

**20.** *Isotopic Exchange Reactions of Organic Compounds. Part II.  
A Survey of the Monocarboxylic Acid Series.*

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The present work is concerned with the isotopic exchange reactions of hydrogen linked with carbon in a series of monocarboxylic acids. The existing evidence on the exchange reaction of acetic acid is conflicting, but it is now shown that exchange of the methyl hydrogen occurs in alkaline aqueous solution, but not in neutral solution, as previously reported.

It has also been found that phenylacetic, acrylic, crotonic, and sorbic acids undergo alkali-catalysed exchange reactions, whereas propionic, butyric, *isobutyric*, benzoic,

*p*-toluic,  $\alpha$ - and  $\beta$ -phenylpropionic, and cinnamic acids do not. No exchange accompanies the acid hydrolysis or saponification of ethyl acetate. These results are discussed in relation to the mechanism of exchange reactions with reference to evidence available from chemical reactions and to theories of structure.

A modified and improved density method of isotopic analysis, accurate to a few parts per million and suitable for small samples, is described.

THE use of deuterium as an indicator in the hydrogen exchange reactions of organic compounds has provided a method of studying not only acidic, pseudo-acidic, and tautomeric substances, but also other compounds which are not normally included in these categories. The method is of unique value because it can provide information in connexion with theories of structure under reversible conditions and is capable of reaching hydrogen atoms linked directly with carbon. It depends neither on the behaviour of molecules under more or less drastic and irreversible reaction conditions, where considerable energy changes may occur, nor on the behaviour of specialised groups in the molecules, and is therefore correspondingly more general in application.

The present work is concerned with the exchange reactions of monocarboxylic acids under conditions in which exchange of the carboxylic hydrogen and exchange proceeding by substitution (Ingold, Raisin, and Wilson, J., 1936, 1637, 1643) are both excluded.

In Part I (Ives and Rydon, J., 1935, 1735) no exchange was detected in the case of butyric acid, a result which was unexpected from some aspects; results which have been recorded for acetic acid are somewhat conflicting, but Liotta and La Mer (*J. Amer. Chem. Soc.*, 1937, 59, 946) summarise the earlier evidence and indicate that any exchange reaction which may occur must be extremely slow. Acetic, propionic, butyric, and isobutyric acids were therefore chosen for the first section of this work, with the object of deciding whether exchange occurs or not in the saturated aliphatic acids. The scope of the work has been restricted by the fact that the exchange reactions which were observed were catalysed by alkali, but proceeded at a rate not much greater than the attack of the alkali on the glass reaction vessels. This circumstance precluded measurements of reaction velocities because the catalyst was progressively destroyed during the course of the reaction. A comparison of the behaviour of different acids has therefore been made under standardised conditions and has not only provided results of some interest, but has also indicated those systems which will repay further study with suitably modified technique.

The method, fully described in the experimental section, was contrived to avoid loss or fractionation at any stage. In the majority of cases the acids were treated with 5 mols. % excess of sodium hydroxide in *N*-solution at 100°. After neutralisation of the catalyst, both solvent and solute were analysed isotopically by a semi-micro density method. It is believed that this method of studying exchange reactions is adequate for definite qualitative conclusions and for providing an indication of the relative magnitudes of well separated velocities. The results for the saturated acids are shown in Table I, in which cols. 4 and 5 give the actual analytical figures for the mol.-fractions of deuterium oxide in the solvent and in the water produced by combustion of the solute respectively. The former do not represent the true isotopic compositions of the solvents during the actual exchange reactions because of the water of neutralisation which is subsequently added. This has been taken into account in calculating the exchange numbers shown in col. 6; these are the apparent numbers of hydrogen atoms exchanged on the assumption that there is no isotopic discrimination during the exchange reaction (cf. Small and Wolfenden, J., 1936, 1811).

The experiments in neutral and acid solutions were included for purposes of comparison with the results of Hall, Bowden, and Jones (*J. Amer. Chem. Soc.*, 1934, 56, 750), Wynne-Jones (*Chem. Reviews*, 1935, 17, 115), and Erlenmeyer, Schoenauer, and Schwartzbach (*Helv. Chim. Acta*, 1937, 20, 726), who find exchange with the acetate ion in neutral solution, and of Klar (*Z. physikal. Chem.*, 1934, B, 26, 335), who reports an acid-catalysed exchange reaction with acetone. It is clear that, although acetic acid shows a very slow exchange reaction in an alkaline medium, the other acids show none (see next paragraph), and in neither of the cases studied does exchange occur in neutral or acid media. Whilst an

TABLE I.

Acid.	Conditions.	Time, hrs.	Mol.-fraction $D_2O \times 10^5$ .		Exchange number.
			Solvent.	Solute.	
Acetic	5 Mols. % excess NaOH .....	100	2442	135	0.161
"	" " " " .....	200	2265	232	0.300
"	" " " " .....	400	2263	315	0.407
"	Neutral .....	100	2460	8	—
"	5 Mols. % excess $H_2SO_4$ .....	100	2433	8	—
Propionic	" " NaOH .....	400	2271	18	0.039
Butyric	" " " " .....	405	2244	6	0.017
"	20 " " " " .....	405	2410	45	—
"	Neutral .....	100	2460	2	—
"	5 Mols. % excess $H_2SO_4$ .....	100	2433	5	—
isoButyric	" " NaOH .....	400	2268	5	0.015
<i>Experiments with ethyl acetate.</i>					
Saponification .....		24	ca. 2000	15	—
Acid hydrolysis .....		24	ca. 2000	2	—

apparent exchange reaction may conceivably be due to experimental error (particularly when the changes in the density of the solvent alone are measured), this can hardly be so when a negative result is obtained. The previous data on the exchange of the acetate ion in neutral solution must therefore be revised, with the possible exception of the observation by Goldfinger and Lasareff (*Compt. rend.*, 1935, **200**, 1671) that exchange occurs on standing for 11 months.

