STUDIES IN ESTERIFICATION.

I. ESTERIFICATION OF THE CYCLOPARAFFIN-MONOCARBOXYLIC ACIDS.

By G. D. Advani and J. J. Sudborough.

INTRODUCTION.

In earlier papers on the esterification of carboxylic acids by the hydrogen chloride catalytic process attention has been drawn to a number of points indicating the close relationship between the structure of the acid and its rate of esterification.

Some of the more important generalisations arrived at so far are—

1. In the series of aliphatic saturated normal monobasic acids the velocity of esterification diminishes in the order: formic, acetic, propionic, *n*-butyric, but from *n*-butyric acid onwards the values for the velocity constants remain practically the same even up to stearic acid.[1]

2. The introduction of substituents into the acetic acid molecule retards the rate of esterification. Thus, in the case of the three compounds :—

(*a*) $CH_2X \cdot CO_2H$
(*b*) $CHX_2 \cdot CO_2H$
(*c*) $CX_3 \cdot CO_2H$

all are esterified less readily than acetic acid, but of the three (*a*) is always esterified most readily and (*c*) least readily; but it does not follow that an acid $CX_3 \cdot CO_2H$ is necessarily esterified more slowly than an acid $CHY_2 \cdot CO_2H$. [2]

[1] Sudborough and Gittins, *J. Chem. Soc.*, 1908, **93**, 210.
[2] Sudborough and Lloyd, *ibid.*, 1899, **75**, 467; Sudborough and Turner 1912, **101**, 237; Gyr *Ber.* 1908, **41**, 4322.

3. The introduction of an olefine linking into the molecule of an aliphatic acid has a marked effect upon the velocity of esterification. In the 1:2 position with respect to the carboxylic group it produces a very marked lowering of the velocity constant, in some cases a fall in the ratio 40 to 1. In the 2:3 position the olefine linking produces a slight accelerating effect, and in the 3:4, or any other position further removed from the carboxylic group, the effect is practically *nil*; in other words, the velocity constants for the saturated acid and its unsaturated analogue are practically the same.[1]

4. The presence of a carboxyl group in the 1, 2, or 3 position with respect to the carboxylic group has an inhibiting effect, but this is not nearly so marked as that due to a 1:2 olefine linking. [2]

5. In the aromatic series an ortho substituent has a marked retarding influence on the rate of esterification,[3] and in most cases two ortho substituents completely inhibit esterification.[4]

Exceptions are met with in the case of two mono-ortho substituted benzoic acids, viz. *o*-benzoylbenzoic acid and acetophenone-*o*-carboxylic acid, $CH_3 \cdot CO \cdot C_6H_4 \cdot CO_2H$, the latter of which is esterified more readily than benzoic acid itself and the former more readily than any other ortho substituted acid examined.[5] Similarly 3:6-dichloro- and tetrachloro-benzoylbenzoic acids, although di-ortho substituted, can be esterified by the catalytic process.[6]

6. In the case of stereoisomeric acids of the crotonic type several generalisations have been drawn.[7] The most important of these are—

(*a*) A comparison of a pair of *cis*, *trans* stereoisomeric acids of the types :—

$$\text{I.}\quad \begin{matrix} X \cdot C \cdot H \\ Y \cdot C \cdot CO_2H \end{matrix} \qquad\qquad \text{II.}\quad \begin{matrix} H \cdot C \cdot X \\ Y \cdot C \cdot CO_2H \end{matrix}$$

shows that the acid (I) in which the substituent X is in the *trans* position with respect to the carboxylic group is esterified more readily than the stereoisomeride (II) in which the substituent X is in the *cis* position.

[1] Sudborough and Roberts, *J. Chem. Soc.*, 1905, **87**, 1840; Sudborough and Thomas, 1907, **91**, 1033; Sudborough and Gittins, 1909, **95**, 315; Sudborough and Thomas, 1911, **99**, 2307; Kailan, *Monatsh.*, 1909, **28**, 1137.

[2] Sudborough, *J. Chem. Soc.*, 1912, **101**, 1227; Kailan, *Monatsh.*, 1907, **28**, 1187.

[3] Kellas, *Zeitsch. physikal Chem.*, 1897, **24**, 221; Goldschmidt, *Zeitsch. Elektrochem.*, 1909, **15**, 4; Sudborough and Turner, *J. Chem. Soc.*, 1912, **101**, 237.

[4] V. Meyer and Sudborough, *Ber.*, 1894, **27**, 510, 1580, 3146.

[5] Sudborough and Turner, *J. Chem. Soc.*, 1912, **101**, 239.

[6] Graebe, *Ber.*, 1900, **33**, 2026.

[7] Sudborough and Lloyd, *J. Chem. Soc.*, 1898, **73**, 81; Sudborough and Roberts, 1905, **87**, 1840; Sudborough and Davies, 1909, **95**, 975.

