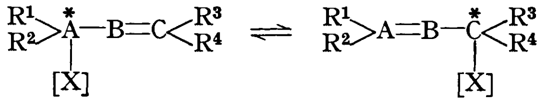
355. *Optical Activity in Relation to Tautomeric Change. Part I. Conditions underlying the Transport of the Centre of Asymmetry in Tautomeric Systems.*

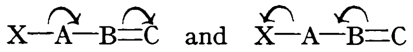
By C. K. INGOLD and C. L. WILSON.

THE immediate question to which the present work was addressed may be stated as follows: Given two mutually convertible triad tautomerides (I and II) each containing only one asymmetric centre (indicated *), which is in each case situated at the point of attachment of the mobile group (represented [X]); it is required to find whether an optically active modification of tautomeride (I) would, on conversion under ordinary non-asymmetric conditions, yield an optically active tautomeride (II) :

(I.)

(II.)

$$\begin{matrix}R^1\\R^2\end{matrix}\!>\!\underset{[X]}{\overset{*}{A}}-B=C\!<\!\begin{matrix}R^3\\R^4\end{matrix} \rightleftharpoons \begin{matrix}R^1\\R^2\end{matrix}\!>\!A=B-\underset{[X]}{\overset{*}{C}}\!<\!\begin{matrix}R^3\\R^4\end{matrix}$$

From the mechanistic point of view two cases arise according as the change is cationotropic (*e.g.*, prototropic) or anionotropic; but the two forms of electron displacement

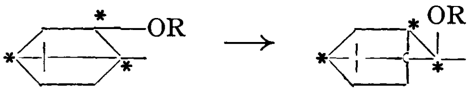


corresponding respectively to these two complementary types of change are so entirely analogous that an answer obtained for either case is expected to hold for both.

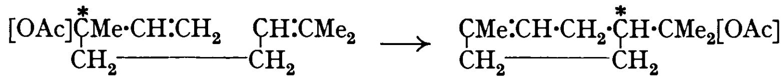
In the problem considered the asymmetric centre becomes transported in the course of the change from the point of detachment of the mobile group to the point of its reunion. This problem is therefore quite distinct from that solved by McKenzie and his co-workers for the pinacol and allied rearrangements, in which optical activity was found to be retained; in these rearrangements the asymmetric centre remains stationary although one of the substituents attached to it becomes replaced, *e.g.*,

$$(CH_2Ph)_2C(OH)\cdot\overset{*}{C}HPh\cdot OH \longrightarrow CH_2Ph\cdot CO\cdot\overset{*}{C}HPh\cdot CH_2Ph$$

The well-known cases in which optical activity is retained during Wagner rearrangement in the terpene series are still more remote from the present question, for in these examples, not only is there no definite migration of an asymmetric centre, but also the molecules contain at least one asymmetric centre external to the rearranging system, *e.g.*,



The only previously known instance of an isomeric change involving movement of the single centre of asymmetry responsible for optical activity is the conversion of linalyl acetate or formate into the corresponding optically active α-terpinyl ester (Stefan, *J. pr. Chem.*, 1898, **58**, 111; Zeitschel, *Ber.*, 1906, **39**, 1780) :



$$\underset{CH_2\text{————}CH_2}{[OAc]\overset{*}{C}Me\cdot CH{:}CH_2\quad CH{:}CMe_2} \longrightarrow \underset{CH_2\text{————}CH_2}{CMe{:}CH\cdot CH_2\cdot\overset{*}{C}H\cdot CMe_2[OAc]}$$

This example differs in two important respects from the fundamental case (I ⇌ II) formulated above. First, the migrating centre of asymmetry does not follow the route of the mobile group and does not arrive at the same destination. Secondly, the interconversion is a ring-chain, pentad, anionotropic change, and, as will be shown later, the circumstance that the displacement of a double bond in this tautomeric system gives rise to a ring rather than to another double bond is far from being trivial in this connexion.

Exploratory experiments (See Experimental, Sections 1—4) concerning both anionotropic and prototropic systems of the form (I ⇌ II) led to the selection of the methylene-azomethine prototropic system $>C[H]\cdot N{:}C<$ (Ingold and Shoppee, J., 1929, 1199) as that most likely to provide suitable examples for the purpose in view; and further preliminary investigations within this field (Experimental, Sections 3 and 4) resulted in the final choice of the pair of tautomerides (III) and (IV) :

(III.)

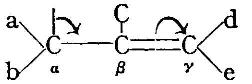
(IV.)

$$\begin{matrix}CH_3\\C_6H_5\end{matrix}\!>\!C[H]\cdot N{:}C\!<\!\begin{matrix}C_6H_5\\C_6H_4Cl(p\text{-})\end{matrix} \rightleftharpoons \begin{matrix}CH_3\\C_6H_5\end{matrix}\!>\!C{:}N\cdot C[H]\!<\!\begin{matrix}C_6H_5\\C_6H_4Cl(p\text{-})\end{matrix}$$

These tautomerides in alcoholic solution become interconvertible in the presence of sodium ethoxide; the reaction occurs at a convenient speed, ceases on destruction of the catalyst, and is unaccompanied by the formation of by-products. No approach to complete conversion is possible because the equilibrium mixture contains almost exactly equal amounts of the two isomerides; but these may be separated through derivatives by a method shown to be suitable for the diagnosis of optical activity.

When the interconversion was effected with one of the optically active modifications of compound (III), the isomeride (IV) produced had no perceptible rotatory power. Had this compound been formed with a rotatory power amounting to 1% of that of its optically pure modification, the retention of activity would certainly have been observed. It was ascertained that this result was not due to the complete racemisation of isomeride (III) prior to its tautomeric conversion; for compound (III) was recovered with a high proportion of its original rotatory power from the same solution which yielded isomeride (IV) in an optically inactive condition.

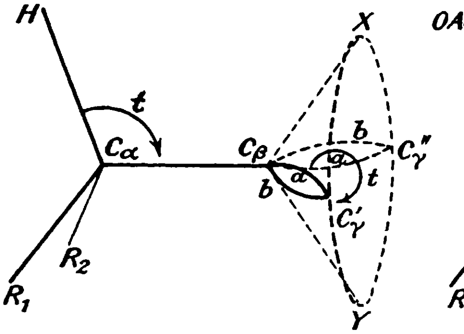
The theoretical object underlying this enquiry is concerned with the problem of whether or not *particular* electron pairs are mechanistically coupled in conjugated electromeric systems. This question has definite meaning in relation to observable phenomena only when considered in its application to systems possessing certain features of dissymmetry. In illustration we may consider a system composed of three carbon (or other octet-forming) atoms, C_α, C_β, and C_γ, with an unshared C_α-duplet (denoted by a " flying " bond-sign) and a $C_\beta C_\gamma$-double linking, the whole system being substituted in such a way that its dissymmetry is limited only by the $C_\beta C_\gamma$-double bond and the potential $C_\alpha C_\beta$-double bond :

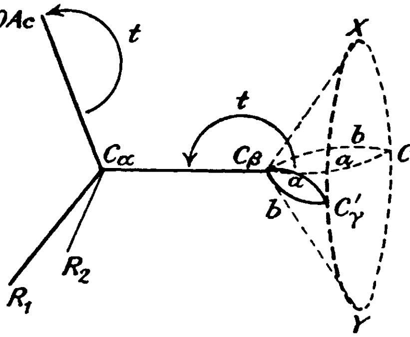


For simplicity we will imagine that dissymmetry through restricted intramolecular rotation is eliminated, *e.g.*, by a configuration in which the unshared C_α-electrons lie symmetrically about the plane of the nuclei of C_α, C_β, and C_γ, and we then enquire whether the unshared electron-pair possesses any dissymmetric property (possibly analogous to spin in a single electron) which can be thrown sufficiently out of balance by the asymmetric atomic environment to enable this electron-pair to establish unequal relationships with the two electron-duplets into which the double link divides on electromeric activation. Apparently the answer is in the negative, in the sense that, either an electron-pair does not contain such a property, or that, if it does, an asymmetric atomic environment is not sufficient to destroy the normal dissymmetric compensation; but before accepting this conclusion, it is necessary to show that it can be reconciled with the retention of optical activity in the conversion of linalyl acetate into terpinyl acetate, and to explain the contrast between this result and that obtained for the system now investigated.