In all cases there is a very small apparent exchange, but a slight deviation from exact stoichiometric equivalence, in either direction, during the final neutralisation of the catalyst is sufficient to account for an error of these dimensions. The result with propionic acid is very close to this margin of error and cannot be taken as real evidence of exchange. Butyric acid in presence of 20 mols. % excess of sodium hydroxide shows an appreciable exchange effect, but in this case the attack of the alkali on the glass reaction vessel was very extensive and the major part of the apparent exchange can be accounted for by the presence of  $Na_2SiO_3 \cdot H_2O$ , which cannot readily be dehydrated at  $100^\circ$ , in the dried solute.

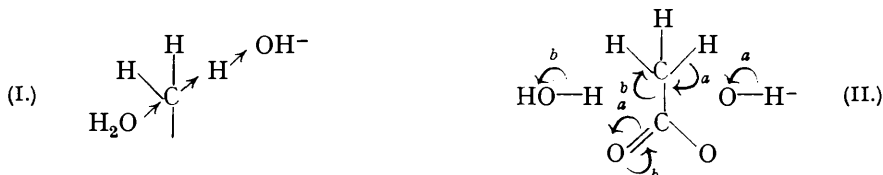
It is highly probable that the mechanism of the acetic acid exchange reaction is identical with that of three-carbon prototropy activated by the carboxyl group in so-called pentad keto-enol tautomerism (Ingold, Shoppee, and Thorpe, *J.*, 1926, 1477). Enolisation in acetic and other monocarboxylic acids or esters has frequently been postulated to explain various modes of reaction (see Part I) and has been extensively discussed in relation to racemisation (McKenzie and Wren, *J.*, 1919, **115**, 602; Conant and Carlson, *J. Amer. Chem. Soc.*, 1932, **54**, 4048; Wilson, *J.*, 1934, 98), but on the other hand, the existence of acetic acid in an enolic form has been rejected (Watson, *J.*, 1925, 2067; *Chem. Reviews*, 1930, **7**, 173). Enolisation is usually interpreted as the formation of an enol, or enolate ion, either as a stable entity or, at least, as a transitory reaction phase with real free existence. Ingold (*J.*, 1933, 1120), however, has rejected the view that the anion of a prototropic system has the enol form, and has suggested that it is, in fact, mesomeric. If this is so, it is clear that prototropy, even when acid-catalysed, does not necessarily involve enolisation (cf. Ingold and Wilson, *J.*, 1934, **93**, 773). Enolisation may in many cases accompany prototropy, because the rate of transformation of the mesomeric ion into the enol form is generally more rapid than its rate of transformation into the keto-form (Hsü and Wilson, *J.*, 1936, 623; but not always, cf. Kimball, *J. Amer. Chem. Soc.*, 1936, **58**, 1963), but this is rather a side reaction than the primary cause of the hydrogen lability.

Since the carbonyl group in its normal state is a hybrid of the non-polar with the semi-polar form (Baker and Ingold, *J.*, 1927, 832; Pauling and Sherman, *J. Chem. Physics*, 1933, **1**, 606; McKay, *Chem. and Ind.*, 1934, **53**, 870), it may be suggested that this degeneracy extends to other parts of the molecule, and that the exchange reaction of acetic acid, or acetone, is primarily a function of the normal configuration of the molecule, rather than of any specific act of enolisation. It is, of course, probable that at the moment of attack electromeric adjustment occurs within the molecule along the path laid down by the mesomeric system. The exchange reaction of acetone has been tentatively ascribed to

enolisation (Schwartz and Steiner, *Z. physikal. Chem.*, 1934, *B*, **25**, 153; Halford, Anderson, and Bates, *J. Amer. Chem. Soc.*, 1934, **56**, 491) and quite definitely by Urey and Teal (*J. Mod. Physics*, 1935, **7**, 34), but it has been admitted that enolisation is not necessarily involved (Halford, Anderson, Bates, and Swisher, *J. Amer. Chem. Soc.*, 1935, **57**, 1663). If the circumstance be considered that both enolisation by the basic mechanism and base-catalysed exchange must be conditioned by the removal of an  $\alpha$ -hydrogen atom (Watson and Yates, *J.*, 1932, 1207), whether this is the initial step or not (cf., *inter alia*, Watson, Nathan, and Laurie, *J. Chem. Physics*, 1935, **3**, 170), it is clear that these must be parallel reactions, and cannot, therefore, be related as cause and effect.

