CXX.—*Symmetrical Triad Prototropic Systems. Part VI. The Effect of Substitution on Tautomeric Mobility and Equilibrium in the αγ-Diphenylpropene System.*

By CHARLES WILLIAM SHOPPEE.

IN Part IV of this series (J., 1929, 447) tautomeric interchange between the isomerides (I $\rightleftharpoons$ II) and (III $\rightleftharpoons$ IV) was shown to occur in the presence of a catalyst, and methods were described whereby the mobility and equilibrium of such systems could be determined. The present paper gives an account of the systems corresponding to (III $\rightleftharpoons$ IV) for a series of *p*-substituents : Me, Cl, Br, I, NMe_2, and $\overset{\oplus}{N}Me_2Et$.

$$\text{(I.)}\quad CH_2Ph{\cdot}CH{:}CH{\cdot}C_6H_4{\cdot}OMe \rightleftharpoons CHPh{:}CH{\cdot}CH_2{\cdot}C_6H_4{\cdot}OMe\quad\text{(II.)}$$

$$\underset{\text{(III.)}}{CH_2Ph{\cdot}C(CO_2Et){:}CH{\cdot}C_6H_4{\cdot}OMe} \rightleftharpoons$$

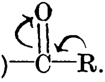
$$\underset{\text{(IV.)}}{CHPh{:}C(CO_2Et){\cdot}CH_2{\cdot}C_6H_4{\cdot}OMe}$$

Before the theoretical significance of the results is discussed, consideration must be given to certain fundamental principles underlying the relation of mobility and equilibrium to the structural features of a tautomeric system.

Substitution and Mobility.—In certain recent papers on prototropy and allied topics there has been a notable tendency to short-circuit the actual theory of the subject by referring to orientation in aromatic substitution as a practical criterion of the polar effects of groups and as, therefore, a direct analogy for their theoretically anticipated behaviour in relation to prototropic and other systems. Aromatic hydrogen-substitutions (even meta-) depend on the negativity of the field at the point of reaction, and the requisite electron availability may result either from the permanent *polarisation* of the molecule due to the electron repulsion (+ *I*) of a substituent, or from the molecular *polarisability* which is enhanced by the presence of a substituent containing unshared electrons, provided that a path exists for the propagation of electron displacements with covalency changes to the point of reaction (+ *T*) (compare Ingold and Shaw, J., 1927, 2923); these will be activating influences. Molecular polarisation resulting from a substituent possessing high electron-affinity (— *I*) will decrease electron-availability at the seat of reaction, and will be a deactivating influence, but polarisability arising from the presence of a substituent capable of sharing additional aromatic electrons and the existence of a free path for the electron transfer (— *T*) will not cause deactivation, because the displacements would lead to a recession of electrons from the seat of reaction, and for this there is no demand. On the other hand, prototropy depends on the positivity of the field at the seat of ionisation; the necessary electron-recession may arise from molecular polarisation due to the electron affinity (— *I*) of a substituent, or from molecular polarisability resulting from the presence of a substituent capable of sharing unshared electrons possessed by the system, provided that a path exists for the electron-transfer (— *T*); these will be facilitating influences. Molecular polarisation due to a substituent-repelling electron (+ *I*) will oppose the production of a positive field at the seat of ionisation, and hence will constitute a retarding influence; molecular polarisability, resulting from the presence of a substituent possessing unshared electrons and capable of sharing these with the system if a path for the electron transfer exists ($+T$), will not lead to electron displacements because such displacements would involve electron-accession to the seat of ionisation and for this there is no demand. In short, whereas

benzene hydrogen-substitution	is facilitated by effects $+I$ and $+T$
	is retarded by effect $-I$ only;
prototropy	is facilitated by effects $-I$ and $-T$
	is retarded by effect $+I$ only;

so that retardation of benzene hydrogen-substitution does not run parallel with facilitation of prototropy, and *vice versa*, unless *tautomeric effects of either sign* ($\pm T$) *are structurally impossible.* Burton and Ingold exemplified this (J., 1928, 904) by stating that $\overset{\oplus}{N}R_3$ and COR activate prototropy by different mechanisms ($-I$, and $-I-T$ respectively), but deactivate the benzene nucleus by the same mechanism ($-I$ only; $-T$ here being inoperative).

The $+T$ effect can enter into the consideration of prototropy only when an activating group of the $-I-T$ type is considered "piece-meal," and the $+T$ effect of one portion is treated as subtractable from the (greater) $-T$ effect of the other, as may be possible, for instance, for COR in (three-carbon) $\text{—}\overset{\overset{\large O}{\|}}{C}\text{—}R$. Since the order of $+T$ effects of R is $O^\ominus > NR_2 > OR > \text{Hals.} > Me$ (zero for the last member), that of the $-T$ effect for COR is $COMe > COHal. > CO_2R > CO{\cdot}NR_2 > CO{\cdot}O^\ominus$, and this is the order of facilitation of prototropy (Ingold, Shoppee, and Thorpe, J., 1926, 1477). The $-I$ effects of the same variants of the group COR are in the different order $COHal. > CO_2R > CO{\cdot}NR_2 > COMe > CO{\cdot}O^\ominus$ (Cooper and Ingold, J., 1927, 838), and this is all that enters into the theory of aromatic substitution ($-T$ is inoperative), and is the order of *m*-orientation. This point has been treated at some length because of Linstead's recent comments (J., 1929, 2498) on the apparent lack of agreement between the two series.