(*b*) A trisubstituted acrylic acid, $CXY{:}CZ{\cdot}CO_2H$ is esterified extremely slowly.

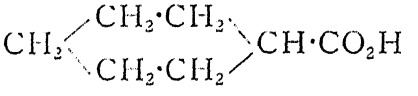
(*c*) A substituent in the 1-position with respect to the carboxyl group has a more pronounced retarding effect than the same substituent in the 2-position either *cis* or *trans*.

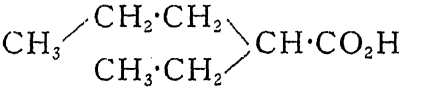
7. The effect of a triple linking in the 1:2 position is similar to that of an olefine linking in the same position.[1]

8. One, two, three or four methyl groups when introduced into the molecule of methyl hydrogen succinate have a distinct inhibiting effect.[2]

As an extension of this work on the relation between constitution and rate of esterification of acids we have taken up the study of the following points:—

1. How far does the closing of the ring and the formation of a cyclic structure affect the rate of esterification of an acid, e.g. is cyclohexanecarboxylic acid esterified more or less readily than the corresponding aliphatic acid, ethylpropylacetic acid.





2. In the case of disubstituted acetic acids is the same phenomenon met with as in the case of the mono-substituted acids, viz. does the effect of an increase in the carbon chain of the substituent cease after ethyl, i.e. have diethyl- and dipropylacetic acids the same rate of esterification.

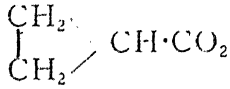
3. A comparison of the rates of esterification of acids of the benzoic series and of their hexahydro-derivatives.

4. Has a 1:2 olefine linking in the molecule of a cyclic acid the same retarding effect as in the case of an aliphatic acid, and is the effect the same if the 1 : 2 linking is a semi-cyclic olefine linking?

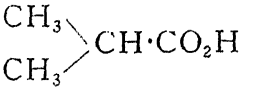
The first of these questions is taken up in the present paper and the others we hope to discuss later.

Our object has been to ascertain the effect of the closing of the ring on the rate of esterification, and for this purpose we have selected the following pairs of acids:—

Cyclopropane-1-carboxylic acid



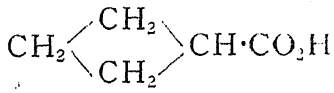
Dimethylacetic acid



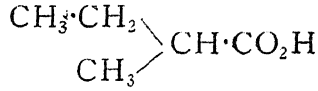
[1] Sudborough and Gittins, *ibid.*, 1909, **95**, 315.

[2] Bone, Sudborough and Sprankling, *ibid*, 1904, **85**, 534.

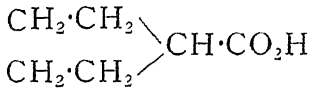
Cyclobutane-1-carboxylic acid



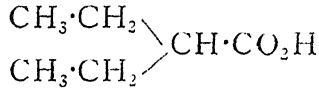
Methylethylacetic acid



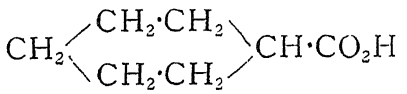
Cyclopentane-1-carboxylic acid



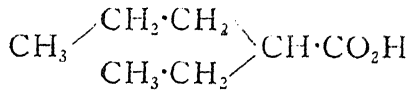
Diethylacetic acid



Cyclohexane-1-carboxylic acid



Ethylpropylacetic acid



The only work hitherto published, which has a direct bearing on the question of the influence of the closing of the ring on chemical reactivity, appears to be that of Menschutkin,[1] who carried out several series of experiments on 'The Velocity of Change in the Polymethylene Series'. In one set of experiments a study was made of the rates of esterification of the polymethylene monohydric alcohols—cyclopentanol, cyclohexanol and cycloheptanol and their methyl derivatives—by heating equimolecular mixtures of the alcohols and acetic anhydride in benzene at 100° and ascertaining the amount of acetyl derivative formed. The relative values for the constants obtained by using the formula

$$K = \frac{1}{t} \cdot \frac{x}{a-x}$$

where $a = 100$, x = extent of change per cent. in t minutes are given in Table I.

TABLE I.

Rates of Esterification of Secondary Alcohols with Acetic Anhydride (Menschutkin).

Cyclic Secondary Alcohol	Constant[2]	Aliphatic Secondary Alcohol	Constant
Cyclopentanol	16·9	Isopropyl alcohol ...	13·2
Cyclohexanol	12·3	Methylpropylcarbinol ...	8·7
Cycloheptanol	10·8	Methylhexylcarbinol ...	8·2

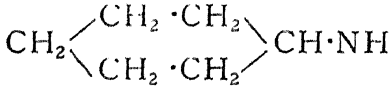
[1] *J. Chem. Soc.*, 1906, 89, 1532.