The exchange reaction of acetic acid may, perhaps, be related to the "methyl effect" of Baker and Nathan (*J.*, 1935, 1844), and it is of interest that Baker, Nathan, and Shoppee (*J.*, 1935, 1847) conclude that this effect is mesomeric in type. This is supported by the observation of Pauling and Sherman (*loc. cit.*) that the C=O bond energy is considerably changed as hydrogen attached to carbon is replaced by alkyl, this change being attributed to the interaction with the carbonyl group of other bonds in the molecule. Further, the large difference between the dissociation constant of formic acid ( $1.87 \times 10^{-4}$ ; recalculated from the data of Auerbach and Zeglin, *Z. physikal. Chem.*, 1922, **103**, 191) and acetic acid ( $1.753 \times 10^{-5}$ ; MacInnes and Shedlovsky, *J. Amer. Chem. Soc.*, 1932, **54**, 1429) may possibly be attributed, not only to the admittedly small inductive effect of the methyl group, but also to a "conjugational effect," similar to that which reduces the strength of  $\alpha\beta$ -unsaturated acids (Ives, Linstead, and Riley, *J.*, 1933, 561).

The mechanism of the exchange, however, cannot be regarded as definitely established. One possibility only can be excluded: the exchange reaction of chloroform (Horiuti and Sakamoto, *Bull. Chem. Soc. Japan*, 1936, **11**, 627) is probably activated by an inductive effect ( $-I$ ), but this cannot be so in the case of the exchange reaction of acetic acid in alkaline solution, since the species concerned are acetate ions, in which the free negative pole would provide a powerful  $+I$  effect (Waters, "Physical Aspects of Organic Chemistry," p. 214), in a sense to retard an exchange reaction. Exchange by an inductomeric effect (Ingold, *Chem. Reviews*, 1934, **15**, 225), which would be facilitated in an anion as compared with a neutral molecule, cannot be definitely rejected. A further question relates to whether the reaction is bimolecular or termolecular (Hsü, Ingold, and Wilson, *J.*, 1935, 1778): its slowness might suggest the latter, but since the points of removal and addition of the proton are coincident, this would probably involve a Walden inversion of the type (I).



It is, however, possible to visualise a tautomeric termolecular mechanism in which the intermediate stage would not attain kinetic independence; this is illustrated in the scheme (II), in which processes (a) and (b) occur as one continuous operation, wherein the system is never separated into its component ions and molecules until the exchange reaction is completed.

The absence of exchange with propionic, butyric, and *isobutyric* acids, as compared with acetic acid, is in accordance with the known inductive effect ( $+I$ ) of alkyl groups (methyl, ethyl, and two methyl groups respectively) which tend to charge the  $\alpha$ -carbon atom negatively and retard exchange: as would be expected, this effect is in the opposite direction to that observed in exchange reactions promoted by an electrophilic catalyst (Ingold, Raisin, and Wilson, *J.*, 1936, 1643). It has also been observed in other connexions that the hydrogen in the  $\alpha$ -position to carbonyl is least reactive to a protophilic reagent when it is tertiary and most active when it is primary, whereas the reverse is true with respect to an electrophilic reagent (cf. Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580). On the views expressed above, exchange of hydrogen elsewhere than in the  $\alpha$ -position is not to be expected in saturated acids.

Lowry's mechanism of hydrolysis of esters (J., 1925, 127, 1379) involves the development of the carbonyl group into its fully activated form, which might be supposed to promote an exchange reaction in the  $\alpha$ -position. It has also been shown that certain optically active esters are more readily racemised by alkali than are the parent acids (Gadamer, *J. pr. Chem.*, 1913, 87, 312; Wren, J., 1918, 113, 210). For this reason, both acid and alkaline hydrolyses of ethyl acetate were carried out in a "heavy" medium, the technique being similar to that employed with the acids. The difficulty of manipulation was greater, and the results shown in the last two lines of Table I, were negative: the slight effect observed in the case of saponification is probably within experimental error.

The remainder of the work now recorded deals with the influence of aryl substitution and unsaturation on the primary exchange reaction of acetic acid. The results are collected in Table II. The conditions were the same in each case: 5 mols. % excess of sodium hydroxide in *N*-solution; 100 hrs.; 100°.

TABLE II.

Acid.	Mol.-fraction of D <sub>2</sub> O × 10 <sup>5</sup> .		Exchange number.	Acid.	Mol.-fraction of D <sub>2</sub> O × 10 <sup>5</sup> .		Exchange number.
	Solvent.	Solute.			Solvent.	Solute.	
Phenylacetic .....	2229	575	1.765	$\beta$ -Phenylpropionic...	2220	8	0.032
" .....	2185	568	1.779	$\alpha$ - " .....	2220	16	0.063
Benzoic .....	2224	2	0.004	Acrylic .....	2214	276	0.365
<i>p</i> -Toluic .....	2224	2	0.006	Crotonic .....	2265	270	0.582
Cinnamic .....	2265	5	0.015	Sorbic .....	2215	160	0.493

The error in the exchange number is directly proportional to the total number of hydrogen atoms per molecule of the acid; the agreement between the duplicate phenylacetic acid experiments therefore indicates an adequate degree of accuracy for the present purposes.

The most striking result, on first inspection, is the apparently anomalous effect of substitution in the two series starting with acetic and acrylic acids. In the former, phenyl substitution promotes exchange (acetic,  $E = 0.161$ ; phenylacetic,  $E = 1.77$ ) and methyl substitution stops it (propionic,  $E = ca. 0.004$ ); in the latter, the reverse is true (acrylic,  $E = 0.365$ ; cinnamic,  $E = 0.015$ ; crotonic,  $E = 0.568$ ). It is believed that this anomaly is satisfactorily explained in the following discussion of the separate cases.

