. The crude 5 : 6-dimethoxyhydrindene melted at 54°, and after purification by crystallisation from dilute alcohol at 55°. Yield, 3·7 g. from 5 g. of hydrindone (Found : C, 74·4 ; H, 8·0. $C_{11}H_{14}O_2$ requires C, 74·1 ; H, 7·9%). The substance gives a pale yellow solution in sulphuric acid which passes into a fine blue on warming.

The methoxy-derivative (2 g.) was heated with hydriodic acid (*d* 1·7) (25 g.) in a current of carbon dioxide for ½ hour after all the oil had gone into solution (about 1½ hours altogether). The contents of the flask, which solidified on cooling, were diluted with water and extracted with ether, the extracts being subsequently washed with sodium bicarbonate solution to remove hydriodic acid and iodine. The *dihydroxyhydrindene*, recrystallised from hot water, was obtained as colourless platelets, m. p. 116°. It can also be crystallised from light petroleum (b. p. 60—80°). It dissolves in concentrated sulphuric acid, giving a pale yellow solution which passes into a fine blue with a reddish fluorescence on warming (Found : C, 71·8 ; H, 6·7. $C_9H_{10}O_2$ requires C, 71·9 ; H, 6·7%).

(b) *From 6-amino-5-hydroxyhydrindene.* The aminohydroxy-compound (3 g.) was dissolved in a solution of sulphuric acid (4 g.) and copper sulphate crystals (0·69 g.) in water (20 c.c.) and diazotised at 0—5°. After ½ hour, the slight excess of nitrous acid was destroyed by the addition of urea. The diazo-solution was then added to a boiling solution of copper sulphate crystals (50 g.) in water (50 c.c.), and boiling continued for a short time until decomposition was complete. The cold solution was extracted with ether, and the tarry product left on removal of the ether extracted with boiling water (150 c.c.), which was again extracted with ether. The residue from the ether, crystallised from light petroleum, gave pure 5 : 6-dihydroxyhydrindene in platelets, m. p. 116° (yield, 0·6 g.). A comparison of the compound thus obtained with that from dimethoxyphenylpropionic acid left no doubt as to their identity. The melting points were identical and the mixed m. p. showed no depression (116°). The colour reactions with sulphuric acid were indistinguishable. Moreover, their crystallographic properties, for the determination of which we are indebted to Mr. E. C. Bullard of Clare College, were found to agree. Examination in polarised light under the microscope showed both to belong to the oblique system with the plane of symmetry perpendicular to the plates and parallel to the cleavage. The optic axial plane was in the plane of symmetry, the normal to the plates lying between the obtuse bisectrix and the one visible optic axis. The angle between the normal and this optic axis was measured for both specimens, the values found being 16·5° for that from dimethoxyhydrindone and 19·5° for that from the aminohydroxyhydrindene, which were equal within the limits of experimental error.

The second optic axis was totally internally reflected, the optic axial angle, estimated from the curvature of the visible brush, being of the order of 45° for both specimens. The refractive indices for light travelling perpendicular to the section were measured by the Beckse line method. That for vibrations perpendicular to the plane of symmetry was 1·62, and for vibrations in the plane of symmetry 1·64, for both specimens. Both specimens were optically positive.

6-*Bromo*-5-*hydroxyhydrindene*.—(a) *From* 5-*hydroxyhydrindene*. A solution of 5-hydroxyhydrindene (4 g.) in acetic acid (50 c.c.) was treated with bromine (4·8 g.) dissolved in twice its volume of acetic acid, the mixture being cooled with ice-water. Water was then added, the product extracted with ether, and the ethereal solution washed with sodium bicarbonate solution to remove acetic acid. The oil left on evaporation of the ether distilled at 143°/14 mm. and crystallised on cooling (yield, 6·4 g.). The crystals were freed from a little adherent oil by pressure between filter-paper and recrystallised from 50% acetic acid cooled in a freezing mixture. The compound has a characteristic odour and melts at 37·7° (Found : Br, 37·1. C_9H_9OBr requires Br, 37·5%).

(b) *From* 6-*amino*-5-*hydroxyhydrindene*. Aminohydroxyhydrindene (1 g.), dissolved in a mixture of 4·6 g. of hydrobromic acid (*d* 1·7) and water (12 c.c.), was diazotised with a solution of sodium nitrite (0·46 g.) in water (5 c.c.). The diazo-solution was poured into a solution of cuprous bromide, prepared from copper sulphate crystals (8 g.), in a mixture of 8·8 c.c. of hydrobromic acid (*d* 1·7) with an equal volume of water kept at 90—100°. The resulting mixture was distilled with steam, and the product extracted with ether from the distillate. It was distilled at 0·5 mm. pressure from a bath at 100°. The distillate, after purification in the same way as the product obtained by bromination of 5-hydroxyhydrindene, proved to be identical with that product. Both substances melted at 37·7° and the mixture melted at the same temperature. The one substance when fused crystallised on addition of a nucleus of the other.

5-*Bromo*-4-*acetamido*-o-*xylene*.—4-Nitro-*o*-xylene, prepared from *o*-xylene by the method of Crossley and Renouf (J., 1909, **95**, 202), was reduced with tin and hydrochloric acid to the corresponding *o*-xylidine and the latter was acetylated with acetic anhydride in the usual manner.

Acetamido-*o*-xylene (7·7 g.) was dissolved in the smallest possible amount of glacial acetic acid, and bromine (8 g.), dissolved in glacial acetic acid (45 c.c.), was added gradually at 0°. A yellow precipitate was formed which dissolved on addition of a small quantity of dilute acetic acid and was reprecipitated by addition of water. Yield, 10·1 g. After crystallisation from dilute acetic acid and then from water, the product melted at 164° (Found : Br, 33·2. $C_{10}H_{12}ONBr$ requires Br, 33·05%).

5-*Bromo*-4-*amino*-o-*xylene*.—Bromoacetamido-*o*-xylene (6·8 g.) was hydrolysed by boiling it gently with a mixture of concentrated sulphuric acid (100 c.c.) and water (100 c.c.). The resulting *bromo*-o-*xylidine* (4·1 g.) melted, after recrystallisation from light petroleum, at 84·5° (Found : Br, 40·2. $C_8H_{10}NBr$ requires Br, 40·0%).

4 : 5-*Dibromo*-o-*xylene*.—Bromoamino-*o*-xylene (1 g.) was dissolved in dilute hydrobromic acid (8 c.c. of acid, *d* 1·7, and 35 c.c. of water) and diazotised with a 10% solution of sodium nitrite. This diazo-solution was added gradually to a solution of cuprous bromide (8·5 g.) in hydrobromic acid (27 c.c. of acid, *d* 1·49, and 9 c.c. of water) kept at 90°. The product was isolated by distillation with steam and extraction with ether. Yield, 1·1 g. After recrystallisation from alcohol it melted at 88° (Found : Br, 60·7. Calc. : Br, 60·6%).

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