[2] The numbers are all comparative and are on the basis of the value for methyl alcohol being represented as 100.

It is clear that in the case of the three cyclic secondary alcohols studied the closing of the ring has produced an increased rate of reactivity towards acetic anhydride, and that this increase is most pronounced in the case of the five-membered ring and least with the seven-membered ring. No values are given for secondary alcohols with a four or three-membered ring. Cyclopentanol appears to react with acetic anhydride more readily than any other secondary alcohol, whether cyclic or aliphatic, e.g. it reacts more readily with the anhydride than the simplest aliphatic secondary alcohol, isopropyl alcohol (dimethylcarbinol).

Cyclohexanol, its 3 and 4-methyl derivatives and the *cis* and *trans*-3:5-dimethyl derivatives are all esterified more readily than the aliphatic secondary alcohols containing six carbon atoms and almost as readily as dimethylcarbinol.

This increased reactivity produced by the closing of the ring does not appear to be restricted to the esterification of alcohols, as in another series of experiments it is shown that ring closure has a similar effect on the alkylation of amines. The cyclic amines used were cyclohexylamine, its 3-methyl, 5-methyl-2-isopropyl, 2:3:5-trimethyl and 1:2:4-trimethyl derivatives. The following numbers show that cyclohexylamine has a higher velocity constant than either isopropylamine or methyl-*n*-propyl-methylamine.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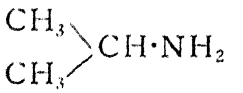
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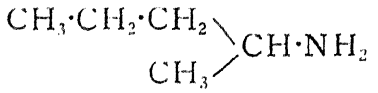
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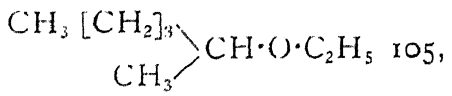
An even more marked effect is noticed when the nitrogen atom forms part of the ring system, as shown by a comparison of the relative alkylation velocities of piperidine and di-*n*-propylhexylamine, viz. 20,575 and 2910.

The study of ether formation from alcohols also shows that ring closing facilitates the reaction as illustrated by the following numbers :—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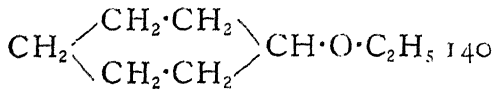
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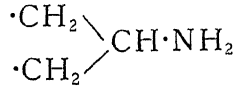
Menschutkin's researches, therefore, lead to the following conclusion :—

In the reactions—

(*a*) The esterification of secondary alcohols by acetic anhydride,

(*b*) The formation of ethers from secondary alcohols, and

(*c*) The alkylation of isoprimary amines of the type



a closing of the ring and the formation of cycloparaffin derivatives increases the rates at which the reactions proceed, at any rate in the case of cyclopentane, cyclohexane and cycloheptane derivatives.

II. PREPARATION OF MATERIALS.

Considerable difficulties were experienced in the preparation of the cycloparaffin-carboxylic acids, and as several different methods were adopted a brief description of these is given.

A. Cyclopropane-1-carboxylic Acid.

Perkin's synthesis from ethylene bromide and ethyl sodiomalonate[1] was first tried, but the yields of the dicarboxylic ester were extremely unsatisfactory, varying from 9 to 14 per cent., and at the end of several weeks only twenty-five grams of cyclopropane-1:1-dicarboxylic acid were obtained, which on distillation gave fourteen grams of a monobasic acid with a boiling point ranging over 130°.

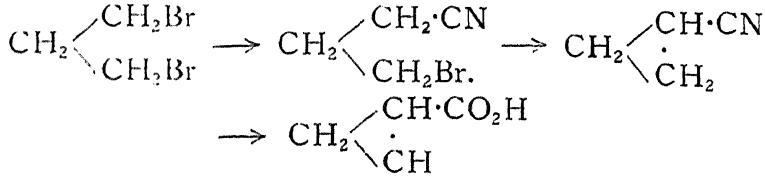
Perkin's method of using ethyl sodiocyanoacetate [2] was also used, and the yields of ester of the cyclic cyanocarboxylic acid increased to 55 to 65 per cent. of the theoretical, but as appreciable losses were met with in the hydrolysis of this ester the final yields were poor. The hydrolysis of the cyclic cyano-ester with aqueous potassium hydroxide was also tried but the results were not satisfactory.

Attempts were also made to prepare the monocarboxylic acid by Henry and Dalle's method,[3] which consists of the following series of reactions :—

Trimethylene chlorobromide ⟶ trimethylene chlorocyanide ⟶ nitrile of cyclopropane-1-carboxylic acid ⟶ cyclopropane-1-carboxylic acid.