*Phenylacetic Acid.*—The tautomeric effect of the phenyl group ( $\pm T$ ) provides an additional means of release of the  $\delta -$  charge induced on the  $\alpha$ -carbon atom by the attack of the hydroxyl ion at the  $\alpha$ -hydrogen atoms: an increased rate of exchange, as compared with acetic acid, is therefore only to be expected. That the activating effect of the phenyl group in this respect is less than that of the carboxyl group is shown by comparison with malonic acid, of which the methylene hydrogen exchanges readily in neutral solution (Münzberg, *Z. physikal. Chem.*, 1935, B, 31, 18; Halford and Anderson, *J. Amer. Chem. Soc.*, 1936, 58, 736), and conforms with the inferior efficiency of the phenyl group in activating three-carbon tautomerism (Ingold and Piggott, J., 1922, 121, 2381). The exchange reaction also corresponds with the known activity of the methylene hydrogen in phenylacetic acid (Perkin condensation; Pschorr, *Ber.*, 1896, 29, 496), but since it is the first example of definite prototropy in a saturated compound containing a phenyl group and a single carboxyl group, it is of interest in connexion with the fact observed by McKenzie and Wren (J., 1920, 117, 680) that  $\alpha$ -aryl-substitution is a necessary condition for the racemisation by alkali of carboxylic acids in which the  $\alpha$ -carbon atom is the centre of asymmetry and carries a hydrogen atom (cf. Wilson, *loc. cit.*).

*Benzoic, p-Toluic, and  $\beta$ -Phenylpropionic Acids.*—The absence of exchange in these cases was not unexpected and is in accord with generally accepted electronic theory. It is probable that the methyl hydrogen of *p*-toluic acid would exchange under the influence of a more active catalyst (cf. Kharasch, Brown, and McNab, *J. Org. Chem.*, 1937, 2, 36, who find exchange with *p*-nitrotoluene catalysed by sodium ethoxide). A comparison of *p*-toluic and phenylacetic acids on the one hand with vinylacetic and crotonic acids (Part I, *loc. cit.*) on the other, indicates that the ethylenic bond is more polarisable than the phenyl

group, both in the activation of exchange and in the transmission of electromeric effects (cf. Waters, J., 1933, 1551).

*α-Phenylpropionic Acid.*—The absence of exchange in this case was unexpected. On polar grounds, it seemed unlikely that the feeble inductive effect of the methyl group could entirely counterbalance the activating tautomeric effect of the phenyl group, and an exchange reaction slower than that of phenylacetic acid, but still appreciable, was anticipated. The influence of steric hindrance, however cannot be excluded, since the exchange reaction is similar in type to the anion substitutions discussed by Ogg and Polanyi (*Trans. Faraday Soc.*, 1935, **31**, 604) in which steric effects play a major part. It is also noteworthy in this connexion that *α*-alkyl hindrance is very appreciable in the saponification of esters (Bryant and Smith, *J. Amer. Chem. Soc.*, 1936, **58**, 1014).

*Acrylic Acid.*—The slow exchange reaction in this case was not unexpected, since a  $\delta +$  charge on the  $\beta$ -carbon atom has been postulated in connexion with the Michael reaction (Cooper, Ingold, and Ingold, J., 1926, 1868) and with hydrogen halide addition (Lucas and Jameson, *J. Amer. Chem. Soc.*, 1924, **46**, 2475); this may be supposed to facilitate the removal of a  $\beta$ -hydrogen atom as a proton. It may also, perhaps, be inferred from the high polarisability of the ethylenic link that the  $\beta$ -hydrogen atoms in acrylic acid would resemble the methyl hydrogens of acetic acid in reactivity. The mechanism of this particular exchange is discussed in relation to that of crotonic acid.

*Crotonic Acid.*—The apparently anomalous effect of the methyl group in promoting exchange disappears if the methyl hydrogen itself is concerned in the exchange reaction, which, *ipso facto*, constitutes evidence that such is the case. This is further supported by the reactivity of the methyl group in crotonic acid in the Claisen reaction with oxalic ester (Lapworth, J., 1901, **79**, 1276). The question of whether the methine hydrogen is also involved is of some importance, and will provide the subject of a further communication.

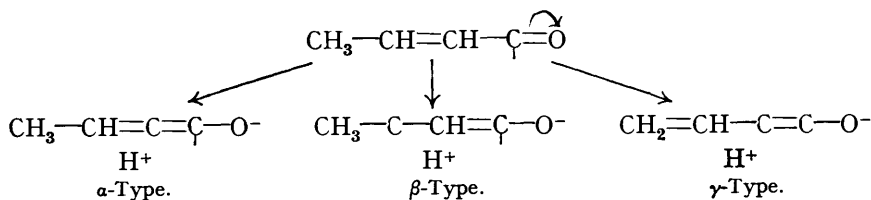
It might be suggested that the exchange reaction of crotonic acid is due to an equilibrium with its isomeride vinylacetic acid. Such an equilibrium, however, must be preceded by an ionisation of the  $\gamma$ -hydrogen, and it is this initial process, rather than any subsequent change, which is the subject of the present discussion. The slowness of the crotonic acid exchange reaction indicates that the position of such an equilibrium, if it exists at all, must be very close to 100%  $\alpha\beta$ .

*Sorbic Acid.*—This acid is of interest in so far as it contains a conjugated system. Again, the evidence of the Claisen reaction (Borsche and Manteuffel, *Ber.*, 1932, **65**, 868) indicates that the methyl hydrogen is involved, but on the other hand, Waters (J., 1933, 1551) ascribes less polarisability to a conjugated chain than to a phenyl group: on this basis a comparison with *p*-toluic acid would imply no exchange on the part of sorbic acid. The possibility that the hydrogen on alternate carbon atoms ( $\beta$  and  $\delta$ ) may be involved cannot be excluded (Lapworth, J., 1898, **73**, 445; Bloom and Ingold, J., 1931, 2765), and it is therefore clear that, whilst the identity of the exchanging hydrogen remains undefined, certain anomalies in the interpretation of the results of exchange experiments must remain.