In the above statement of the problem the propagation of asymmetry through the action of a dissymmetric influence on intramolecular rotations was assumed to be inoperative; but this effect is bound to intervene in greater or less degree in all actual examples. This may be called the asymmetric synthesis effect; for asymmetric synthesis depends on the production of a new asymmetric centre in the presence of a molecular electric field which not only is non-uniform but also gives a time-average, which, calculated over the totality of reaction periods for a large assembly of molecules, does not acquire any complete element of symmetry through intramolecular rotation because of the influences which dissymmetrically affect such rotations. It is clear, from reference to known results concerning asymmetric synthesis, that the effect of dissymmetrically influenced rotations in throwing the new asymmetric centre out of external compensation is usually small and frequently undetectable. The application to a prototropic system is indicated in formula (V), in which X and Y mark the intersections between the fixed plane $HC_\alpha C_\beta$ and the circular locus of C_γ, and *a* and *b* are imaginary labels applied to the two duplets, or potential duplets, of the $C_\beta C_\gamma$-double bond. Evidently the transport of asymmetry would be maximal were C_γ permanently held in such a position as C_γ', when either, if there is no Walden inversion at C_β, electrons *a*, or if there is, electrons *b*, will be preferentially coupled with the $C_\alpha H$-electrons in the tautomeric process *tt*. Since to each point on the semicircle $XC_\gamma'Y$ there corresponds a point on the other semicircle $YC_\gamma''X$ at which the respective relations of the *a* and of the *b* electrons to the $C_\alpha H$-electrons become interchanged, the propagation of asymmetry by the asymmetric synthesis effect is normally dependent on the fulfilment of the condition that, owing to the non-equivalence of the external electric fields due to R_1 and R_2, C_γ should spend a greater proportion of its time, or rather should be more likely to be found at a moment of reaction, in one of these semicircles than in the other. The case of an analogous anionotropic system is indicated in formula (VI). In conformity with known analogies, our results show that the propagation of asymmetry by this mechanism is normally very small. Turning now to the cyclic transformation of linalyl acetate, it becomes immediately evident that, since reaction can occur only when the molecule is suitably articulated for ring formation, as is indicated in formula (VII), C_γ is effectively fixed at a point corresponding to C_γ', not in the sense that C_γ necessarily spends more of its life there than elsewhere prior to reaction, but in the sense that C_γ is in, or very close to, that position for every molecule during the whole of its reaction period. A similar statement applies to the atoms C_δ and C_ϵ of the pentad system, and thus the whole effect on the transmission of asymmetry is as if intramolecular rotation were, not merely asymmetrically influenced, but wholly stopped, and stopped, moreover, with the groups in precisely those relative positions which make for a maximal propagation of asymmetry by the effect which has been correlated with asymmetric synthesis.

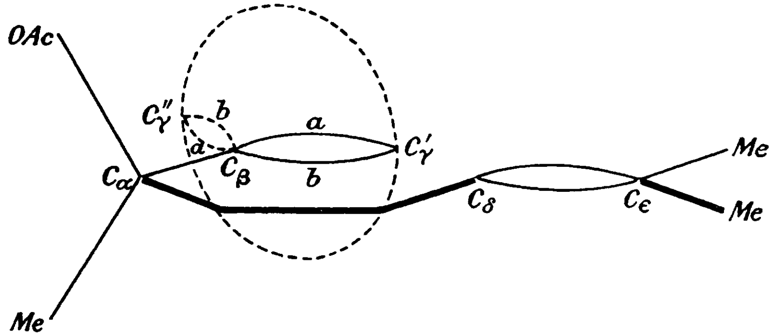
(V.)





(VI.)

(VII.)



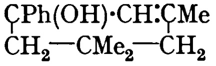
An explanatory statement concerning the synthetical experiments, and the investigations of tautomeric mobility and equilibrium, which formed a necessary preliminary to this investigation, will be found preceding the corresponding experimental descriptions in each of Sections 1—4 of the experimental portion. The details of the investigation outlined above are given in Section 5.

EXPERIMENTAL.

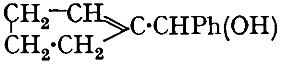
Section 1. *Exploratory Experiments on Anionotropic Systems Derived from α-Phenyl- and α-Ethyl-crotyl Alcohols.*

The anionotropic conversion of α-phenylallyl esters into cinnamyl esters is known to be quantitative (Burton and Ingold, J., 1928, 904), and, since a complete conversion would obviate the necessity for a difficult separation of isomerides in the projected experiment with optically active compounds, anionotropic systems containing an α-phenyl group, and the further substituents required to provide the necessary asymmetry, were first considered. Since, moreover, the presence in one tautomeride of *cis*- and *trans*-forms, both externally compensated, would complicate optical resolution, it was hoped to avoid this by including the triad system in a ring; and thus, as a preliminary to the preparation of the cyclic compound (VIII) from *iso*phorone and a Grignard reagent, the reaction was studied between

(VIII.)



$$\begin{array}{l}\text{CPh(OH)}\cdot\text{CH:CMe}\\ \text{CH}_2\text{—CMe}_2\text{—CH}_2\end{array}$$



$$\begin{array}{l}\text{CH}_2\text{—CH}\\ \text{CH}_2\cdot\text{CH}_2\end{array}\!\!>\text{C}\cdot\text{CHPh(OH)}$$

(IX.)

mesityl oxide and phenylmagnesium bromide. The resultant alcohol, $\text{CMePh(OH)}\cdot\text{CH:CMe}_2$, could not be esterified and readily underwent dehydration, behaviours which were attributed to its tertiary alcoholic character, and accordingly the analogous secondary alcohols CHPh(OH)·CH:CHMe and CHEt(OH)·CH:CHMe were subsequently examined. These compounds could be esterified, and from the former a hydrogen succinate was obtained, which could possibly have been used for optical resolution; but all the compounds of these series were without exception difficult to purify, and apparently were mixtures of geometrical isomerides. Thus the presence of a ring, of a secondary hydroxyl group, and of an aryl group attached to the carbinol carbon atom, are indicated to be essential conditions, so that although these experiments have not directly led to the production of a triad anionotropic system suitable for the investigation of asymmetric transference, they are regarded as suggesting that the system represented in (IX), or its *cyclo*hexene homologue, would have the required properties. We hope to pursue the subject along these lines.