[1] *J. Chem. Soc.*, 1885, **47**, 815. [2] *Ibid.*, 1899, **75**, 921.
[3] *Bull. Acad Roy. Belg.*, 1901, 249 ; 1902, 36.

As no trimethylene chlorobromide, $ClCH_2 \cdot CH_2 \cdot CH_2 \cdot Br$, was available when the experiments were started, we substituted trimethylene bromide, $BrCH_2 \cdot CH_2 \cdot CH_2 \cdot Br$, and carried out the following series of reactions :—



The trimethylene bromide was prepared from commercial trimethylene-glycol by heating with constant boiling hydrobromic acid and sulphuric acid according to Kamm and Marvel's method.[1] The yields varied from 77-88 per cent. of the theoretical and the boiling point was 158-161° under a pressure of 682 mm.

Bromobutyronitrile was made by Derick and Hess's modification[2] of Gabriel's method.[3] The former authors give the yield of nitrile as 42 per cent. of the theoretical, but we have increased this to 60-66 per cent. Table II gives the yields obtained in individual experiments.

TABLE II.

Yields of 3-bromobutyronitrile.

Experimenter	Grams of Trimethylene bromide used	Grams of Potassium cyanide	Grams of Trimethylene bromide recovered	Grams of 3-bromobutyro nitrile	Percentage of theoretical yield
Derick and Hess	404	65	175	70	42
Advani ...	400	65	217	70	50
Do. ...	200	41	109	49	66
Do. ...	200	41	112	44	60
Do. ...	220	50	105	55	64

The following is a short description of the method :—

A quantity (41 grams) of finely powdered 98-100 per cent. potassium cyanide (1·25 molecules) was shaken with 500 cc. of anhydrous methyl alcohol until almost completely dissolved, 200 grams of

[1] *J. Amer. Chem. Soc.*, 1920, **42**, 307.

[2] *Ibid.*, 1918, **40**, 547.

[3] *Ber.* 1889, **22**, 3336.

trimethylene bromide (2 mols.) were added and the whole heated in a reflux apparatus on a water bath for six to seven hours. The precipitated potassium bromide was removed, washed with a little anhydrous methyl alcohol, and the alcohol distilled off from the filtrate. The residual liquid was dried with calcium chloride and then distilled under reduced pressure. The first fraction passed over below 70° at 11 mm. pressure and consisted of trimethylene bromide and was followed by the bromonitrile which boiled at 80-85° under 11 mm. pressure.

The next two operations were carried out according to the methods of Dalle [1] and Bruylants,[2] using 3-bromobutyronitrile instead of the corresponding chloro-compound.

Sixty-five grams of powdered potassium hydroxide were placed in a 200 cc. distilling flask heated in an oil bath at 180° and ninety grams of the nitrile were run in drop by drop during the course of 1·5 hours. As soon as the drops began to fall distillate collected and a total of twenty-five grams of distillate were obtained in the form of two distinct layers. The intermediate compound was not purified, but twenty-five grams of finely powdered potassium hydroxide were added to the total distillate and the whole heated over a microburner for two hours. An extremely vigorous reaction took place and on cooling the product solidified with the exception of a few cc. of red-coloured oil. A small quantity of water was added and the flask fitted with an air condenser heated on the sand bath for two hours. The product was then acidified, extracted with ether and the ether removed and the residual oil distilled. From ninety grams of the original bromonitrile only ten grams of an acid boiling at 176-179° under a pressure of 686 mm. were obtained, corresponding with a 25 per cent. yield.

Since the completion of the experimental work just described two papers dealing with cyclopropanecarboxylic acids have appeared. In the first, by Dox and Yoder,[3] a modification of Perkin's method is described by means of which the yield of ester of the dicarboxylic acid is raised from 27 to 40 per cent. These authors did not hydrolyse the ester nor yet prepare the monocarboxylic acid. In the second paper by Jones and Scott [4] experiments are described using ethyl malonate and also ethyl cyanoacetate. They recommend the latter, also efficient stirring and omission of washing to remove colour. The yield of ethyl 1-cyano-cyclopropane-1-carboxylate is given as 76 per cent. of the theoretical as compared with 55–65 per cent. in our experiments. They do not give the yields of dibasic acid obtained on hydrolysing the cyano-ester, but in preparing the monobasic acid

[1] *Rec. trav. chim.*, 1902, **21**, 126.
[2] *Ibid.*, 1909, **28**, 183.
[3] *J. Amer. Chem. Soc.*, 1921, **43**, 2097.
[4] *Ibid.*, 1922, **44**, 413

they distilled the dibasic acid under reduced pressure and obtained after two distillations eleven grams of monobasic acid boiling at 182-184°, corresponding with 47 per cent. of the theoretical yield from the dibasic acid.