Some evidence, however, may be gathered by considering the possible mechanisms of the exchange reactions with reference to the constitution of the intermediate ions. Crotonic and acrylic acids are discussed for this purpose, since they probably represent two different modes of reaction. It is assumed that the primary electron-release effect which activates exchange is the tendency of the carbonyl group to assume a dipolar form:

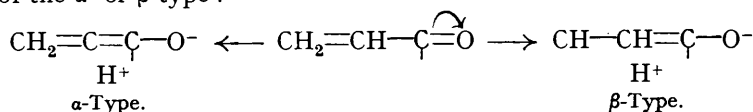
$$\text{>C}=\overset{\curvearrowright}{\text{O}} \longrightarrow \text{>}\overset{+}{\text{C}}-\overset{-}{\text{O}}$$
and that this tendency is transmitted electromerically to the seat of exchange. This is justified in the case of the  $\alpha\beta$ -unsaturated acids by the evidence of the depression of the dissociation constants of such acids by the so-called "conjugational effect" (Ives, Linstead, and Riley, *loc. cit.*; Dippy and Lewis, J., 1937, 1008), which postulates a path along which electromeric adjustment can occur between the carboxyl group and the rest of the molecule: the dissociation of the acid is concerned with one end of this path, and the exchange reaction with the other.

For the sake of clarity, we shall assume that the intermediate ion has the unperturbed enol form; that the exchange of  $\alpha$ -,  $\beta$ -, or  $\gamma$ -hydrogen in crotonic acid must involve quite characteristic and different types of intermediate ion is clear from the following scheme:

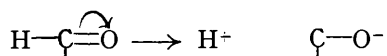


The three possibilities are denoted the  $\alpha$ -,  $\beta$ -, and  $\gamma$ -types of exchange, and require the following structural changes to accompany the formation of the ion. (1)  $\alpha$ -Type: no valency disturbance; loss of conjugation with development of allene structure. (2)  $\beta$ -Type: the formation of a bivalent carbon atom; loss of double bond and therefore loss of conjugation. (3)  $\gamma$ -Type: no valency disturbance; no loss of conjugation.

Consideration of the probable energy requirements of these operations indicates that terminal exchange is most likely in crotonic acid, and, also, in sorbic acid for similar reasons. Again, this problem is of interest in connexion with the "methyl effect" of Baker and Nathan (*loc. cit.*). On the other hand, the exchange reaction of acrylic acid is necessarily of the  $\alpha$ - or  $\beta$ -type:



and the exchange reaction of formic acid (Small and Wolfenden, *loc. cit.*; Münzberg, *loc. cit.*) would appear, paradoxically, to be of the  $\beta$ -type (bivalent carbon, loss of double bond):



*Cinnamic Acid.*—The lack of exchange can be attributed to the direct coupling of the carboxyl double bond with the phenyl group by means of the ethylenic link. This depression of reactivity indicates that the molecule has a mesomeric structure; evidence in support of this view is available from the following sources.

(1) Resonance energies, calculated from the data given by Pauling and Sherman (*loc. cit.*), Pauling (*J. Amer. Chem. Soc.*, 1932, **54**, 3570), Kharasch (*Bur. Stand. J. Res.*, 1929, **2**, 359), and Landolt-Börnstein are recorded, in volt-electrons, in Table III, the possible error in the values amounting to about 0.2 v.-e.

TABLE III.

Acetic acid .....	1.33	Acrylic acid .....	1.30	Benzoic acid .....	3.26
Propionic acid .....	1.37	Crotonic acid .....	1.45	Phenylacetic acid .....	2.80
Butyric acid .....	1.29	Sorbic acid .....	1.86	<i>p</i> -Toluic acid .....	2.98
<i>iso</i> Butyric acid .....	1.53			$\beta$ -Phenylpropionic acid ...	2.95
				Cinnamic acid .....	3.66
Phenyl (Pauling and Sherman, <i>loc. cit.</i> ) .....					1.71
"   from $\beta$ -phenylpropionic and propionic acids .....					1.58
"   from phenylacetic and acetic acids .....					1.47
"   from cinnamic and acrylic acids .....					2.36
—CH=CH— from crotonic and acetic acids .....					0.12
"   from cinnamic and benzoic acids .....					0.40
—CH=CH— replacing —CH <sub>2</sub> —CH <sub>2</sub> — {					
from crotonic and butyric acids .....					0.16
from cinnamic and $\beta$ -phenylpropionic acids .....					0.71

Intercomparison of these results in the manner indicated in the table shows that the resonance energy of cinnamic acid is higher than would be anticipated, by about 0.5 v.-e. (12 kg.-cals.), which is considerably greater than any likely error in the thermal data. Other points of interest will be apparent from these figures.

(2) The influence of phenyl substitution in three-carbon tautomeric systems indicates that an increase of stability results from the formation of a cinnamic acid structure (*cf.* Baker, "Tautomerism," p. 158).