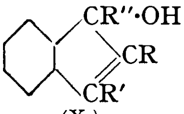
α-Phenyl-αγ-dimethylcrotyl Alcohol.—Freshly distilled mesityl oxide (49 g.) was added below 0° during 1·5 hours to a dry ethereal solution of the Grignard reagent prepared from redistilled bromobenzene (79 g.) and magnesium (12 g.). The stirring and cooling were continued for another 1·5 hours and the product was decomposed with ice and saturated ammonium chloride solution (600 c.c.). The product, a viscous oil, was undoubtedly the alcohol named, but it could not be purified for analysis because on attempted distillation it eliminated water (collected and identified) and yielded the hydrocarbon mentioned below. Attempts to prepare esters from the undistilled alcohol by treatment with acetic anhydride or with *p*-nitrobenzoyl chloride in pyridine solution also resulted in loss of water. The hydrocarbon was a highly refractive oil of distinctive odour and b. p. 94—96°/16 mm. (Found: C, 90·3; H, 8·7. $C_{12}H_{14}$ requires C, 91·1; H, 8·9%). We believe it to be *γ-phenyl-α-methylbutadiene* because on ozonolysis we obtained formaldehyde, benzoic acid, and a neutral substance responding to the iodoform test, and also because this constitution corresponds to the normal direction of dehydration. The substance is, however, probably identical with the hydrocarbon described by Klages (*Ber.*, 1904, **37**, 2305) as α-phenyl-αγγ-trimethylallene, because on oxidation with acid permanganate (*idem, ibid.*) it gave the products, acetophenone and benzoic acid, on which Klages based this constitution. We think it more probable, however, that the acid oxidation involves an unusual mechanism. On keeping, the hydrocarbon polymerises.

α-Phenylcrotyl Alcohol.—This was prepared in 81% yield by Burton's method (J., 1929, 455); it had b. p. 88—90°/1 mm. and $n_D^{18^\circ}$ 1·5412 (Found: C, 81·0; H, 7·9. Calc.: C, 81·0; H, 8·2%). The alcohol was heated with phthalic anhydride both alone and in pyridine for various periods, but in no case was any acidic product isolated other than phthalic acid. The neutral product on distillation yielded a highly refracting oil, b. p. 50—51°/0·4 mm., $n_D^{18^\circ}$ 1·6093 (Found: C, 91·1; H, 7·7. Calc.: C, 92·2; H, 7·8%), which was identified as α-phenylbutadiene by conversion into *cis*-3-phenyl-Δ^4-tetrahydrophthalic anhydride, needles m. p. 118—120° (Found: C, 73·3; H, 5·35. Calc.: C, 73·6; H, 5·3%), by condensation with maleic anhydride (Diels and Alder, *Ber.*, 1929, **62**, 2081). A less volatile by-product was obtained as a viscous oil, b. p. 160°/1 mm. [Found: C, 91·6; H, 7·8; *M* (Rast), 262, 275. Calc.: C, 92·2; H, 7·8%; *M*, 260], evidently the dimeride of phenylbutadiene to which Lebedev (*J. Russ. Phys. Chem. Soc.*, 1913, **45**, 1329; cf. Iwanow, *ibid.*, 1916, **48**, 1000) has assigned the constitution of 3-phenyl-1-styryl-Δ^4-*cyclo*hexene. It was characterised by the product formed on bromination in chloroform at − 10°. This substance, precipitated by the addition of light petroleum and crystallised either from benzene–light petroleum or from ethyl alcohol, had m. p. 226—227° (decomp.) (Found: Br, 47·5. Calc.: Br, 48·1%) (cf. Döbner and Staudinger, *Ber.*, 1903, **36**, 4325; Rüber, *Ber.*, 1902, **35**, 2697; von der Heide, *Ber.*, 1904, **37**, 2103). In an attempt to prepare the hydrogen succinate, the alcohol was heated with succinic anhydride at 100° for 30 hours and the product divided into a neutral and an acid fraction with ether and sodium carbonate. The acid portion consisted of succinic acid only, whilst the neutral, on crystallisation from light petroleum, gave needles, m. p. 72—80°, which after two further crystallisations from the same solvent and three from ethyl alcohol melted over the same temperature range. Possibly the m. p. indicates the original alcohol to be a mixture of *cis*- and *trans*-isomerides as analysis gave figures agreeing closely with those required for *α-phenylcrotyl succinate* [Found : C, 76·2; H, 6·9; *M* (Rast), 362, 361. $C_{24}H_{26}O_4$ requires C, 76·2; H, 6·9%; *M*, 378], and, in conformity with this constitution, treatment with ozone in chloroform solution at 0° followed by decomposition of the ozonide with water yielded benzoic acid and acetaldehyde, the latter being identified as its 2 : 4-dinitrophenylhydrazone (m. p. and mixed m. p. 157—158°). When the condensation with succinic anhydride was repeated with pyridine as solvent, the products were the above neutral ester (20%) and *α-phenylcrotyl hydrogen succinate* (80%), which separated from light petroleum in plates, m. p. 74—77° raised by numerous crystallisations from the same solvent to 76—78° [Found : C, 67·6; H, 6·5; *M* (Rast), 264, 249. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%; *M*, 248].

α-Ethylcrotyl Alcohol.—Prepared in the usual way from crotonaldehyde (dried by potassium carbonate and freshly distilled, b. p. 102·5—102·8°) and methylmagnesium bromide or iodide in ether, this substance had b. p. 135—142°/770 mm. and gave a liquid *p*-nitrobenzoate and hydrogen phthalate. Geometrical isomerides were therefore believed to be present, and in an attempt to separate them the material was divided into the following fractions (764·8 mm.) : (1) below 136·5°, 2%; (2) 136·7—136·9°, 4%; (3) 136·9—137·0°, 4%; (4) 137·0—137·1°, 30%; (5) 137·1°, 30%; (6) 137·1—137·2°, 20%. Fraction (5) on being heated with *p*-nitrobenzoyl chloride in pyridine solution at 100° for 4 hours gave *α-ethylcrotyl* p-*nitrobenzoate*, which crystallised with difficulty from light petroleum below — 20° as laminæ, m. p. 42—43·5° (Found : C, 62·4; H, 6·0; N, 5·8. $C_{13}H_{15}O_4N$ requires C, 62·6; H, 6·1; N, 5·6%). The 3 : 5-*dinitrobenzoate*, prepared similarly and crystallised repeatedly from light petroleum, formed laminæ, m. p. 47—48° (Found : C, 53·3; H, 4·8; N, 9·6. $C_{13}H_{14}O_6N_2$ requires C, 53·1; H, 4·8; N, 9·5%). The hydrogen succinate and hydrogen phthalate were also prepared in pyridine solution, but the former was a liquid, and the latter, a solid, m. p. 51—53°, could not be crystallised from the usual organic solvents, since either it was too soluble or it separated as an oil even below — 20°.

Section 2. *Exploratory Experiments on Anionotropic Systems Derived from 1-Hydroxyindene.*

The object of these experiments was to prepare an alcohol of the type (X). Indenones, which should yield alcohols of the required type on treatment with Grignard reagents, have been prepared by Rupe, Steiger, and Fiedler (*Ber.*, 1914, **47**, 66) from benzophenone, α-bromocarboxylic esters, and zinc, the Reformatsky product being subsequently dehydrated and cyclised with sulphuric acid. The method necessitates that the group R′ in the expected alcohol shall be an aryl group, because when aryl alphyl ketones, such as acetophenone, are used in the Reformatsky reaction, dehydration of the product gives an ethylene derivative of the wrong geometrical form for cyclisation. It follows that R″ must also be an aryl group, since otherwise the expected alcohol on esterification would yield a stable tautomeride incapable of conversion into a second form. We have prepared a compound of the formula indicated, with R′ = R″ = Ph and R = Me. Attempts to create asymmetry and provide a means of resolution by the introduction of an amino- or substituted amino-group were unsuccessful; attempted nitration of the alcohol yielded tars, and it was not found possible to replace bromobenzene by either *m*-bromoaniline or *p*-bromodimethylaniline in the Grignard reaction which yields the alcohol. In the latter experiments pyridine was tried as a solvent and this led to the observation of the direct alkylation (in our case, arylation) of this base by the Grignard reagent, a reaction recently reported (for the case of benzylation) by Bergmann and Rosenthal (*J. pr. Chem.*, 1932, **135**, 267) : evidently the reaction is general.