Cyclobutane-1-carboxylic Acid.

In the earlier experiments Perkin's method[1] of synthesis was adopted. Although the yields of dibasic acid were much better than in the case of the cyclopropanedicarboxylic acid, there were appreciable losses in the conversion of the dibasic into the monobasic acid. Experiments were also made using ethyl cyanoacetate in place of ethyl malonate but the hydrolysis of the cyanocyclobutanecarboxylic ester did not proceed smoothly. Dox and Yoder's method[2] was finally adopted and the following is a brief description of the process :—

A solution containing eighty grams of ethyl malonate and twenty-three grams of sodium dissolved in 300 cc. of 99 per cent. ethyl alcohol was gradually added to 105 grams of trimethylene bromide dissolved in 50 cc. of absolute alcohol, and contained in a reflux apparatus placed in a water bath at 80° and provided with an arrangement for vigorously stirring the mixture. Two hours were required for adding the whole of the sodium derivative and the stirring was continued for a further period of two hours. At the end of this time a few drops of the liquid when diluted with water showed only a very slightly alkaline reaction. Most of the alcohol was distilled off whilst the stirrer was kept working and then sufficient water was added to dissolve the sodium bromide and the mass extracted five times with ether. After washing, drying and removing the ether 112 grams of residual oil were obtained and were distilled under reduced pressure when a fraction of seventy grams boiling at 90-110° under 9 mm. pressure was isolated and this on redistillation gave forty-nine grams of a fragrant smelling oil boiling at 100-110° under 12 mm. pressure, corresponding with a 50 per cent. yield as compared with Dox and Yoder's 42 per cent.

For hydrolysing the dibasic ester Perkin's method was followed. Thirty-three grams of the ester were saponified with thirty grams of potassium hydroxide dissolved in 20 cc. of water and 180 cc. of 95 per cent. alcohol by heating in a reflux apparatus on a boiling water bath for three hours. After the usual procedure twenty grams of a solid acid melting at 152-154° were obtained, corresponding with a yield of 83 per cent. of the theoretical, and on distilling the dibasic acid from

[1] *J. Chem. Soc.*, 1887, **51**, 8, 229.

[2] *J. Amer. Chem. Soc.*, 1921, **43**, 680.

a small distilling flask with the aid of a microburner nine grams of an acid boiling at 190-192° under 685 mm. pressure were obtained, corresponding with a 65 per cent. yield, so that the yield of monobasic acid calculated on the weight of ethyl malonate used is only 27 per cent. of the theoretical.

Cyclopentane-1-carboxylic Acid.

Two methods are available for the preparation of this acid. One by Wislicenus and Gartner[1] starts with calcium adipate and passes through the stages ketone, secondary alcohol, alkyl iodide, nitrile, carboxylic acid. The second method due to Haworth and Perkin[2] consists in the condensation of tetramethylene bromide, 1:4-dibromobutane, with the sodium derivative of ethyl malonate. On account of the high price of adipic acid the latter method was selected. Two methods are available for preparing the 1 : 4-dibromobutane. The one due to Hamonet[3] makes use of β-chloropropionic acid which is difficult to prepare and hence the second method due to Braun and Beschke,[4] and the starting point of which is trimethylene bromide, was adopted.

1:4-*Dibromobutane.*

The preparation of this bromide is tedious, but after several weeks' work sixty-five grams were obtained. The various steps in the preparation are indicated in the following scheme :—

Trimethylene bromide $BrCH_2 \cdot CH_2 \cdot CH_2Br$ —(1)→ 3-Phenoxypropyl bromide $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2Br$

—(2)→ 3-Phenoxypropyl cyanide $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CN$ —(3)→ 4-Phenoxy-*n*-butylamine $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$

—(4)→ 4-Phenoxy-benzoyl-*n*-butylamine $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NHBz$ —(5)→ 4-Phenoxy-*n*-butyl chloride $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2Cl$

—(6)→ 1 : 4-Diphenoxy-*n*-butane $OPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OPh$ —(7)→ 1 : 4-Dibromo-*n*-butane $CH_2Br \cdot CH_2 \cdot CH_2 \cdot CH_2Br$

As Braun and Beschke do not give yields and experimental details for all seven reactions, we record in Table III the yields we have obtained.

[1] *Annalen*, 1893, **275**, 333.
[2] *Ber.*, 1893, **26**, 2246.
[3] *Compt. rend.*, 1901, **132**, 346.
[4] *Ber.*, 1906, **39**, 4357.

TABLE III.

Percentage yields of products in the different stages in preparation of 1 : 4-dibromobutane.