In continuation of previous investigations (J., 1929, 447, 1199), in which it was shown that systems of the forms

$$\text{(V.)}\quad CH_2Ph{\cdot}CH{:}CH{\cdot}C_6H_4R \underset{k_2}{\overset{k_1}{\rightleftharpoons}} CHPh{:}CH{\cdot}CH_2{\cdot}C_6H_4R \quad \text{(VI.)}$$

$$\underset{\text{(VII.)}}{CH_2Ph{\cdot}C(CO_2Et){:}CH{\cdot}C_6H_4R} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \underset{\text{(VIII.)}}{CHPh{:}C(CO_2Et){\cdot}CH_2{\cdot}C_6H_4R}$$

$$\text{(IX.)}\quad CH_2Ph{\cdot}N{:}CH{\cdot}C_6H_4R \underset{k_2}{\overset{k_1}{\rightleftharpoons}} CHPh{:}N{\cdot}CH_2{\cdot}C_6H_4R \quad \text{(X.)}$$

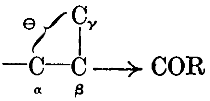
became mobile in the presence of sodium ethoxide, it has now been proved for the system (VII $\rightleftharpoons$ VIII)—system (IX $\rightleftharpoons$ X) is still being investigated—that the effect of R on the velocity of interconversion under constant conditions of temperature and catalysis is as follows (time units, hours)[*] :

Group R	NMe_2.	OMe.	I.	Br.	Cl.
$k_1 + k_2$	<<0·050	0·058	0·39	0·64	1·02
Moment	+1·39	−0·80	−1·25	−1·51	−1·56

The bottom row of the table contains the recorded values of the molecular electric moments of the compounds C_6H_5R in E.S.U. $\times 10^{-18}$, the attached sign indicating the polarity of R; the numbers are direct measures of the state of polarisation ($\pm I$) induced by R directly attached to the aromatic nucleus in a series of compounds such as those investigated. The parallelism between this measure of $- I$ and the mobility figures will be obvious.

None of the groups investigated is known to exert a $- T$ effect; if it had been capable of so doing, the parallelism would, of course, have failed (*e.g.*, COR, CN, NO_2). On the other hand, the groups tabulated are all structurally capable of $+ T$ effects, but this, as already explained, does not enter into prototropy (when the *whole* activating group is considered and not merely a part of it). The cases, therefore, differ from those studied by Kon and Linstead, which involve the $- T$ effect, and an alternative statement of the difference is that the systems examined by these investigators are pentad keto-enols, involving the common enolide ion $C{=}C{-}C{=}C{-}\overset{\ominus}{O}$.

Although the three-carbon systems here examined contain a group (carbethoxyl) normally capable of a $- T$ effect, the position of this (β-) is such that this effect cannot be propagated by tautomeric electron displacements to the seat of ionisation. A feeble $- I$ effect should, however, reach the ionising centre, and in addition to this, polar and steric disturbances due to the spatial proximity of the group are to be anticipated.



In this connexion, Linstead's argument (*loc. cit.*) that the preliminary ionic dissociation is unimolecular, whereas the final recombination of ions is bimolecular, and that this furnishes a basis for consideration of the mechanism of steric inhibition in prototropy,

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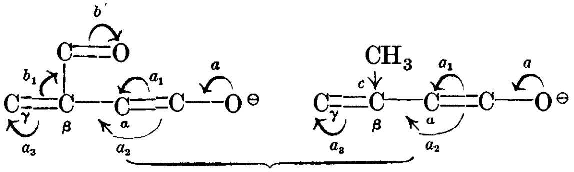
[*] The value for R = Me is of the same order as for R = OMe, but is not tabulated because the velocity coefficients were not good enough to give an accurate significance to their mean. Theoretically, Me should fit in between OMe and NMe_2.

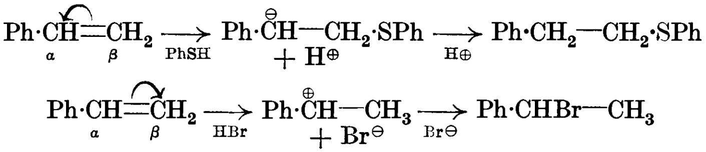
is unacceptable to the writer, who regards the catalyst as promoting ionic dissociation; from this point of view the dissociation must at least be bimolecular, for it is common knowledge that it depends on the catalyst (*e.g.*, OEt$^{\ominus}$ ion) as well as on the compound ionised.

Substitution and Equilibrium.—The general theory of the effect of substitution on equilibrium in three-carbon systems containing activating groups of the $-I-T$ type (pentad keto-enol and pentad cyano-imino systems) has already been given (Ingold, Shoppee, and Thorpe, *loc. cit.*; Ingold, *Ann. Reports*, 1927, 111; 1928, 118; Bennett, *ibid.*, 1929, 119), and is in excellent agreement with the available data, including the most recent results (Kon and Linstead, J., 1929, 1269; Kandiah and Linstead, *ibid.*, p. 2139); nevertheless, confusion has again arisen, through the application of the process previously described as short-circuiting. Ingold, Shoppee, and Thorpe discussed the effect of a β-carbethoxyl group and showed that it should lead ($-T$ effect) to predominance of the βγ-unsaturated form (*e.g.*, in the system citraconic ester–itaconic ester, the latter is the favoured phase). Linstead has concluded from this (*loc. cit.*) that the theory implies that a β-methyl group ($+I$ effect) should produce the opposite result, that is, a stable αβ-form, which is contrary to fact (Goldberg and Linstead, J., 1928, 2343). It cannot be too strongly insisted that the effect of $+I$ cannot be deduced by mechanical inversion of that of $-T$, and that all such short cuts involve unsound procedure, with the sole exceptions of that for $+I$ to $-I$, and its converse. In the case considered, the formulæ (XI) show the enolide ions in the critical stage immediately preceding their combination with a proton. The $-T$ effect of the β-carbethoxyl group (b, b_1) acts on the displaceable double-bond electrons, inhibiting a_3; the $+I$ effect of the β-methyl group (c) acts on the β-carbon atom, charging it negatively and directing the electrons away from a_2 into the alternative route a_1; since a_3 depends on initiation from a_2 (which in turn depends on a), the $+I$ effect (c) will also, indirectly, inhibit a_3. The facts (that the influences of β-methyl and β-carbethoxyl groups are qualitatively similar) are thus in complete agreement with the theory.



(XI.)