(X.)

3-*Phenyl*-2-*methylindenone.*—Ethyl β-hydroxy-ββ-diphenyl-α-methylpropionate was obtained in 70% yield from benzophenone (90 g.), ethyl α-bromopropionate (100 g.), and zinc (35 g.), with benzene (200 c.c.) as solvent (Rupe, Steiger, and Fiedler, *loc. cit.*). The benzene solution was washed with dilute sulphuric acid and evaporated, and the product was triturated with ethyl alcohol at 0°, dried, and dissolved (96 g.) in cold concentrated sulphuric acid (800 c.c.). 3-Phenyl-2-methylindenone, obtained (65 g.) by subsequently pouring the solution on ice, crystallised from ethyl alcohol in orange needles, m. p. 85°. The 2 : 4-*dinitrophenylhydrazone* separated from xylene in deep red needles, m. p. 259° (decomp.) (Found : N, 13·2. $C_{22}H_{16}O_4N_4$ requires N, 14·0%). The unsaturated ketone was reduced with hydrogen in the presence of a platinum oxide catalyst to 3-phenyl-2-methylindanone, an oil, the 2 : 4-*dinitrophenylhydrazone* of which crystallised from alcohol in red needles, m. p. 176—177° (Found : N, 13·7. $C_{22}H_{18}O_4N_4$ requires N, 14·0%).

1-*Hydroxy*-1 : 3-*diphenyl*-2-*methylindene*.—When an ethereal solution of the indenone was added to one of the Grignard reagent prepared from bromobenzene, a brilliant red coloration was produced, which became permanent when 1 mol. of indenone had been introduced, and on working up the product half the original indenone was recovered. By employing 2·5 mols. of Grignard reagent the whole of the indenone was caused to react, and the solution remained colourless. The product, on distillation at 1 mm. and crystallisation from light petroleum at below 0°, yielded prisms, m. p. 92° [Found : C, 88·4; H, 6·0; *M* (Rast), 296, 284. $C_{22}H_{18}O$ requires C, 88·6; H, 6·1%; *M*, 298]. This alcohol, 1-*hydroxy*-1 : 3-*diphenyl*-2-*methylindene*, on reduction with hydrogen in the presence of a platinum oxide catalyst gave the corresponding saturated alcohol, which on distillation lost water, forming 1 : 3-*diphenyl*-2-*methylindene*, a viscous oil, which subsequently solidified, and then crystallised from ethyl alcohol in plates, m. p. 108° [Found : C, 93·5; H, 6·4; *M* (Rast), 260, 262. $C_{22}H_{18}$ requires C, 93·6; H, 6·4%; *M*, 282]. Experiments with the object of introducing an aminophenyl, or dimethylaminophenyl, group by the action on the indenone of a basic Grignard compound in the presence of pyridine were unsuccessful. In one of the experiments, in which *p*-bromodimethylaniline was employed, a substance was isolated which crystallised from benzene in buff laminæ, m. p. 228—229°, gave an orange picrate, and appeared on analysis to be a p-*dimethylaminophenylpyridine* (Found : C, 78·4; H, 7·4; N, 13·8; *M*, 191, 207. $C_{13}H_{14}N_2$ requires C, 78·7; H, 7·1; N, 14·2%; *M*, 198).

Section 3. *Exploratory Experiments on Methyleneazomethine Prototropic Systems derived from 9-Aminofluorene.*

Attention was directed to the methyleneazomethine prototropic system partly on account of the ease with which optically active substances containing this system could be synthesised from previously resolved amines, and partly because the difficulty arising from the formation of geometrical isomerides may be avoided by separating and examining the tautomerides through their basic hydrolysis products, which contain the original asymmetric centres undisturbed. Originally it was hoped to obtain systems showing unidirectional interchange, and it was considered that such a result would be favoured by loading one end of the triad system with an *o*-diphenylene residue as in the example,


$\begin{matrix}C_6H_4\\|\\C_6H_4\end{matrix}\!\!>CH\cdot N{:}CPhMe$ (XI). α-Phenylethylidene-9-fluorenylamine was prepared and isomerised, but in both these reactions by-products were formed, and the example was therefore considered unsuitable for the purpose in view.

9-*Fluorenylamine*.—The method of reduction of fluorenoneoxime recommended by Schmidt and Stützel (*Ber.*, 1908, **41**, 1243) and Kuhn and Jacob (*Ber.*, 1925, **58**, 1438) yielded in our hands a considerable proportion of aceto-9-fluorenylamide, and a modified procedure was accordingly adopted. Zinc dust (70 g.) was added in small portions to a mechanically stirred solution of the oxime (40 g.) in glacial acetic acid (267 c.c.) and water (13 c.c.), the rate of addition being regulated so as to maintain the liquid in gentle ebullition under reflux. Heat was applied after the addition was complete in order to continue the boiling for a further hour, and then water (400 c.c.) was added. The solution was filtered, and the residue extracted with hot 5% acetic acid (200 c.c.). The combined acetic acid solutions on cooling yielded a small precipitate of aceto-9-fluorenylamide, and a further quantity of the same substance could be extracted from the zinc residues by means of ethyl acetate. The acetic acid solution was mixed with an equal volume of concentrated hydrochloric acid, and the mixture was kept at 0° for 12 hours. The 9-fluorenylamine hydrochloride thus precipitated was washed with cold concentrated hydrochloric acid, dried, and basified with ammonia, the amine being finally crystallised from light petroleum (yield 90%; m. p. 62—63°).

α-Phenylethylidene-9-fluorenylamine.—Equivalent quantities of 9-fluorenylamine and acetophenone were heated at 100° with a small amount of ethyl alcohol for 5 hours. During the reaction a green colour developed, which increased in intensity with rise of temperature and was destroyed by dilution with alcohol. It was noticed that a similar colour was formed in the cold when the amine and ketone were together dissolved in piperidine, and that it varied in intensity with temperature and concentration, and was destroyed by the access of air, in a manner reminiscent of free radicals. The condensation product was separated by crystallisation from alcohol into a more soluble fraction, *α-phenylethylidene-9-fluorenylamine*, which separated from light petroleum in needles, m. p. 156·5—157·5° (yield 50%) (Found : C, 89·2; H, 6·1; N, 5·1. $C_{21}H_{17}N$ requires C, 89·0; H, 6·1; N, 5·0%), and a less soluble portion (see below). The azomethine decomposes on heating above its m. p. or on keeping for many months. If uncontaminated with traces of fluorenylidenefluorenylamine (see below) it gives no coloration with alcoholic sodium ethoxide. With 20% hydrochloric acid a red-brown colour was formed, and on warming hydrolysis occurred with production of 9-fluorenylamine (identified as its benzoyl derivative, m. p. and mixed m. p. 260°) and acetophenone (identified as semicarbazone, m. p. and mixed m. p. 202°), thus showing that no tautomeric conversion had occurred during preparation. On attempting to prepare the azomethine at 140—145°, difluorenyl was formed, m. p. 239—240° (Found : C, 94·3; H, 5·5. Calc. : C, 94·5; H, 5·5%), and this substance was also obtained on heating fluorenylamine alone at 180°.