No. of Reaction	Change	Percentage yield of product
1	Trimethylene bromide to phenoxy bromide ...	65 to 75
2	Phenoxy bromide to phenoxy cyanide ...	65 to 75
3 and 4	Phenoxy cyanide to benzoyl derivative of 4-phenoxy-1-butylamine.	68 to 80
5	Benzoyl derivative to 4-phenoxy-butyl chloride ...	50 to 60
6	Phenoxy chloride to diphenoxybutane ...	80 to 90
7	Diphenoxybutane to 1 : 4-dibromobutane ...	60 to 70

Braun and Beschke report a 70 per cent. yield in reaction 4, a quantitative yield in No. 5, but no yield is given for Nos. 6 or 7. They give details of reactions 1 to 4, but no details for reactions 5–7. Details for these latter reactions are as follows :—

Eighteen grams of 4-phenoxy-*n*-butyl chloride, boiling at 129° under a pressure of 4 mm.,[1] were added to a sodium phenoxide solution prepared by dissolving 4·6 grams of sodium in 75 cc. of absolute alcohol and adding nineteen grams of phenol. The whole was boiled for four hours in a reflux apparatus on the water bath, then allowed to cool and the solid removed by filtration. The alcoholic filtrate was again boiled for four hours, cooled and filtered. The sodium chloride was removed from the solid by washing with water, and the yields of diphenoxy compound were, from the first operation 75 to 80 per cent. and from the second 5 to 10 per cent. of the theoretical. The melting point of the uncrystallised product, viz. 98 to 99°, indicated that it was practically pure as Braun and Beschke give the melting point as 99° after recrystallisation.

A few experiments were also made with 1-chloro-3-bromopropane (trimethylene chlorobromide) obtained from Kahlbaum, and it was found that in order completely to replace the chlorine by cyanogen it was necessary to boil the reaction mixture for twenty-four hours or more as compared with eight hours for the phenoxy bromide. Comparative experiments proved that it is more convenient first to replace bromine by cyanogen and then chlorine by phenoxy, than to replace bromine by phenoxy and then chlorine by cyanogen.

[1] Braun and Beschke give 147° at 12 mm.

The use of 1-chloro-3-bromopropane does not appreciably affect the final yields; but an important point is that in the first operation, whichever it may be, replacement of Br by CN or OPh, there is no necessity for using double the theoretical quantity of the chlorobromide, as was found advisable in the case of trimethylene bromide, in order to avoid the formation of large quantities of 1 : 3 dicyanopropane or of 1 : 3-diphenoxypropane.

In the final reaction, No. 7, the following process was found to be most convenient:—

Twelve grams of the diphenoxybutane and 25 cc. hydrobromic acid saturated at 0° (66 per cent. hydrogen bromide) were carefully sealed in a thick-walled glass tube and heated at 130-140° for six to eight hours. The yield of 1:4-dibromobutane varied from 60 to 70 per cent. and a preliminary examination failed to detect the formation of 4-phenoxybutyl bromide.

After these experiments were concluded a paper was published by Marvel and Tanenbaum [1] in which improvements in Braun and Beschke's method are described. The first two stages in their preparation are as given above, but their yields are better, viz. 80 to 85 per cent. in the first operation and 90 to 94 per cent. in the second. In the first reaction instead of using absolute alcohol and sodium they use a concentrated aqueous solution of sodium hydroxide, which they add drop by drop to a mixture of trimethylene bromide, phenol and water which is kept boiling and vigorously stirred. In the second operation they use sodium cyanide and not the potassium salt. Both these changes appear to be distinct improvements. In reaction 3 instead of reducing the nitrile they convert it into ethyl 4-phenoxy-*n*-butyrate, $OPh{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2Et$, by refluxing with a mixture of ethyl alcohol and sulphuric acid and obtain an 80 per cent. yield. The ester is then reduced by means of sodium and a mixture of alcohol and toluene [2] to 4-phenoxy-*n*-butyl alcohol, the yield being 68 per cent. provided the alcohol used is quite free from water, as even small amounts of the latter reduce the yield to 40 per cent. The phenoxybutyl alcohol is converted into a mixture of 1:4-dibromobutane and 4-phenoxybutyl bromide, $OPh{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$, by treatment with a mixture of concentrated sulphuric acid and hydrobromic acid of constant boiling point or with hydrobromic acid of specific gravity 1·57. The yield of the dibromo-compound in this operation is 40 per cent. and a 40 per cent. yield of the monobromo-compound is also obtained.

[1] *J. Amer. Chem. Soc.*, 1922, **44**, 2645.
[2] Levene and Allen, *J. biol. Chem.* 1916, **27**, 433.

The authors mention that they have been able to obtain an 80 to 85 per cent. yield of 4-phenoxybutylamine by reducing the nitrile with sodium in a mixture of alcohol and toluene. If this is correct, then by Braun and Beschke's method of directly reducing the nitrile to the amine, benzoylating and carrying out the reactions as indicated on p. 50 the final yield of 1: 4-dibromobutane would be 25 to 30 per cent. of the theoretical, assuming the yields to be those given by Marvel and Tanenbaum, whereas their own method of conversion into the ester followed by reduction, etc., give a final yield of only 16 to 20 per cent. of the dibromo derivative.