Reference is also necessary to another point raised by Linstead, namely, the effect of β- and γ-phenyl substituents. The polar effect of the phenyl group is represented by $\pm T$, that is, it is able to furnish either electron-accession to or electron-recession from an adjacent carbon atom, according to the sign of the field required at the seat of reaction. This duplex polar capacity of the phenyl group is manifested in its ability to activate both prototropy (these papers) and anionotropy (Burton and Ingold, *loc. cit.*), and to confer stability on free radicals (*idem, Proc. Leeds Phil. Soc.*, 1929, i, 421). Owing to its ambi-polar charge-distributing mechanism, phenyl tends to absorb the charge on C_α in either polarisation $\mathrm{Ph{-}C_\alpha{=}C_\beta}$, $\mathrm{Ph{-}C_\alpha{=}C_\beta}$, with the result, *inter alia*, that $\mathrm{Aryl{\cdot}CH{:}CH{\cdot}CH_2[H]}$ and $\mathrm{Aryl{\cdot}CH{:}CH{\cdot}CH_2[Br]}$ are stable tautomerides; to attribute such phenomena to a special " non-polar element of stability associated with conjugated systems " is to conceal their essentially polar nature. Probably the simplest illustration of the duplex polar functions of phenyl is that additions of either polar sign to styrene are uniformly initiated at C_β (Ingold, *Ann. Reports*, 1928, 146); for instance, addition of thiophenol to styrene occurs through the strongly basic (prone to co-ordinate) potential anion $\mathrm{PhS^{\ominus}}$, whereas in the addition of hydrogen bromide the relatively unstable potential kation (proton) commences the attack; addition is probably initiated by a partly polarised molecule, with subsequent liberation of the more stable ion of the additive complex :

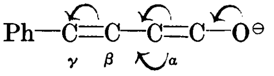


$$\mathrm{Ph{\cdot}\underset{\alpha}{CH}{=}\underset{\beta}{CH_2}} \xrightarrow[\mathrm{PhSH}]{} \mathrm{Ph{\cdot}\overset{\ominus}{C}H{-}CH_2{\cdot}SPh} \atop {+\,\mathrm{H^{\oplus}}} \xrightarrow[\mathrm{H^{\oplus}}]{} \mathrm{Ph{\cdot}CH_2{-}CH_2{\cdot}SPh}$$

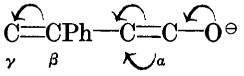
$$\mathrm{Ph{\cdot}\underset{\alpha}{CH}{=}\underset{\beta}{CH_2}} \xrightarrow[\mathrm{HBr}]{} \mathrm{Ph{\cdot}\overset{\oplus}{C}H{-}CH_3} \atop {+\,\mathrm{Br^{\ominus}}} \xrightarrow[\mathrm{Br^{\ominus}}]{} \mathrm{Ph{\cdot}CHBr{-}CH_3}$$

Now in the case of a γ-phenyl substituent, consideration of formula (XII), which shows the enolide ion in the critical stage preceding co-ordination of the proton, indicates that charge absorption will deactivate C_γ (like C_α in styrene) and the proton will combine at C_α;

(XII.)



$$\mathrm{Ph{-}\underset{\gamma}{C}{=}\underset{\beta}{C}{-}\underset{\alpha}{C}{=}C{-}O^{\ominus}}$$



$$\mathrm{\underset{\gamma}{C}{=}\underset{\beta}{C}Ph{-}\underset{\alpha}{C}{=}C{-}O^{\ominus}}$$

(XIII.)

the phenyl group could activate C_β towards a proton (like C_β in styrene), but the structure is such that C_β cannot take advantage of this tendency. In the case of a β-phenyl substituent (XIII), the phenyl group will activate C_γ towards a proton (like C_β in styrene) and this will favour combination at C_γ; the other effect, namely, deactivation of C_β (like C_α in styrene), does not enter into the problem for obvious reasons. Once again it is seen that the theory is adequate when properly applied.

In the experimental work here described, special attention has been given to the establishment of a small, but apparently real, anomaly, for which several explanations, none of which can as yet be proved, are possible. The system examined is the simple three-carbon system formulated on p. 970 (VII $\rightleftharpoons$ VIII), and the substituents R are of the forms normally characterised by the effects $-I$, $-I+T$, and $+I$. In the simple three-carbon system the anionic charge is necessarily borne by carbon and the essential consideration determining equilibrium pertains to the relative ionisability of the isomerides. Obviously the predominance of form (VII) (see equation) should diminish as the electron-affinity of R decreases (from $-I$ to $+I$). The table shows that, although the three kinds of groups are arranged in the right way, the members of the central group are inverted amongst themselves.

Type	$-I$	$-I+T$			$+I$
R	$\overset{\oplus}{N}Me_2Et$	OMe	Br	Cl	Me
VII (%)	>90	56·5	54·0	50·0	48·0

It is thought that this anomaly is probably related to the similar anomalies revealed in Tasman's results on the alkaline hydrolysis of phthalides (*Rec. trav. chim.*, 1927, **46**, 653) and in Kindler's on the alkaline saponification of benzoic esters (*Annalen*, 1926, **450**, 1), though in the latter two examples of aromatic side-chain reactivity the anomaly relates to the halogens only and does not include methoxyl. It is possible (but the point must await proof) that these apparent inversions are dependent on changes shown to be possible by Sidgwick's limiting-valency rule, and in a classification of groups relating to an aspect of aromatic substitution more closely analogous to prototropy than ordinary hydrogen substitution, a $-T$ effect has tentatively been ascribed to halogens (other than fluorine) in the presence of basic reagents.

EXPERIMENTAL.

Methyl Compounds.

α-p-*Methylbenzylcinnamic Acid* (formula as VIII).—*p*-Methylcinnamic acid was obtained in 70% yield by condensing *p*-tolualdehyde with malonic acid in pyridine solution in the presence of piperidine on the steam-bath. β-*p*-Tolylpropionic acid can be obtained from it by reduction with phosphorus and hydriodic acid (von Miller and Rohde, *Ber.*, 1890, **23**, 1898), but is contaminated with a considerable quantity of *p*-toluic acid : the use of 3% sodium amalgam (Krober, *ibid.*, p. 1053) gives a pure product.

Sodium β-*p*-tolylpropionate (45 g.), benzaldehyde (26 g.), and acetic anhydride (30 g.) were heated together at 160° for 10 hours, the melt was poured into a solution of crystallised sodium carbonate (150 g.) and extracted with ether, and the extract washed twice with 2*N*-sodium hydroxide. The ethereal extract contained a hydrocarbon, and the alkaline washings on acidification yielded 2 g. of *α*-p-*methylbenzylcinnamic acid*, which separated from dilute alcohol in long prisms, m. p. 181°, and instantly decolorised alkaline permanganate (as did also all the substituted cinnamic acids described later in this paper) (Found: C, 81·0; H, 6·4. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·3%). A further quantity was obtained from the sodium carbonate solution by acidification and fractional crystallisation of the product from dilute alcohol.