Fluorenylidene-9-fluorenylamine.—The less soluble fraction referred to in the preceding paragraph was further subdivided by the use of chloroform into a less soluble portion (m. p. 230—250°), which could not be crystallised and has not been identified, and a more soluble substance, *fluorenylidene-9-fluorenylamine*, which crystallised from light petroleum in minute sulphur-yellow needles, m. p. 175° (decomp.) (Found : C, 90·1, 90·4, 90·8; H, 4·9, 5·1, 4·9; N, 4·1, 4·4. $C_{26}H_{17}N$ requires C, 90·9; H, 5·0; N, 4·1%). The same substance was obtained by heating fluorenylamine with fluorenone either in alcohol at its b. p. for 7 hours, or without a solvent at 100° for 4 hours. The azomethine on solution in cold alcoholic alkali gives a deep blue-green colour, which increases in intensity on warming; but the base obtained by reduction with sodium amalgam and dilute acetic acid gives no colour under the same conditions. On hydrolysis with warm 20% hydrochloric acid the azomethine yielded 9-fluorenylamine (identified through the benzoyl derivative) and fluorenone (m. p. and mixed m. p. in each case). Fluorenylidene-9-fluorenylamine was also obtained as a by-product on repeating Schmidt and Stützel's preparation (*Ber.*, 1908, **41**, 1243) of benzylidene-9-fluorenylamine.

Isomerisation of α-Phenylethylidene-9-fluorenylamine.—The change was effected by warming the substance with 1·33*N*-alcoholic sodium ethoxide at 85° for 4 hours. The mixture of azomethines obtained on pouring into water could not be directly separated, and they were therefore hydrolysed with warm 20% hydrochloric acid. In addition to 9-fluorenylamine and acetophenone, identified as already described, the product contained fluorenone (m. p. and mixed m. p.) and α-phenylethylamine [isolated as picrate, m. p. 187°, and identified through the *benzoate*, m. p. 141° (Found : C, 74·2; H, 6·9; N, 5·8. $C_{15}H_{17}O_2N$ requires C, 74·0; H, 7·0; N, 5·8%)]. The hydrolysis product also contained a small quantity of a red substance, the amount of which increased on increasing the time allowed for isomerisation. Attempts to prepare fluorenylidene-α-phenylethylamine by condensation of α-phenylethylamine with either fluorenone or 9 : 9-dichlorofluorene were unfruitful.

Section 4. *Exploratory Experiments on Methyleneazomethine Prototropic Systems derived from Benzhydrylamine.*

The experiments of the preceding section having shown that systems derived from 9-fluorenylamine were insufficiently stable for the purpose in view, attention was directed to related derivatives of benzhydrylamine. It is shown below that these have the necessary stability and tautomeric mobility, although the examples examined, which are of the type

$$Ar^1Ar^2CH{\cdot}N{:}CAr^3R \rightleftharpoons Ar^1Ar^2C{:}N{\cdot}CHAr^3R$$

do not exhibit unidirectional change. However, it had become clear from contemporary work by Shoppee on methyleneazomethine equilibria in general (J., 1931, 1225, *et seq.*), that an effectively unidirectional conversion was likely to be extremely difficult to realise, and it therefore now became our aim not to find a system with a one-sided equilibrium, but to find one such that the basic hydrolysis products representing the equilibrium mixture could be formed and quantitatively separated without loss of optical activity. In the first of the several series of systems investigated, $Ar^1 = Ar^2 = Ar^3 = Ph$ and $R = H$. Later R was changed to Me in order to give one asymmetric centre, and Ar^1 was changed to p-MeC_6H_4 or p-ClC_6H_4 in order to provide the other, and in this way a system suitable for the proposed investigation was found. Incidentally, the opportunity was taken to measure the mobility and equilibrium of the system formulated below, which is completely balanced, excepting that a phenyl group at one end takes the place of a hydrogen atom at the other. The equilibrium proportions are indicated in parentheses :

$$(43\%)\ CHPh_2{\cdot}N{:}CPhH \rightleftharpoons CPh_2{:}N{\cdot}CH_2Ph\ (57\%).$$

Benzylidenebenzhydrylamine.—Benzhydrylamine was obtained (yield 90%) by a modification of Billon's method (*Compt. rend.*, 1923, **179**, 1054; 1926, **182**, 470). Benzophenoneoxime (15 g.) and sodium (17 g.; cut into thin strips) were placed in a large flask under reflux and ethyl alcohol (130 c.c.) was quickly added. After removal of any unchanged sodium, water (15 c.c.) was added, and the alcohol removed on a water-bath. After a further addition of water, the base was extracted with ether, dried with potassium carbonate, and distilled. Preparation by the method of Busch and Leefhelm (*J. pr. Chem.*, 1908, **77**, 14) was unsatisfactory in our hands, but we obtained it by Gabriel's method. *Phthalobenzhydrylimide* was obtained in yields up to 40% by boiling for 4 hours a xylene solution of benzhydryl bromide with either potassium phthalimide or phthalimide in potassium carbonate. The xylene was removed by distillation in steam, and the substituted imide was isolated by crystallisation from glacial acetic acid and thus obtained as needles, m. p. 149—150° (Found : C, 80·7; H, 4·8; N, 4·7. $C_{21}H_{15}O_2N$ requires C, 80·5; H, 4·8; N, 4·5%), identical with the sample prepared from phthalic anhydride and benzhydrylamine. Attempts to prepare this substance from benzhydryl bromide with omission of the xylene led to the production of a large amount of tetraphenylethylene. The imide was converted into benzhydrylamine in almost quantitative yield by Ing and Manske's method (J., 1926, 2348). Condensation of the amine with benzaldehyde proceeded with the evolution of heat in the absence of a solvent, and the product, crystallised from alcohol, had m. p. 101—102° (Michaelis, *Ber.*, 1893, **26**, 2169, records m. p. 98—99°). On hydrolysis with hydrochloric acid it yielded only benzhydrylamine and benzaldehyde.

Benzhydrylidenebenzylamine.—This was prepared by heating a mixture of benzophenone dichloride and benzylamine at 100° for one hour. Ether and water were added, and the excess of benzylamine in the dried ethereal extract was removed by extraction with 2% acetic acid. The extract was subsequently washed with aqueous sodium carbonate, dried with anhydrous sodium acetate, and evaporated. The azomethine, crystallised from light petroleum, had m. p. 60—61° (cf. Hantzsch and Hornbostel, *Ber.*, 1897, **30**, 3006), and on hydrolysis with warm dilute hydrochloric acid gave only benzophenone and benzylamine.

Interconversion of Benzylidenebenzhydrylamine and Benzhydrylidenebenzylamine.—The two azomethines undergo smooth interconversion on being heated at 85° in 3% ethyl-alcoholic solution containing sodium ethoxide in 1·33*N*-concentration. The reaction can be stopped at any moment by the addition of water, and the mixed azomethines can be readily isolated without loss as a strictly binary mixture. The velocity and equilibrium constants of the reaction were therefore determined by thermal analysis. The fusion diagram was based on the following observations :

Benzylidenebenzhydrylamine (%) ...	0·0	14·7	25·8	30·1	50·7	62·6	78·9	100·0
M. p.	60·9°	55·0°	51·3°	59·8°	77·9°	85·1°	92·7°	101·8°

The corresponding points lie on a two-branch curve indicating a eutectic mixture, m. p. 50°, containing 25% of benzylidenebenzhydrylamine. The dynamical observations are contained in the following table. The m. p.'s are uncorrected, but were obtained by the method and with the apparatus used for the construction of the m. p. diagram.

Benzylidenebenzhydrylamine = A; benzhydrylidenebenzylamine = B.

Time (mins.).	M. p.	A, %.	$k_1 + k_2$ (min.$^{-1}$).	Time (mins.).	M. p.	A, %.	$k_1 + k_2$ (min.$^{-1}$).	Time (mins.).	M. p.	A, %.	$k_1 + k_2$ (min.$^{-1}$).
Initially A.								Initially B.			
0	101·8°	100	—	200	72·3	43	—	0	60·9	0	—
1	92·5	79	0·460	300	72·6	43	—	1	52·3	20	0·508
3	82·1	57	0·468	430	72·5	43	—	4	67·5	38	0·538
5	75·1	47	0·531	600	72·4	43	—	255	72·4	43	—
20	72·5	43	—								

These results show that the equilibrium mixture contains 43% of benzylidenebenzhydrylamine, and that the unimolecular velocity coefficient ($k_1 + k_2$) is 0·50 min.$^{-1}$.