Condensation of 1:4-Dibromobutane with Ethyl Sodiomalonate.

The condensation of ethyl sodiomalonate with pure 1:4-dibromobutane has apparently never been carried out, as the reagent used by Perkin contained 25 per cent. of 1:5-dibromopentane. The procedure we adopted was as follows :—

To a well-cooled[1] solution of 4·6 grams of sodium in 100 cc. of 99 per cent. alcohol a mixture of eighteen grams of ethyl malonate and twenty-two grams of 1:4-dibromobutane was added. The flask was finally placed in a water bath at 80° and the contents vigorously stirred for two to three hours, at the end of which time a few drops of the liquid when diluted with water showed a neutral reaction. The precipitated sodium bromide, the yield of which was theoretical, was removed and washed with absolute alcohol. From the alcoholic liquid and washings twenty-three grams of an oil were obtained from which on distillation twenty grams of a fragrant oil boiling at 115 to 120° under a pressure of 16 mm. were obtained. This corresponds with a 90 per cent. yield and the residue in the flask which solidified on cooling was too small for investigation.

To hydrolyse the dibasic ester twenty grams of the oil were boiled for three hours with twenty grams of potassium hydroxide, 10 cc. of water and 50 cc. of methyl alcohol. After removal of the methyl alcohol and acidifying the alkaline liquid with hydrochloric acid the solution was extracted eight times with ether. The yield of dibasic acid was only nine grams corresponding with a 62 per cent. yield. Its melting point was 178-180°. When thirteen grams of the dibasic acid were distilled from a small flask, 8·5 grams of the monobasic acid, cyclopentane-1-carboxylic acid, were obtained as an oil boiling at 207 to 211° under a pressure of 687 mm. and corresponding with a 90 per cent. yield.

[1] This cooling was necessary as otherwise the reaction was extremely violent and most of the reaction mixture was ejected from the flask.

Cyclohexane-1-carboxylic Acid.

A small amount of this acid was prepared from benzoic acid by Perkin's method [1] of reduction with sodium and amyl alcohol and destruction of unsaturated acids with cold saturated permanganate solution. The yields were poor, varying from 28 to 33 per cent. of the theoretical, and the acid boiled at 226–228° under a pressure of 683 mm., but did not solidify until impregnated with a crystal of the solid acid.

Ethylpropylacetic Acid.

This acid was prepared from a specimen of Schuchardt's ethylpropylmalonic acid melting at 107° instead of 117°. Fifty grams of the acid heated at 180° in an oil bath gave thirty-four grams of an oil with a boiling point ranging over 20° and on fractional distillation the monobasic acid was obtained as an oil boiling at 204-206° under a pressure of 683 mm.

III. PURIFICATION OF MATERIALS.

Acids.—All the acids were fractionally distilled before use. Table IV gives the boiling points of the acids actually used. These boiling points were determined with the aid of short standard thermometers.

TABLE IV.

Boiling Points of Acids.

Acid	Boiling point in degrees Centigrade	Pressure in mm.
Propionic	136·4—136·8	683
Isobutyric	150·0—150·4	683
Methylethylacetic	171—173	683
Diethylacetic	187—189	683
Ethylpropylacetic	204—206	683
Cyclopropane-carboxylic	175·0—176·4	683
Cyclobutane-carboxylic	190—191	683
Cyclopentane-carboxylic	208—210	683
Cyclohexane-carboxylic	226—228	683

[1] *J. Chem. Soc.*, 1905, 87, 663.

Ethyl Alcohol.—The alcohol used had a concentration of 98·9 per cent. by weight and was dehydrated by repeatedly heating with fresh amounts of calcium turnings. In the first operation 2·5 litres of the alcohol were boiled in a reflux apparatus for eight hours with twenty grams of fresh calcium turnings and the alcohol distilled. The process of heating with calcium and distillation was repeated with fifteen grams, then with ten grams and finally with five grams.

After the third treatment the alcohol had the density

$$D_4^{25} = 0{\cdot}78511 \text{ to } 0{\cdot}78506$$

corresponding with 100 per cent. of ethyl alcohol.[1] After the fourth treatment the colour of the alcohol was invariably pale yellow to golden yellow and no precipitate of calcium hydroxide could be observed. In all preparations of 100 per cent. alcohol care was taken that this stage was reached.

IV. ESTERIFICATION.

The thermostat used was the same as the one already described,[2] and was regulated for 25°.