(3) Cinnamic acid is less ionised than acrylic acid in aqueous solution ( $K \times 10^5 = 3.65$

and 5.56 respectively; Dippy and Lewis, *loc. cit.*): if the strengths of unsaturated acids are mainly conditioned by polarisability (Ives, Linstead, and Riley; cf., however, Dippy and Lewis, *loc. cit.*), the reduced strength of cinnamic acid corresponds with a permanent (mesomeric) polarisation in the molecule.

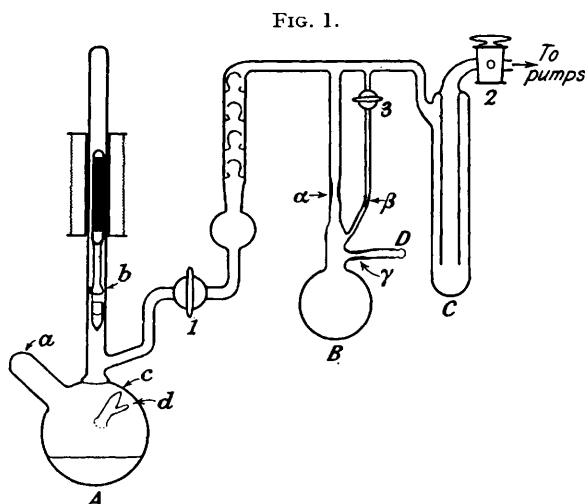
(4) Finally, Duquesnois (*Bull. Soc. chim.*, 1937, 4, 193) and Lespagnol and Bruneel (*J. Pharm. Chim.*, 1937, 25, 454) have shown that cinnamic acid and its aldehyde and esters are less reactive to halogens in the dark than cinnamyl alcohol or styrene. This corresponds with a reduced polarisability of the ethylenic bond (cf. Anantakrishnan and Ingold, J., 1935, 1396) which might be inferred from a mesomeric degeneracy of the molecules containing the conjugated system in question.

#### EXPERIMENTAL.

*Preparation of Materials.*—The organic materials were purchased, or prepared by standard methods, and carefully purified. The purity was checked by determination of m. p., b. p., equivalent (by titration), or density. Concentrated carbonate-free sodium hydroxide (prepared from the metal) was rendered  $1.050 \pm 0.002N$ . by dilution with 2.5% deuterium oxide and standardised micro-volumetrically. Other standard solutions were prepared similarly.

Weighed amounts of 8N-sulphuric acid or anhydrous sodium carbonate were used for neutralisation of the alkaline and acid catalysts respectively.

*Exchange Experiments.*—The exchange reactions were carried out in Pyrex bombs of 100 c.c. capacity. These were prepared from Pyrex flasks and were of the form indicated in Fig. 1, where a bomb, *A*, is shown in connexion with the solvent-recovery apparatus. Each bomb carried, in addition to the original neck (*a*), three side tubes; one of these (*b*, 30 mm.  $\times$  10 mm.) was closed at the lower end by a septum blown directly into the wall of the flask, and is referred to subsequently as the "fall-tube." The fall-tube was fitted with a closed side branch, near the bomb, by which it could be sealed to the solvent-recovery



apparatus when desired. The other two tubes (*c* and *d*) were for the respective purposes of introducing the standard solution and of evacuation immediately before starting the reaction.

The bombs were prepared for use by suitable cleaning and thorough drying in vacuum. Weighed quantities of the standard solutions were introduced, and the bombs left sealed until used. The quantity of the particular acid under investigation, calculated to give a  $x$ -solution in the form of the sodium salt, was weighed out into a capsule and introduced through the neck of the bomb (*a*), which had been opened for this purpose. After the neck had been resealed, the contents of the bomb were frozen at a temperature of  $-80^\circ$ , and the bomb rapidly evacuated through the side tube *d*, which was then sealed. After thawing and thorough mixing of the contents, the bomb was placed in a boiling water-bath, or, for the hydrolyses, in a thermostat at  $75^\circ$ .

*Recovery of Water.*—*From solvent.* Before removal of the bomb from the water-bath, at the conclusion of the exchange period, the calculated quantity of the 8N-sulphuric acid was weighed out into a small, stout Pyrex "bucket," which was fitted with a fine platinum hook. This bucket could be suspended from a glass-sheathed armature, for manipulation inside the fall-tube by means of a solenoid. After removal from the water-bath, the bomb was cooled and sealed on to the solvent-recovery apparatus in the position shown in Fig. 1: the armature, with suspended bucket, was lowered into the fall-tube, and the latter sealed. The apparatus was then cautiously evacuated: any loss by evaporation from the sulphuric acid during this operation represents a negligible error in the subsequent calculations. Tap 1 (Fig. 1) was then closed, a heavy current passed through the solenoid, and the bucket driven through the septum



without allowing the armature to drop. The current through the solenoid was then reduced, the armature raised, and a "shelf" provided on which it could rest by heating the wall of the fall-tube so that it gently "caved in." The contents of the bomb were thoroughly mixed: in some cases, where solid acid separated, prolonged shaking and boiling were necessary before this was complete. Trap *C* was then cooled to  $-80^{\circ}$ , tap 1 opened, and the pressure in the apparatus reduced to about 0.01 mm. Tap 2 was then closed, the cooling bath removed from trap *C*, and vessel *B* cooled in ice. The bomb *A* was next surrounded by a water-bath, which was gradually raised to the b. p. and maintained there until the residue in the bomb was dry. Constriction  $\alpha$  was then sealed, tap 3 closed, and trap *C* again cooled to  $-80^{\circ}$ . The apparatus was then opened to the pumps for a few minutes and subsequently left closed for about  $\frac{1}{2}$  hour; any condensate in *C* was now transferred to vessel *B* by suitable manipulation of taps, warming, and cooling. This procedure was repeated until no appreciable condensation of water occurred in trap *C*. The whole of the solvent was then collected in *B* by cooling this to  $-80^{\circ}$  with tap 3 open, and *B* was finally sealed off (at  $\alpha$  and  $\beta$ ) and removed from the apparatus. After being thawed and mixed, a sample of about 0.3 c.c. of the recovered solvent was poured into the side tube *D* which was provided with a thin-walled end: *D* was then sealed off (at  $\gamma$ ) and stored for isotopic analysis.