Benzhydrylidenebenzhydrylamine.—Condensation between benzhydrylamine and aromatic ketones could not be smoothly effected. For instance, with acetophenone at 180°, the principal product was an azomethine, m. p. 152°, which on hydrolysis with warm 2*N*-sulphuric acid yielded benzophenone (m. p. and mixed m. p.) and benzhydrylamine, identified as its benzoate (m. p. and mixed m. p. 158—159°). *Benzhydrylidenebenzhydrylamine* was obtained by heating benzhydrylamine (3·5 mols.) with benzophenone chloride (1 mol.) at 100° for ten minutes. The product was treated with ether and water, and the benzhydrylamine was precipitated from the separated ethereal solution by passage of carbon dioxide, the azomethine being then obtained by evaporation of the ether. It crystallised from alcohol, light petroleum, or glacial acetic acid in prisms, m. p. 152°, identical with the product of this m. p. obtained in the preceding experiment [Found : C, 89·3; H, 5·8; N, 4·1; *M* (Rast), 304, 326. $C_{26}H_{21}N$ requires C, 89·9; H, 6·1; N, 4·0%; *M*, 347].

Benzhydrylidene-α-phenylethylamine.—α-Phenylethylamine could not be condensed with benzophenone, but reacted rapidly (3·5 mols.) at 140° with benzophenone chloride (1 mol.), and at 100° reaction was complete in 3 hours. The ethereal solution of the product was washed successively with water, 2% acetic acid, and aqueous sodium hydrogen carbonate, dried with sodium acetate, and evaporated. The *benzylidene-α-phenylethylamine* separated from light petroleum in prisms, m. p. 52°, very soluble in the usual organic solvents (Found : C, 88·3; H, 6·6; N, 5·1. $C_{21}H_{19}N$ requires C, 88·4; H, 6·7; N, 4·9%).

p-*Methylbenzhydrylidene-α-phenylethylamine and its Isomerisation.*—*p*-Methylbenzophenone chloride, prepared by Overton's method (*Ber.*, 1893, **26**, 26), was condensed with α-phenylethylamine as described for the preceding example. The p-*methylbenzhydrylidene-α-phenylethylamine*, a very pale yellow-green oil, b. p. 198—201°/0·1 mm. (Found : C, 87·7; H, 7·1; N, 4·7. $C_{22}H_{21}N$ requires C, 88·2; H, 7·1; N, 4·7%), could not be crystallised, but on acid hydrolysis yielded only *p*-methylbenzophenone and α-phenylethylamine. Isomerisation in the presence of 1·33*N*-ethyl-alcoholic sodium ethoxide at 85° for 54 hours yielded a mixture of azomethines, which on acid hydrolysis gave, in addition to *p*-methylbenzophenone and α-phenylethylamine, only a small amount of acetophenone and a less volatile amine. This result was taken to indicate a small speed of isomerisation, the alternative explanation of a one-sided equilibrium being rendered improbable by analogy, and accordingly in the next series of experiments the methyl group was replaced by a chlorine substituent, because this is expected on theoretical grounds to increase the rate of prototropic change.

p-*Chlorobenzhydrylidene-α-phenylethylamine and its Isomerisation.*—*p*-Chlorobenzophenone, obtained (yield 86%) by Gomberg and Cone's method (*Ber.*, 1906, **39**, 3278), b. p. 322—325°, m. p. 72—73° after crystallisation from alcohol, was converted by Overton's method (*loc. cit.*) into the chloride, a colourless oil, b. p. 160°/1, 170°/2, 180°/3·5, 185—186°/4, 191—193°/13, 196—199°/16, 203—206°/20, 207—209°/22 mm. (Found : Cl, 39·0. Calc. : Cl, 39·2%). Condensation with α-phenylethylamine (3·5 mols.) was effected by heating the mixed reactants slowly to 100° and maintaining them at that temperature for 3 hours. The p-*chlorobenzhydrylidene-α-phenylethylamine* isolated in the usual way had b. p. 195—198°/0·05 mm. (Found : C, 78·9; H, 5·9; N, 4·7; Cl, 10·8. $C_{21}H_{18}NCl$ requires C, 78·8; H, 5·7; N, 4·4; Cl, 11·1%). On hydrolysis with warm dilute sulphuric acid it yielded only *p*-chlorobenzophenone (m. p. and mixed m. p.) and α-phenylethylamine, [identified as the benzoate (Found : C, 74·2; H, 6·9; N, 5·8. Calc. : C, 74·0; H, 7·0; N, 5·8%)]. When this azomethine was heated for 8 hours at 85° with 1·33*N*-ethyl-alcoholic sodium ethoxide a mixture of Schiff's bases was obtained, which, on acid hydrolysis, yielded a mixture of ketones from which acetophenone, identified as the semicarbazone (m. p. and mixed m. p.) was separated by distillation in steam. In other similar experiments *p*-chlorobenzhydrylamine was isolated as its hydrochloride, m. p. 304—305° (decomp.) (see Section 5). Semiquantitative experiments showed that the equilibrium mixture contained approximately equal proportions of the two isomerides, and that half-conversion to equilibrium occurred in about two days under the conditions stated. The change was unaccompanied by side reactions, even under prolonged treatment with the catalyst, and, since *p*-chlorobenzhydrylamine can readily be separated from α-phenylethylamine, the example appeared suitable for investigation with optically active materials.

Section 5. *Isomerisation of Optically Active* p-*Chlorobenzhydrylidene-α-phenylethylamine.*

Optical Resolution of α-Phenylethylamine.—In the earlier stages of this work the racemic base (Found for the benzoate : C, 74·2; H, 6·9; N, 5·8. Calc. : C, 74·0; H, 7·0; N, 5·8%)

was resolved with *d*-bromocamphorsulphonic acid by Kipping and Hunter's method (J., 1903, **83**, 1148). The success of the resolution was found to depend largely on the different rates of crystallisation of the salts of the *l*- and the *dl*-base. The former separated from approximately 0·5*M* aqueous solution at the ordinary temperature, in about 23% yield, as prismatic crystals during the first few hours, after which feathery crystals of the salt of the *dl*-base began to appear. The optically impure *d*-base was obtained from the mother-liquor. The first-mentioned salt, after two further crystallisations from water, had m. p. 206—207°, $[\alpha]_{5893}^{19\cdot5^\circ}$ 62·1°; $[\alpha]_{5461}^{19\cdot5}$ 77·6° ($c = 2\cdot455$ in water) (Kipping and Hunter record $[\alpha]_{5893}^{?}$ 62·8°). The free bases were liberated by the calculated amount of barium hydroxide, distilled in steam, collected in ether after the addition of potassium carbonate, and distilled under reduced pressure after drying over sodium. The optically pure *l*-base had b. p. 54°/1 mm. and $\alpha - 22\cdot92^\circ$ ($l = 50$ mm., $t = 16\cdot5^\circ$, $\lambda = 5461$), and its *benzoate* had m. p. 163—163·5° (Found : C, 73·7; H, 7·2; N, 5·9. $C_{15}H_{17}O_2N$ requires C, 74·0; H, 7·0; N, 5·8%). Optically impure *d*-base, α 5·6—6·3° ($l = 50$ mm., $t = 19^\circ$, $\lambda = 5461$), was used in some of the experiments described below. The optically pure *d*-base was prepared by resolution with malic acid as described by Lovèn (*J. pr. Chem.*, 1905, **72**, 310). The separated salt after one further crystallisation from water was optically pure and yielded an amine, b. p. 187°/760 mm., $\alpha + 22\cdot22^\circ$ ($l = 50$ mm., $t = 17^\circ$, $\lambda = 5461$).