α-Benzyl-p-*methylcinnamic Acid* (formula as VII).—*p*-Tolualdehyde (48 g.), sodium β-phenylpropionate (69 g.), and acetic anhydride (49 g.) were heated at 150° for 8 hours and the procedure described above (sodium carbonate, 300 g.) was then followed. The sodium hydroxide washings on acidification yielded *α-benzyl*-p-*methylcinnamic acid* (2 g.), which separated from alcohol in needles, m. p. 200° (Found: C, 80·8; H, 6·3%). A further quantity (5 g.) was isolated from the sodium carbonate solution. The ethereal extract yielded 25·5 g. of *p*-tolualdehyde, b. p. 92—94°/13 mm., and a hydrocarbon.

The following m. p.'s are uncorrected, but were determined under identical conditions. The m. p.'s of artificial mixtures of the two preceding acids lie on a two-branch curve, the eutectic point of which corresponds to a mixture, m. p. 163°, containing 64·0% of α-*p*-methylbenzylcinnamic acid (A).

A, %	0·0	20·8	35·2	47·9	56·8	68·2	85·1	100·0
M. p.	200·0°	190·0°	181·5°	175·5°	168·0°	165·0°	173·5°	181·0°

Interconversion of the Ethyl Esters.—Preparation of the esters. These two esters, and those described subsequently, were obtained by the action of ethyl iodide upon the silver salts. *Ethyl α*-p-*methylbenzylcinnamate* (VIII; R = Me) is a colourless oil, b. p. 178—180°/1 mm., 197—198°/6 mm. (Found: C, 81·2; H, 7·2. $C_{19}H_{20}O_2$ requires C, 81·4; H, 7·2%). *Ethyl α-benzyl*-p-*methylcinnamate* (VII; R = Me) also is a colourless oil, b. p. 205—207°/7 mm., $n_D^{22°}$ 1·58415 (Found: C, 81·0; H, 7·4%).

Alkaline hydrolysis of the esters. The standard conditions and the method of isolation described for the methoxy-compounds (J., 1929, 447) were employed. As only a small quantity (0·01 g.) was used for a m. p. determination, the whole of the hydrolysis product was first melted, to ensure homogeneity. The ester (VII) gave 96% of unpurified acid, m. p. 200·0°, and the ester (VIII) gave 95%, m. p. 180·5° (the m. p.'s of the pure acids are 200·0° and 181·0°, respectively).

These results establish (*a*) that no interconversion of the isomerides takes place in the presence of hydroxide ions at 100° under the conditions given, and (*b*) that, since the yields are practically quantitative in both cases, and no impurities affecting the m. p.'s of the acids are introduced, hydrolysis and subsequent thermal analysis of the acids can be used to follow the interconversion of the esters.

Stability of the esters to heat. Redistillation of the esters and subsequent hydrolysis gave the same results. The esters were interconverted under the standard conditions (1·45*N*-alcoholic sodium ethoxide at 85°), the approach towards equilibrium being followed by hydrolysis under the standard conditions, and thermal analysis.

Isomeride used.	Time at 85° with NaOEt (hours).	M. p. of acids.	Isomeride VIII, %.	$k_1 + k_2$ (hour^{-1}).
VII	0·0	200·0°	0·0	—
	4·0	191·5	17·0	0·099
	10·5	179·0	39·0	0·132
	22·0	172·5	50·5	0·059
	31·0	172·0	51·0	0·065
	48·0	171·5	52·0	—
	68·0	171·5	52·0	—
VIII	48·0	171·5	52·0	—
	22·0	162·0	64·0	0·063
	2·0	176·0	89·0	0·115
	0·0	181·0	100·0	—

Equilibrium : VIII (52·0%) $\rightleftharpoons$ (48·0%) VII; $k_1 + k_2$ (mean) = 0·088 hr.$^{-1}$; $k_1/k_2 = 1·083$; $k_1 = 0·0046$; $k_2 = 0·0042$.

Chloro-compounds.

α-p-*Chlorobenzylcinnamic Acid* (formula as VIII).—*p*-Chlorocinnamic acid was obtained by condensing *p*-chlorobenzaldehyde (50 g.) and malonic acid (37 g.) with piperidine (5 c.c.) in pyridine (125 c.c.); it separated from alcohol in fine colourless needles (yield, 85%), m. p. 244—245°. Gabriel and Herzberg (*Ber.*, 1883, **16**, 2037) described it as yellow and indistinctly crystalline, m. p. 240—242°. The acid was rapidly reduced by 3% sodium amalgam at about 45° and gave a 75% yield of β-*p*-chlorophenylpropionic acid, m. p. 122° after crystallisation from dilute acetic acid.

Sodium β-*p*-chlorophenylpropionate (62 g.), benzaldehyde (32 g.), and acetic anhydride (34 g.) were heated at 160° for 8 hours and the melt was poured into a solution of 100 g. of crystallised sodium carbonate. After 12 hours, the white solid was filtered off, washed with ether, suspended in warm water, and agitated with hydrochloric acid. The precipitate was filtered off and twice crystallised from alcohol, α-p-*chlorobenzylcinnamic acid* being obtained in clusters of prisms (10 g.), m. p. 194·5° (Found : C, 70·0; H, 4·9. $C_{16}H_{13}O_2Cl$ requires C, 70·4; H, 4·8%).

Extraction of the aqueous liquor with ether gave a solution containing a chlorohydrocarbon and the above acid (4 g., removed by sodium hydroxide); on acidification, the sodium carbonate solution gave a further quantity of the acid (57 g., crude).

p-*Chloro-α-benzylcinnamic Acid* (formula as VII).—Sodium β-phenylpropionate (49 g.), *p*-chlorobenzaldehyde (40 g.), and acetic anhydride (35 g.) were heated together for 8 hours at 160°, and the melt was poured into a solution of 100 g. of crystallised sodium carbonate. The solution was extracted with ether and then acidified. The acid product separated from boiling alcohol in colourless needles, m. p. 163°, unchanged by further crystallisation (Found : C, 68·5, 68·6; H, 4·5%). These figures indicate that the product consisted of a mixture of the required acid (82%) and *p*-chlorocinnamic acid (18%); these could not be separated by fractional crystallisation. The mixed acids (10 g.) were treated with two successive quantities of sodium carbonate (50 c.c.; 2·2 g. Na_2CO_3 in 150 c.c. water), from which, by acidification of the two filtrates, three fractions, A, B, and C, were obtained.