This whole procedure was applied to all cases, except those in which a neutral medium was used for the exchange reaction: here no neutralisation of the catalyst was required, the bucket was eliminated, and the armature used only as a breaker. In the hydrolysis experiments, the alcoholic solvent was not collected, since a precise knowledge of its isotopic composition was not required. The quantity of sodium carbonate used to neutralise the products of the acid hydrolysis was calculated on the basis of  $K = [\text{Me}\cdot\text{CO}_2\text{Et}][\text{H}_2\text{O}]/[\text{EtOH}][\text{Me}\cdot\text{CO}_2\text{H}] = 4.0$ .

*From residue.* The bomb was opened, and the dry residue scraped out as completely as possible. After being powdered, it was tested for neutrality with both alcoholic and aqueous phenolphthalein: in the majority of cases it was neutral to the former and slightly alkaline to the latter, in conformity with the required stoichiometric accuracy, owing to the hydrolysis of sodium salts of weak acids. After transference to a boat, the residue was dried at  $100^{\circ}$  in a high vacuum, and then burned in dry air or oxygen, the combustion water being collected at  $-80^{\circ}$ . Particular care was taken to ensure complete recovery of this water, which was finally transferred in vacuum to a sampling tube similar to that described in connexion with the solvent-recovery apparatus.

*Isotopic Analysis.*—The difficulty of avoiding errors in the density method of isotopic analysis is considerably increased when the quantity of water available is small (in the present case, 0.2—0.4 c.c.); the method described in Part I (*loc. cit.*) has therefore been modified in several important respects, although the general sequence of operations has been retained. Errors due to small losses during purification have been avoided by carrying out the purification, measurement of density, and recovery of the samples in a vacuum; 0.2579 g. of water lost 0.0003 g. in weight after undergoing this sequence of operations three times.

The purification apparatus is illustrated in Fig. 2. All ground joints were lubricated with "Apiezon L" grease. The pumping system consisted of a three-stage mercury-diffusion pump, backed by an oil pump, a trap cooled to  $-80^{\circ}$  to prevent back diffusion of mercury vapour, and a discharge tube as a rough vacuum gauge. Air could be admitted to the apparatus when desired through a suitable purification and drying train. The section of apparatus between the points *a* and *c* was subjected to cleaning operations and final steaming from conductivity water, and the whole apparatus was pumped to a hard vacuum and thoroughly baked before use in each case.

Vessel *A*, which could be opened to the silica combustion tube by the usual device of septum and breaker, was used for the preliminary heating with silver oxide. (The sample was released in *A*, after evacuation, baking, and sealing, by shaking, so that the thin wall of the sample tube was broken.) Trap *B* contained a trace of silver oxide and was cooled to  $-80^{\circ}$  when used as receiver for the distillation of the sample through the combustion tube. During this process, considerable quantities of gas were evolved and it was necessary from time to time to reduce the pressure in the apparatus, but at no stage of the process was continuous pumping necessary. This gas evolution practically ceased (apart from a small residual effect due to the dissociation of the copper oxide) on completion of the distillation. The constriction *a* was then sealed, and the sample kept at room temperature, in presence of the trace of silver oxide, for  $\frac{1}{2}$  hour. Trap *C* was now cooled to  $-80^{\circ}$ , and the last traces of gas removed from the system by pumping until the ultimate vacuum obtainable was reached. The final distillation into the flotation

vessel *D* was then carried out, without pumping, with the receiver at  $-80^{\circ}$ . On completion of this operation, the flotation vessel was withdrawn by sealing off at the constriction *b*. The avoidance of ebullition during this final distillation was found to be important.

The next stage of the purification was carried out in the flotation vessel, shown in Fig. 3. Bulb *D*, of about 2 c.c. capacity, was used as receiver in the distillation just described, *b* being the constriction at which the vessel was sealed off from the rest of the apparatus. The sample was poured into the compartment *A*, a thin-ended sampling tube in which the sample was finally recovered. This was followed by a distillation, between  $40^{\circ}$  and  $0^{\circ}$ , into the tube *B*, which was of 2 mm. diameter and contained a silica float of volume 10–15 mm.<sup>3</sup>. The sample was next poured into *D* through the narrow capillary *C*, rinsed round, and poured back into *A*, with the vessel in an inverted position. This cycle of distillation and pouring operations was repeated 3 or 4 times, with the result that soluble impurities collected in *A*, and the density of the sample decreased to a limiting constant value. The total decrease in density resulting from this procedure was, on the average, about 15 p.p.m., but in some cases was even greater.

FIG. 2.