Formation and Hydrolysis of Optically Active p-*Chlorobenzhydrylidene-α-phenylethylamine.*—These condensations were carried out as described for the *dl*-substance in Section 4. In the first series of experiments with optically impure *d*-base, the azomethine obtained had $[\alpha]_{5893}^{20^\circ} - 4\cdot32^\circ$, $[\alpha]_{5461}^{19^\circ} - 5\cdot58^\circ$ ($c = 5\cdot56$ in ethyl alcohol), and a peculiar phenomenon was observed on hydrolysing this and similar samples by means of mineral acid, and recovering the α-phenylethylamine as a check on possible racemisation during the reactions involved. It was found that the amine recovered by hydrolysis of the azomethine frequently had a higher rotatory power than the amine originally condensed with the ketone chloride, the amine converted into hydrochloride during this condensation having a correspondingly lower rotatory power. The process uniformly employed in hydrolysing optically active samples of azomethines was to warm them on the water-bath for 15 minutes with distilled 20% hydrochloric acid. After extraction of the ketones by ether, the solution was saturated with potassium carbonate and the basic product, extracted with ether and dried with potassium carbonate, was distilled under reduced pressure. Details of the condensations with partly resolved α-phenylethylamine are recorded in the following table, col. 1 of which indicates the chronological order of the observations. Cols. 2 and 3 record the weights of amine and chloride used for condensation, and cols. 4, 7, and 10 show the rotations (α for $l = 50$ mm., $\lambda = 5461$) of the original amine, the amine recovered from the hydrochloride formed in the condensation, and the amine recovered by hydrolysis of the azomethine, respectively. The temperatures corresponding to these observations are in cols. 5, 8, and 11. In some of the experiments optical uniformity was controlled by collecting the distilled base in several roughly equal fractions; the fractions polarimetrically examined are indicated in cols. 6, 9, and 12.

	Reactants (g.).		Original amine.			Amine from hydrochloride.			Amine from azomethine.		
No.	Amine.	Chloride.	α.	Temp.	Frac.	α.	Temp.	Frac.	α.	Temp.	Frac.
1	12	9	5·31°	19°	—	—	—	—	6·51°	20°	—
2	37	27	5·56	19	—	4·71°	20°	—	8·64	20	—
3	4	2·72	4·71	20	—	(4·81	20	—	4·81	20	—) *
4	10	5·4	4·71	20	—	3·56	20	—	7·69	20	—
5	12	8	5·22	—	—	5·02	20	1	5·52	21	1
						5·07	20	2	5·38	21	2
6	13·5	8	3·51	21	1	2·95	21·3	1	5·05	21·3	1
			3·50	21	3	2·93	21·3	3	5·02	21·7	2
7	7·5	5·4	4·34	—	—	4·30	21	1	4·65	21	2
						4·31	21	2			
						4·24	21	3			
8	11	6	4·14	21	—	4·14	—	1	4·48	20	3
						4·18	20·5	2	4·45	20·1	4
						4·13	—	3			
9	7	5	3·95	20·5	1	3·82	19·7	2	4·63	20	2
			3·97	20	2	3·88	20·5	3			
						3·84	19·8	4			

* The whole of the reaction mixture was hydrolysed in this experiment.

The phenomenon is shown particularly in observations 1, 2, 4, and 6, but it was not commented upon in the introduction because, as the other experiments show, it could not with certainty be reproduced. It is conceivably due to an asymmetric influence of an optically active solvent, the solvent in the present case being the optically active reagent present in excess; and the difficulty of reproduction may possibly be concerned with the circumstance that the reaction mixture becomes heterogeneous, the hydrochloride separating sometimes as crystals and sometimes as oily drops, which subsequently solidify. Unsuccessful attempts were made to trace the effect to an optically active impurity, and the result of one such test appears in the table, in that the amine of lower rotation recovered from Expt. 2 is used as the starting amine in Expts. 3 and 4. The phenomenon was, of course, not observed when optically pure α-phenylethylamine was employed in the condensation; for instance, a sample of *d*-base, having $\alpha + 22{\cdot}2°$, yielded an azomethine and a hydrochloride, from each of which an amine was recovered, having $\alpha + 22{\cdot}2°$ ($l = 50$ mm., $t = 17°$, $\lambda = 5461$). Similar results were obtained using the *l*-base, having $\alpha - 22{\cdot}9°$ ($l = 50$ mm., $t = 16{\cdot}5°$, $\lambda = 5461$). The azomethine, prepared from the *l*-amine, was dextrorotatory and had $[\alpha]^{18°}_{5893}$ 13·9°, $[\alpha]^{18°}_{5461}$ 19·4° (1·932 g. in 25 c.c. ethyl-alcoholic solution).

Isomerisation of Optically Active p-*Chlorobenzhydrylidene-α-phenylethylamine.*—The samples of optically active azomethine were treated for various lengths of time with boiling ethyl-alcoholic sodium ethoxide. The mixed azomethines were isolated and hydrolysed as usual, and in the first series of experiments the basic hydrolysis products were distilled below 100° under reduced pressure to remove α-phenylethylamine. The residual *p*-chlorobenzhydrylamine was converted into its hydrochloride, which was crystallised once from water. The samples of recovered *p*-chlorobenzhydrylamine showed no appreciable optical activity; *e.g.*, in an experiment in which the azomethine from optically pure *l*-amine was heated with ten parts of 1·45*N*-sodium ethoxide for 147·5 hours, the α-phenylethylamine recovered on hydrolysis had $\alpha - 17{\cdot}4°$ ($l = 50$ mm., $t = 18°$, $\lambda = 5461$), whilst the recovered *p*-chlorobenzhydrylamine had $\alpha - 0{\cdot}014°$ ($l = 100$ mm., $t = 18°$, $\lambda = 5893$) and $\alpha - 0{\cdot}01°$ ($l = 50$ mm., $t = 18°$, $\lambda = 5461$). In view of the possibility that the crystallisation of the hydrochloride in these experiments might be purifying the racemic salt from an accompanying optically active isomeride, a second series of experiments was carried out in which the basic hydrolysis products of the converted azomethine were separated by fractional distillation only. For instance, the azomethine prepared from pure *d*-α-phenylethylamine, $\alpha + 22{\cdot}22°$ ($l = 50$ mm., $t = 17°$, $\lambda = 5461$), after treatment with 1·33*N*-sodium ethoxide for 173 hours under the usual conditions and subsequent hydrolysis, gave α-phenylethylamine having b. p. 59°/0·2 mm. and $\alpha + 15{\cdot}2°$ ($l = 50$ mm., $t = 18°$, $\lambda = 5461$), and *p*-chlorobenzhydrylamine having b. p. 149—150°/0·1 mm. and $\alpha - 0{\cdot}018°$, and after a further distillation $\alpha - 0{\cdot}008°$ ($l = 50$ mm., $t = 18°$, $\lambda = 5461$). It is shown later that the distillation of optically active *p*-chlorobenzhydrylamine under these conditions causes no detectable racemisation.