Fraction A, recrystallised from alcohol, melted at 223—225° and consisted largely of *p*-chlorocinnamic acid.

Fractions B and C, recrystallised from alcohol, gave p-*chloro-α-benzylcinnamic acid* in colourless needles, m. p. 171·5° (Found : C, 70·3; H, 4·7%).

Mixtures of α-*p*-chlorobenzylcinnamic and *p*-chloro-α-benzylcinnamic acids melted as follows : A denotes the former acid.

A, %	0	20·6	31·6	36·2	42·0	45·9	50·3	53·6	69·7	100·0
M. p.	171·5°	162·5°	156·5°	153·5°	155·0°	161·0°	165·0°	168·0°	178·0°	194·5°

Interconversion of the Ethyl Esters.—Ethyl α-p-*chlorobenzylcinnamate* (VIII; R = Cl) has b. p. 197°/3 mm. and separates from ligroin (b. p. 40—60°) in prisms, m. p. 55° (Found : C, 71·8; H, 5·8. $C_{18}H_{17}O_2Cl$ requires C, 71·9; H, 5·7%). Ethyl *p*-chloro-α-benzylcinnamate (VII; R = Cl) has b. p. 208°/6 mm. (Found: C, 71·8; H, 5·7%).

Under standard conditions, hydrolysis of (VIII) afforded a quantitative yield of the corresponding acid, m. p. (crude) 194°, and (VII) gave a 99% yield of its acid, m. p. 170·5°.

The interconversion of the esters in 1·45*N*-alcoholic sodium ethoxide was observed in the manner described for the methoxy- and methyl compounds.

Isomeride used.	Time at 85° with NaOEt (hours).	M. p. of acids.	Isomeride VIII, %.	$k_1 + k_2$ (hours^{-1}).
VII	0	171·5°	0	—
	1·0	148·0*	41·0	(1·71)
	2·0	157·5	43·5	1·02
	16·0	165·0	50·0	—
VIII	32·0	165·0	50·0	—
	16·0	165·0	50·0	—
	8·0	165·0	50·0	—
	2·0	169·5	56·0	1·07
	1·0	176·5	67·0	1·08
	0·5	185·0	82·0	0·90
	0	194·5	100·0	—

* This is very near the eutectic.

Equilibrium : VIII (50·0%) $\rightleftharpoons$ VII (50·0%) ; $k_1 + k_2$ (mean) = 1·02 hr.$^{-1}$; $k_1/k_2 = 1{\cdot}00$; $k_1 = k_2 = 0{\cdot}51$.

Bromo-compounds.

α-p-*Bromobenzylcinnamic Acid* (formula as VIII).—Sodium β-*p*-bromophenylpropionate (Gabriel and Zimmermann, *Ber.*, 1880, **13**, 1683) (67 g.), benzaldehyde (28 g.), and acetic anhydride (33 g.) were heated together for 10 hours at 160° and the melt was submitted to the usual treatment. The sodium hydroxide washings of the ethereal extract yielded on acidification α-p-*bromobenzylcinnamic acid*, which crystallised from alcohol in prisms, m. p. 200° (Found : C, 60·8 ; H, 4·1. $C_{16}H_{13}O_2Br$ requires C, 60·5 ; H, 4·1%). The sodium carbonate liquor gave a large quantity of an acid, which was not investigated, and the ethereal extract contained a bromohydrocarbon.

p-*Bromo-α-benzylcinnamic Acid* (formula as VII).—*p*-Bromobenzaldehyde (Jackson and White, *Ber.*, 1878, **11**, 1023) (24 g.), sodium β-phenylpropionate (23 g.), and acetic anhydride (17 g.) were similarly treated. The sodium hydroxide washings gave p-*bromo-α-benzylcinnamic acid*, which was obtained in fine long needles, m. p. 193°, after several crystallisations from ethyl acetate–ligroin (Found : C, 60·5 ; H, 4·0%). The sodium carbonate solution yielded a large quantity of *p*-bromocinnamic acid, m. p. 257° after two crystallisations from boiling absolute alcohol (Found : C, 47·8 ; H, 3·0. Calc. for $C_9H_7O_2Br$: C, 47·6 ; H, 3·1%). The ethereal extract contained a bromohydrocarbon.

Mixtures of the two acids melted as follows : A denotes α-*p*-bromobenzylcinnamic acid :

A, %	0	15·9	35·1	57·2	68·0	86·2	100·0
M. p.	193·0°	186·0°	177·0°	178·0°	184·0°	192·5°	200·0°

Interconversion of the Ethyl Esters.—*Ethyl* α-p-*bromobenzylcinnamate* (VIII; R = Br) is a colourless oil, b. p. 200°/1 mm.

(Found : C, 62·6; H, 4·9. $C_{18}H_{17}O_2Br$ requires C, 62·6; H, 4·9%). Hydrolysis under the standard conditions affords the corresponding acid, m. p. 200° without purification, in 98% yield. *Ethyl* p-*bromo-α-benzylcinnamate* (VII; R = Br) is a colourless oil, b. p. 200°/3 mm. (Found : C, 62·6; H, 5·0%); on hydrolysis under the standard conditions it gives the corresponding acid, m. p. 193° without purification, in 98·5% yield.

The esters were interconverted under the standard conditions and the process was followed by hydrolysis (standard conditions) and thermal analysis. In the case marked with an asterisk 0·45 g. of ester was used.