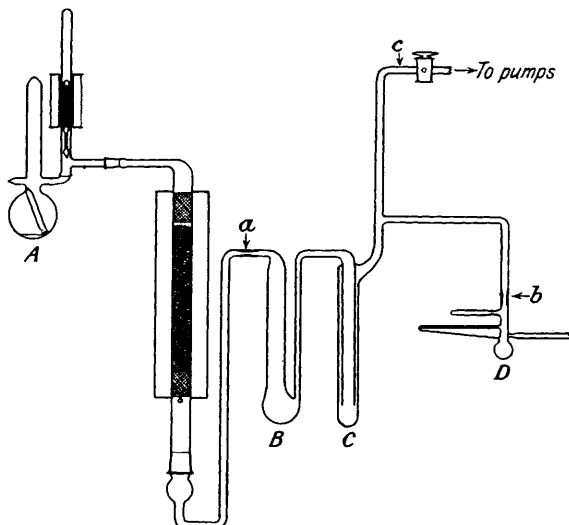
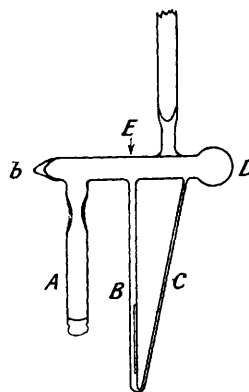


FIG. 3.



A difficulty with "heavy" samples was experienced, owing to the fractionation occurring in the distillation from *A* into *B*. This was so considerable that the distillate in the narrow tube *B* was far from homogeneous, being "light" at the bottom and "heavy" at the top (cf. Hall, Anderson, and Jones, *J. Amer. Chem. Soc.*, 1934, 56, 749). Diffusion being exceedingly slow, it was necessary to mix the sample by pouring it through *C* into *D*, rinsing round and pouring it back again, before a measurement could be carried out.

The method of flotation need not be described in detail. The rate of movement of the float was observed and plotted against temperature in the usual way. The difficulty of "sticktion" was avoided by not measuring any rate of motion in excess of about 0.2 mm. per minute, corresponding with a temperature range of about  $0.01^{\circ}$ . Between each determination the float was removed from the vessel, so that the latter might be steamed, by making an opening at the point *E*. When not in use, the float was kept in fuming nitric acid, and was manipulated by means of a narrow tube with a flat constriction. This provided a holder for the float in which it could be washed, and from which it could be extruded directly into the flotation vessel by means of a thin platinum wire. No difficulty due to fortuitous density changes was experienced with any of the floats used.

The thermostat and thermometer were the same as those used in Part I, but the temperature scale was corrected by calibration against a platinum thermometer with a fundamental interval of 14 ohms. Ice and steam points were determined with the usual precautions and corrections, and the third fixed point necessary to relate platinum and Centigrade temperatures was obtained with the aid of sodium sulphate decahydrate recrystallised to constant transition temperature. The accuracy of the scale thus obtained did not exceed  $\pm 0.01^{\circ}$ , and, in the author's opinion, greater accuracy is unobtainable without great experimental elaboration, particularly with

regard to the fixed points. A check on this scale was provided by the temperature of the transition  $\text{MnCl}_2 \cdot 4\text{H}_2\text{O} \rightleftharpoons \text{MnCl}_2 \cdot 2\text{H}_2\text{O} + \text{satd. soln.}$ : a value of  $58.12^\circ$  was obtained (Richards and Wrede, *Proc. Amer. Acad. Sci.*, 1907, **43**, 343 give  $58.09^\circ$ ). The accuracy within the temperature range used ( $22$ — $32^\circ$ ) was undoubtedly better than indicated by this comparison. Duplicate measurements of the density of "heavy" samples with floats of slightly different density gave substantially identical results, the largest discrepancy observed being 3 p.p.m.

*Calculation of Densities and Mol.-fractions of Deuterium Oxide.*—Tronstad, Nordhagen, and Brun (*Nature*, 1935, **136**, 515) have shown that the earlier values for the specific gravity of deuterium oxide were too high, owing to the presence of  $^{18}\text{O}$ . The earlier data of Lewis and Macdonald (*J. Amer. Chem. Soc.*, 1933, **55**, 3057) and of Luten (*Physical Rev.*, 1934, **45**, 161), however, provide the only information available with regard to the variation of specific gravity with temperature and with mol.-fraction in mixtures with normal water. The earlier figures have therefore been used, and it is clear that any possible error in the exchange numbers from this source must be negligible.

The formula for the density of mixtures of deuterium oxide and normal water was quoted wrongly in Part I (p. 1742): the correct formula is  $d_4^{25^\circ} = 0.9970 + 0.1078x - 0.0012x(1 - x)$ .

In calculating mol.-fractions of deuterium oxide in the solvent actually used in an exchange reaction, allowance was made for the dilution which occurs on neutralisation of the catalyst. The solvent was examined in every case, but it was not possible to prepare "deuterium balance sheets" because slight variations occurred from experiment to experiment due to small losses, and also possibly small dilutions, in the operations of sealing and exhausting the bombs. The subsequent procedure, however, must have been so nearly quantitative as to render this precaution superfluous, and in any case, the effect of exchange on the density of the solvent was usually close to experimental error. Such small variations in the solvent do not affect the final result to any appreciable extent, because the solvent remaining *after* these operations was examined in each case.

Densities of normal water at various temperatures were interpolated graphically from the data given in International Critical Tables. Allowance was made for the thermal expansion of the silica float, which has an appreciable effect over the wider temperature range.

The author records his thanks to Dr. H. R. Nettleton for the loan of apparatus and helpful advice in connexion with the platinum-resistance thermometry.

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[Received, October 20th, 1937.]