p-*Chlorobenzhydrylamine.*—A solution of hydroxylamine hydrochloride (210 g.) in water (420 c.c.) was added gradually to a well-cooled mixture of a solution of *p*-chlorobenzophenone (200 g.) in ethyl alcohol (2000 c.c.) with a solution of potassium hydroxide (510 g.) in water (420 c.c.). After the mixture has been kept for 20 hours at room temperature, water (4 l.) was added, and the oxime (yield quantitative) was precipitated with carbon dioxide, collected, washed, and dried. Zinc dust (120 g.) was added in small portions to a hot, mechanically stirred mixture, under reflux, of the oxime (100 g.), acetic acid (500 c.c.), and water (50 c.c.), the vigorous reaction caused by each addition being allowed to subside before the next addition was made. After the whole of the zinc had been introduced, heating (steam-bath) was continued for a further hour, and the mixture was then diluted with water (300 c.c.), cooled, and filtered. The residue was washed with a small amount of hot dilute acetic acid, and the combined filtrates were mixed with 2 vols. of concentrated hydrochloric acid. The mixture was kept below 0° for 24 hours, and the amine hydrochloride was collected, washed with cold concentrated hydrochloric acid and with ether, and basified with ammonia. The p-*chlorobenzhydrylamine*, yield 60—70%, was obtained as an oil, b. p. 161°/0·9 mm., 188—189°/13 mm., 193°/14·5 mm. (Found : C, 71·5; H, 5·6; N, 6·1; Cl, 16·7. $C_{13}H_{12}NCl$ requires C, 71·7; H, 5·6; N, 6·4; Cl, 16·3%), which, unlike benzhydrylamine, does not absorb carbon dioxide. The benzoate has m. p. 163·5—164°, and the *hydrochloride*, which is sparingly soluble in cold concentrated hydrochloric acid and crystallises in needles from water or alcohol, had m. p. 304—305° (decomp.) (Found : C, 61·7; H, 5·2; N, 5·0; Cl, 28·1; ionic Cl, 13·4. $C_{13}H_{13}NCl_2$ requires C, 61·4; H, 5·2; N, 5·5; Cl, 27·9; ionic Cl, 13·9%). The ethereal washings from the hydrochloride obtained in the above preparation yielded an oil, which on rubbing with light petroleum deposited crystals; these on crystallisation from benzene gave slender needles, m. p. 132°, identified as *aceto*-p-*chlorobenzhydrylamide* by comparison with a specimen prepared from the amine in the usual way (Found : C, 69·7; H, 5·4; Cl, 13·7. $C_{15}H_{14}ONCl$ requires C, 69·3; H, 5·4; Cl, 13·7%).

Optical Resolution of p-*Chlorobenzhydrylamine.*—Resolution of the *dl*-base could not be effected through the d-α-*bromocamphor*-π-*sulphonate*, which crystallised from water or alcohol in rosettes of needles, m. p. 251° (Found : C, 52·5; H, 5·2. $C_{23}H_{27}O_4NClBrS$ requires C, 52·2; H, 5·2%). Partial separation was obtained by means of the malates, which crystallised during 5 days from a solution of the *dl*-base (113 g.) and *l*-malic acid (60 g.) in ethyl alcohol (3 l.). By further crystallisation from alcohol the salt was divided into a neutral l-*malate*, m. p. 171°, $[\alpha]_{5461}^{21^\circ}$ − 5·40° (1 g. in 25 c.c. methyl alcohol) (Found : C, 62·9; H, 5·3; N, 4·4. $C_{30}H_{30}O_5N_2Cl_2$ requires C, 63·2; H, 5·3; N, 4·9%), and a *hydrogen* l-*malate*, m. p. 160° (decomp.), $[\alpha]_{5461}^{19^\circ}$ + 0·46° (1 g. in 25 c.c. methyl alcohol) (Found : N, 3·8. $C_{17}H_{18}O_5NCl$ requires N, 4·0%). The free base recovered from the neutral salt had α + 0·43° (t = 19°), that from the acid salt had α − 0·20° (t = 19°), and that derived from the combined mother-liquors had α + 0·17° (t = 20°) (all l = 50 mm., λ = 5461). These bases could be distilled without perceptible racemisation at temperatures below 160° and reduced pressure. A better separation of the optical enantiomerides was obtained by the use of *d*-camphor-10-sulphonic acid (Loudon, this vol., p. 823). l-p-*Chlorobenzhydrylamine* d-*bromocamphor*-10-*sulphonate*, after 15 crystallisations from ethyl alcohol, had m. p. 218° (Found : C, 61·3; H, 6·2. $C_{23}H_{28}O_4NClS$ requires C, 61·5; H, 6·3%), and yielded *l*-*p*-chlorobenzhydrylamine having α − 1·95° (l = 50 mm., t = 19°, λ = 5461). Several further crystallisations of the salt raised the rotation of the base to α − 2·06° (l = 50 mm., t = 20°, λ = 4561), which even then was probably not quite optically pure. The resolution shows, however, that the rotation of this base is at least 200 times the error of determination of null rotations.

α-*Phenylethylidene*-p-*chlorobenzhydrylamine and its Isomerisation.*—The condensation between acetophenone and *p*-chlorobenzhydrylamine could not be effected at temperatures below those at which side reactions also take place, with the liberation of ionic chlorine. By determinations of the rate of appearance of ionic chlorine and of the proportions of azomethines simultaneously produced (see below), it was ascertained that a product containing a high proportion of azomethine could best be obtained by heating the reagents in an open flask at 140° for 66 hours. The azomethine could not be satisfactorily purified by distillation and by washing with dilute acetic acid, and the quantity present in the undistilled material obtained after removal of the reactants was therefore estimated. The crude reaction product was dissolved in ether, and washed successively with water, 3% acetic acid, and sodium hydrogen carbonate. The ethereal solution was dried with potassium carbonate and evaporated, and the residue was heated on the water-bath under a low pressure, in order to remove acetophenone. The weighed sample for analysis was first heated at 110°/0·1 mm. over phosphoric oxide, in order to remove the last traces of volatile impurities, and then dissolved in alcohol and precipitated with 2 : 4-dinitrophenylhydrazine in alcoholic sulphuric acid (Brady, J., 1931, 756). The hydrazone, which was quite pure (m. p. 239°), was collected (Gooch), washed with alcohol, dried at 140°, and weighed. An allowance was made for its solubility in alcohol, 0·0058 g./100 c.c. at 20°. The samples examined contained 69—77% of the *azomethine* [Found : C, 78·5; H, 5·5; Cl, 11·7; M (Rast), 278, 263. $C_{21}H_{18}NCl$ requires C, 78·9; H, 5·9; Cl, 10·8%; M, 278], and were contaminated with unchanged *p*-chlorobenzhydrylamine, since on acid hydrolysis in the usual manner this amine was obtained in excess of the quantity corresponding to the acetophenone. The azomethine was heated at 85° for 168 hours with 1·33*N*-ethyl-alcoholic sodium ethoxide, and the product was isolated and hydrolysed with hydrochloric acid as usual. The basic hydrolysis products on distillation yielded α-phenylethylamine, b. p. 80°/18 mm. (benzoate, m. p. and mixed m. p. 141°), and *p*-chlorobenzhydrylamine, b. p. 150°/0·12 mm. (Found : C, 71·1; H, 5·5; Cl, 15·8. Calc. : C, 71·7; H, 5·6; Cl, 16·3%), whilst the neutral products yielded *p*-chlorobenzophenone (m. p. and mixed m. p. 72—73°) and acetophenone. When the condensation between acetophenone and *p*-chlorobenzhydrylamine was repeated with the optically active form of that base, considerable racemisation occurred, so that less meaning attaches to the null rotation shown by the α-phenylethylamine obtained by isomerisation and subsequent hydrolysis than to the similar result of the analogous experiment with *p*-chlorobenzhydrylidene-α-phenylethylamine.

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