Isomeride used.	Time at 85° with NaOEt (hours).	M. p. of acids.	Isomeride VIII, %.	$k_1 + k_2$ (hour^{-1}).
VII	0	193·0°	0	—
	2·0	178·0	33·0	0·631
	24·0	172·0	46·0	—
VIII	36·0	172·0	46·0	—
	24·0	172·0	46·0	—
	12·0	171·5	46·5	(0·375)
	4·8	172·5	48·0	0·671
	2·0	181·0	62·5	0·592
	1·0*	185·5	71·0	0·659
	0	200·0	100·0	—

Equilibrium : VIII (46·0%) $\rightleftharpoons$ VII (54·0%); $k_1 + k_2$ (mean) = 0·64 hr.$^{-1}$; $k_1/k_2 = 0{\cdot}852$; $k_1 = 0{\cdot}30$; $k_2 = 0{\cdot}34$.

Iodo-compounds.

*α-*p*-Iodobenzylcinnamic Acid* (formula as VIII).—*p*-Iodobenzaldehyde was prepared by oxidation of *p*-iodobenzyl bromide with copper nitrate solution and had m. p. 76°. The aldehyde (20 g.) and malonic acid (9 g.) were condensed in pyridine solution with piperidine (2 c.c.); the *p*-iodocinnamic acid obtained separated from boiling alcohol in colourless prismatic needles, m. p. 264° (decomp.) (Gabriel and Herzberg, *Ber.*, 1883, **16**, 2039, describe the acid as yellow and incompletely crystalline, decomposing at 255° without melting) (Found : C, 39·4; H, 2·6. Calc. for $C_9H_7O_2I$: C, 39·4; H, 2·6%).

Gabriel and Herzberg obtained the dihydro-acid by reduction with phosphorus and hydriodic acid for a short period (undefined). Little reduction takes place under these conditions, and the use of sodium amalgam in alkaline solution at 45° yields only β-phenylpropionic acid. β-*p*-Iodophenylpropionic acid is best obtained by iodination of β-phenylpropionic acid in 50% acetic acid with a 10% excess of iodine monochloride. The mixture, which becomes hot, is kept on the steam-bath for ½ hour. After 12 hours, the product is dissolved in ether and the solution is washed with aqueous sodium thiosulphate and with water, dried, and evaporated. A large part of the residual oil solidifies after 48 hours; the acid is drained and then crystallised from 40% acetic acid; m. p. 139°. Yield, 14 g. from 50 g. of β-phenylpropionic acid.

Sodium β-*p*-iodophenylpropionate (34·5 g.), benzaldehyde (12·5 g.), and acetic anhydride (13 g.) were heated at 150—155° for 6 hours and the melt was poured into a solution of sodium carbonate (50 g.). After 12 hours, the solid (sodium salt of the required acid) was removed and washed with ether; the filtrate was extracted with ether. The extract, after being washed with *N*-sodium hydroxide, contained an iodohydrocarbon. The sodium carbonate solution, acidified with 2*N*-hydrochloric acid at 0°, gave α-p-*iodobenzylcinnamic acid* (5 g.), m. p. 219·5° after crystallisation from glacial acetic acid (Found : C, 52·5; H, 3·5. $C_{16}H_{13}O_2I$ requires C, 52·7; H, 3·6%). The sodium hydroxide washings also gave a small quantity of this acid.

p-*Iodo*-α-*benzylcinnamic Acid* (formula as VII).—*p*-Iodobenzaldehyde (46 g.), sodium β-phenylpropionate (34 g.), and acetic anhydride (25 g.) were heated together at 170—180° for 7 hours; the melt was poured into excess of sodium carbonate solution and treated as in the preceding case. The ethereal extract and the sodium hydroxide washings contained an iodohydrocarbon and β-phenylpropionic acid respectively.

The solid initially precipitated by the sodium carbonate was suspended in 2*N*-hydrochloric acid at 40—45° and stirred for ½ hour; the product was a mixture of *p*-iodocinnamic acid (2 parts) and *p*-iodo-α-benzylcinnamic acid (1 part), which could not be separated by fractional crystallisation (Found : C, 44·7, 44·8; H, 3·0, 3·1%). The mixture (10 g.) was converted through the acid chlorides (by thionyl chloride) into the ethyl esters, which were distilled. The lower fraction obtained (5 g.), b. p. 175—180°/5 mm., mainly at 177°/5 mm., crystallised readily, and separated from ice-cold ligroin (b. p. 40—60°) in long needles, m. p. 37—37·5°, consisting of ethyl *p*-iodocinnamate, identical with a specimen prepared from synthetic *p*-iodocinnamic acid. The second fraction (3·5 g.), b. p. 180—230°/5 mm., partly solidified; after being drained, the solid was crystallised from ligroin (b. p. 40—60°), giving *ethyl* p-*iodo*-α-*benzylcinnamate*, m. p. 53·5° (Found : C, 54·9; H, 4·4. $C_{18}H_{17}O_2I$ requires C, 55·1; H, 4·4%). On hydrolysis under the standard conditions, this ester gave pure *p*-iodo-α-benzylcinnamic acid, m. p. 232° after crystallisation from alcohol (Found: C, 52·3; H, 3·7%).

On account of the decomposition which occurred in the later stages of the foregoing distillation, the following separation is to be preferred. The mixed acids (25 g.) were treated with a solution of

2·2 g. of sodium carbonate at 100° and the hot liquid was filtered. The filtrate gave a granular precipitate (A) on acidification. Repetition of the process afforded a flocculent precipitate (B). Recrystallisation of (A) and (B) from alcohol gave *p*-iodocinnamic acid (13 g.) and *p*-iodo-α-benzylcinnamic acid (7 g.), m. p. 229—230°, respectively. The sodium hydroxide washings (above) also gave a very small quantity of the latter acid.

Mixtures of α-*p*-iodobenzylcinnamic acid (C) and *p*-iodo-α-benzylcinnamic acid melted as follows :

C, %	0	19·0	39·0	47·2	57·0	61·0	66·4	79·1	100·0
M. p.	232·0°	222·0°	210·5°	206·5°	201·5°	199·0°	204·0°	210·0°	219·5°

Interconversion of the Ethyl Esters.—Ethyl α-p-*iodobenzylcinnamate* (VIII; R = I) has b. p. 212—214°/2 mm., and melts at 46·5° after crystallisation from ligroin (b. p. 40—60°) (Found : C, 55·0; H, 4·4. $C_{18}H_{17}O_2I$ requires C, 55·1; H, 4·4%). Ethyl *p*-iodo-α-benzylcinnamate (VII; R = I), m. p. 53·5°, prepared from the silver salt was identical with the ester described above.

Hydrolysis. The esters (VII) and (VIII) gave quantitative yields of the respective acids, m. p.'s 232° and 219°, on hydrolysis with aqueous-alcoholic alkali (standard conditions). They are hydrolysed with extraordinary ease by acids, even by cold 2*N*-acetic acid.

Action of sodium ethoxide. Treatment of either ester with 1·45*N*-sodium ethoxide at 85° caused conversion into the other, since, by hydrolysis under the standard conditions and fractional crystallisation of the product from acetic acid, both acids were obtained. Owing to the presence of impurities produced by a secondary reaction, probably involving the iodine atom, the composition of the equilibrium mixture of the acids could not be determined from the melting-point diagram. The esters could not be distilled owing to hydrolysis taking place, and the following procedure was therefore adopted.

Preliminary experiments indicated that the ester (VII) was more prone to decomposition than the isomeride (VIII); and that the quantity of the new isomeride produced during very short periods of interconversion ($\frac{1}{4}$—$\frac{1}{2}$ hour) was insufficient to give, after hydrolysis, a saturated solution of the corresponding acid in ethyl acetate at 0°. To minimise errors due to the secondary reaction, the ester (VIII) was employed : it was treated with 1·45*N*-sodium ethoxide at 85°, the product hydrolysed under the standard conditions, and the acids isolated in the usual manner. A known weight (0·20 g.) of the cooled fused acids was dissolved in ethyl acetate, and the solution concentrated by evaporation in a graduated test-tube as far as was possible without separation of solid. The solution, its volume having been noted, was kept for 16 hours in the ice-chest and the crystalline product was then collected and weighed. Its composition was determined by thermal analysis (the mixtures showing binary character), and a correction made for the solubility of each isomeride in a saturated ethyl acetate solution of the other at 0°.

Time at 85° with NaOEt (hrs.).	Wt. crude acids (g.).	Wt. cryst. acids (g.).	Vol. EtAc (c.c.).	M. p. of cryst. acids.	% Isomeride VII.	% VII, corr. for solubility.	$k_1 + k_2$ (hr.$^{-1}$).
2	0·1990	0·1428	1·7	203·0°*	35·0	33·7	0·47
3	0·1994	0·1425	2·0	200·0*	38·5	36·8	0·37
4	0·1998	0·1522	2·0	200·5†	42·0	40·2	0·33

* Depressed by trace of acid (VII). † Elevated by trace of acid (VII).

Owing to the secondary reaction, the equilibrium point could not be ascertained. The velocity coefficients are calculated on the basis of the assumed equilibrium VIII (45%) $\rightleftharpoons$ (55%) VII, which is approximately that found for the bromo-esters.

The solubility of α-*p*-iodobenzylcinnamic acid (0·00592 g./c.c.) and of *p*-iodo-α-benzylcinnamic acid (0·00157 g./c.c.) in a saturated ethyl acetate solution of the other was determined by saturating ethyl acetate with both acids, keeping the solution at 0° for 16 hours, and evaporating a known volume of the solvent; the composition of the residue was found by thermal analysis.

Dimethylamino-compounds.

α-p-*Dimethylaminobenzylcinnamic Acid* (formula as VIII).—*p*-Dimethylaminobenzaldehyde (300 g.) and malonic acid (213 g.) were heated in pyridine (500 c.c.) in the presence of piperidine (20 c.c.) for some hours on the steam-bath. When the mixture ceased to evolve carbon dioxide, it was poured into a large volume of ice-water containing 500 c.c. of glacial acetic acid. The precipitate crystallised from boiling alcohol in yellow plates (335 g.), m. p. 225° (vig. decomp.). Weil (*Monatsh.*, 1908, **29**, 899) gives m. p. 216° (decomp.).

The foregoing acid (250 g.) was reduced with 3% sodium amalgam at 45—50°, and the product isolated by acidification with hydrochloric acid (Congo) and treatment with saturated sodium acetate solution. The β-*p*-dimethylaminophenylpropionic acid formed colourless prisms, m. p. 106°, from dilute alcohol: a further quantity was obtained by extraction of the mother-liquor with ether (total yield, 140 g.). The sodium salt (120 g.), benzaldehyde (60 g.), and acetic anhydride (66 g.) were heated together for 9 hours while the temperature rose from 160° to 180°, the melt was then poured into an excess of sodium carbonate solution, and the mixture was extracted with ether after standing. The aqueous liquid, by acidification and treatment with sodium acetate solution with mechanical stirring, afforded α-p-*dimethylaminobenzylcinnamic acid* (24 g.), m. p. 146° after repeated crystallisation from methyl alcohol (Found: C, 76·7; H, 6·7. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8%). A little more was obtained by acidification of the sodium hydroxide washings of the ethereal extract; the latter contained a small quantity of the *p*-dimethylamino-base.

p-*Dimethylamino*-α-*benzylcinnamic Acid* (as VII).—Condensation of potassium β-phenylpropionate (63 g.), *p*-dimethylaminobenzaldehyde (50 g.), and acetic anhydride (38 g.) at 160—170° for 9 hours, and isolation of that portion of the product soluble in hydrochloric acid but precipitated by sodium acetate, furnished an acid, m. p. 232° (decomp.) after crystallisation from methyl alcohol. The quantity was insufficient for analysis, but the following observations indicate that the acid was *p*-dimethylamino-α-benzylcinnamic acid.

α-*p*-Dimethylaminobenzylcinnamic acid was heated with sodium ethoxide solution under the standard conditions for 48 hours; the product was isolated by acidification and addition of sodium acetate. Crystallisation from methyl alcohol yielded α-*p*-dimethylaminobenzylcinnamic acid, m. p. 144°, and a less soluble acid, m. p. 230° (decomp.) after repeated crystallisation (m. p. of a mixture with the above acid, 229° decomp.). Ozonolysis in glacial acetic acid solution yielded an acid, m. p. above 200° (*p*-dimethylaminobenzoic acid ?), in quantity insufficient for complete purification; benzoic acid was not obtained.

α-*p*-Dimethylaminobenzyl- and *p*-dimethylamino-α-benzyl-cinnamic acids do not yield a m. p.–composition diagram of the usual form, probably owing to decomposition of the latter acid. Since thermal analysis could not be employed to estimate the composition of mixtures of the acids, the ethyl esters were investigated. *Ethyl* α-p-*dimethylaminobenzylcinnamate* (VIII; R = NMe_2) was obtained from the silver salt of the corresponding acid by treatment with 1 mol. of ethyl iodide in an equal volume of chloroform; it separated from ligroin (b. p. 40—60°) in rectangular prisms, m. p. 62·5° (Found: C, 77·6; H, 7·4. $C_{20}H_{23}O_2N$ requires C, 77·6; H, 7·5%). On hydrolysis under the standard conditions it gave the corresponding acid, m. p. 146° without purification. As partial hydrolysis during isolation of the mixed esters obtained by equilibration of this ester with 1·45*N*-sodium ethoxide could not be prevented, the preparation of the isomeric ester (VII) and the plotting of a m. p.–composition diagram for the esters were not proceeded with.

The conversion of the ester (VIII) into its isomeride in the presence of 1·45*N*-sodium ethoxide could be proved qualitatively only after 65 hours' treatment: from 0·50 g. of the ester (VIII), 0·02 g. of *p*-dimethylamino-α-benzylcinnamic acid, m. p. 229—230°, was isolated after hydrolysis under the standard conditions; the remainder (0·38 g.) consisted of the more soluble isomeric acid. These experiments indicate a minimum conversion of about 4% in 65 hours; in the absence of knowledge relating to the position of equilibrium, and assuming this to be of the same order as that found for the methoxy-compounds (J., 1928, 447), it appears that the mobility of the dimethylamino-compounds is much smaller than that of the methoxy-compounds.

Dimethylethylammonium Compounds.

Internal Salt of p-β-*Carboxy-γ-phenylallylphenyldimethylethylammonium Hydroxide.*—Silver α-*p*-dimethylaminobenzylcinnamate was treated with an excess of ethyl iodide on the steam-bath for ½ hour. The mixture of crystalline solid and silver iodide produced was extracted with much boiling acetone. The extract, on addition of ligroin, cooling, and stirring, gave the *molecular compound* of *p*-β-carbethoxy-γ-phenylallylphenyldimethylethylammonium iodide and silver iodide (1 mol.) in colourless pearly plates, m. p. 155—156° (Found: C, 38·4; H, 4·0; ionic I, 18·5, 18·6; AgI, 34·3. $C_{22}H_{28}O_2NI,AgI$ requires C, 37·8; H, 4·0; ionic I, 18·1; AgI, 33·6%). By treatment with silver hydroxide in warm aqueous acetone solution, filtration, evaporation, and addition of alcoholic picric acid, p-β-*carbethoxy-γ-phenylallylphenyldimethylethylammonium picrate*, m. p. 130° after crystallisation from methyl alcohol, was obtained (Found: C, 58·6; H, 5·2. $C_{28}H_{30}O_9N_4$ requires C, 59·3; H, 5·3%).

The molecular compound was boiled in aqueous-acetone solution with silver chloride, and the filtered solution evaporated; prolonged desiccation yielded a resinous solid, which could not be purified. This was probably the betaine, since it contained no ionisable halogen and gave with sodium picrate a sodium salt-picrate, m. p. 270° (decomp.). A satisfactory analysis could not be obtained, but ozonolysis in glacial acetic acid solution gave an almost quantitative yield of benzoic acid:

$$\overset{\oplus}{N}Me_2Et\cdot C_6H_4\cdot CH_2\cdot C(CO_2{}^{\ominus})\overset{\vdots}{\underset{\vdots}{=}}CH\cdot C_6H_5 \xrightarrow{O_3} CO_2H\cdot C_6H_5$$

The resinous solid (0·50 g.) was treated with a solution of 0·54 g. of sodium in 15 c.c. of ethyl alcohol (giving an active ethoxide-ion concentration equal to that of 1·45*N*-sodium ethoxide) for 24 hours at 85°. The cooled product was poured into water, neutralised with hydrochloric acid, and evaporated to dryness. The residue was extracted with successive small quantities of hot glacial acetic acid and the combined extracts were treated with ozonised oxygen. From the ether-soluble portion of the decomposition products, only a trace of benzoic acid (a few mg.) could be isolated. The water-soluble portion yielded no identifiable substance.

Attempts were made to synthesise the pairs of isomerides in which the *p*-substituents were NHAc or CN. *p*-Cyanobenzaldehyde, m. p. 100°, prepared from *p*-cyanobenzyl bromide, condensed with sodium β-phenylpropionate and acetic anhydride at 160° to yield almost entirely *p*-cyanocinnamic acid, m. p. 254° after crystallisation from nitrobenzene (Found: C, 68·5; H, 3·6. Calc. for $C_{10}H_7O_2N$: C, 69·4; H, 4·0%). *p*-Acetamidobenzaldehyde, sodium β-phenylpropionate, and acetic anhydride at 180—200° gave an *acid*, m. p. 267° after repeated crystallisation from nitrobenzene, to which no formula has been assigned (Found: C, 71·2, 71·3; H, 5·5, 5·8; N, 5·7, 5·7%). *p*-Acetamidocinnamic acid, yellow prismatic needles, m. p. 261° (decomp.), was readily obtained in 78% yield from *p*-acetamidobenzaldehyde and malonic acid in the presence of piperidine. Reduction of this with sodium amalgam at 40—45° in the presence of carbon dioxide afforded β-*p*-acetamidophenylpropionic acid, which crystallised from 2*N*-acetic acid as the *monohydrate*, m. p. 124° after softening at 87—88° (Found: C, 59·3; H, 6·6. $C_{11}H_{13}O_3N,H_2O$ requires C, 58·8; H, 6·7%). Desiccation gave the anhydrous acid, m. p. 143°. Sodium β-*p*-acetylphenylpropionate, benzaldehyde, and acetic anhydride condensed at 160—170° to furnish an *acid*, m. p. 233—234°, of unknown constitution (Found: C, 71·0; H, 5·8; N, 4·9, 4·9%).

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