The method adopted was slightly different from that used by Sudborough and Lloyd.[3] A Jena glass bottle, which had been previously kept in contact with hydrochloric acid for some time, was used for keeping the main reaction solution and at intervals portions were removed for titration by means of a 20 cc. pipette. For this purpose standard sodium hydroxide, kept in a bottle protected from atmospheric carbon dioxide, was used with phenolphthalein as indicator.

Goldschmidt [4] was the first to observe the great anticatalytic effect of water on esterification and later Goldschmidt and Udby[5] were able to show that the equation for a unimolecular reaction—

$$K = 1/t \log a/a\text{-}x \qquad \text{i}$$

never gives constant values when anhydrous alcohol is used. They have propounded a theory of esterification of acids according to which it is not the free hydrogen ion which is the catalyst but a compound of this ion with the alcohol molecule—

$$C_2H_5{\cdot}OH + H^{\cdot} \rightleftarrows C_2H_5{\cdot}OHH^{\cdot}$$

Thus the total hydrogen ions, that is the sum of the free and combined ions, remains constant. On the addition of water it is assumed

[1] *Bull. Bur. Standards*, 1913, **9**, 424.

[2] Cumming, *Trans. Faraday Soc.*, 1911, **7**, 257; this Journal, 1915, **1**, 110; 1921, **4**,185; 1922, **5**, 7.

[3] *J. Chem. Soc.*, 1899, **75**, 471.

[4] *Ber.*, 1896, **29**, 2208

[5] *Zeitsch. physikal. Chem.*, 1907, **60**, 728.

that the water molecules tend to rob the complex ions $C_2H_5 \cdot OHH^{\cdot}$ of their hydrogen ions

$$C_2H_5 \cdot OHH^{\cdot} + H_2O \longrightarrow C_2H_5 \cdot OH + H_2OH^{\cdot}$$

and thus diminish the concentration of the active catalyst

$$C_2H_5 \cdot OHH^{\cdot}.$$

On these premises they have worked out a complex formula which gives more constant values for K. They have also deduced a modified form of this equation, viz.—

$$K_c t = (n + r + a) \log a/a\text{-}x \quad -x \qquad \text{ii}$$

where K_c is the constant at concentration c of the catalyst.

t is the time in hours.

n is the number of gram molecules of water at the beginning.

r is a constant known as the hydrolytic constant and is equal to 0·15 in the case of most acids examined by Goldschmidt and Udby.

a is the original concentration of the organic acid in gram molecules per litre.

x is the change in concentration of the organic acid expressed in gram molecules per litre.

In our experiments we have used both the ordinary equation for a unimolecular reaction, viz., i, and also Goldschmidt and Udby's modified formula ii. As anhydrous alcohol was used, in all our experiments the value of n is zero.

In order to ascertain if our results are directly comparable with those of Goldschmidt and Udby we have determined the esterification constant of propionic acid and compared our values with theirs. With a concentration of hydrogen chloride of 0·02 N. we obtained the value 0·547 calculated for 0·1 N. catalyst, and using 0·1 N. hydrogen chloride a value 0·530. Using this latter concentration of catalyst Goldschmidt obtained the value 0·550, so that the two values agree within about 3·5 per cent.

In Tables V–XIII the various columns 1 to 5 indicate—

COLUMN

1 Time in hours.
2 Value of a-x in cc.
3 Percentage conversion into ester.
4 Value of K calculated from equation i.
5 Value of K calculated from equation ii.

A = Normality of the organic acid.

B = Normality of the alkali used for titration.

C = Normality of the hydrogen chloride.

a = Number of cc. of the alkali required for neutralising the organic acid in 20 cc. of solution at zero time.

V. PROPIONIC ACID.

1					2				
A = 0·0986 N. B = 0·0677 N.			C = 0·0199 N. a = 29·15.		A = 0·0850 N. B = 0·0684 N.			C = 0·1045 N. a = 24·85.	
1	2	3	4	5	1	2	3	4	5
0	29·15	...	...	...	0	24·85	...	...	...
·5	20·77	28·7	0·2940	0·111	·1	17·65	29·0	1·477	0·555
·75	17·87	38·7	0·2832	0·111	·2	12·95	47·9	1·415	0·563
1	15·67	46·2	0·2694	0·111	·3	9·75	61·8	1·355	0·561
1·25	13·57	53·4	0·2552	0·104	·5	5·85	76·5	1·256	0·550
1·75	10·62	63·6	0·2504	0·108	·7	3·60	85·5	1·199	0·547
2	9·42	67·7	0·2452	0·107	·9	2·20	91·1	1·170	0·547
2·25	8·32	70·8	0·2420	0·107	1·1	1·40	94·4	1·136	0·542
4·25	3·52	87·9	0·2160	0·109	1·5	0·70	97·2	1·037	...

Mean value of K = 0·109 = 0·557

Mean value calculated for 0·1 N. catalyst = 0·547 = 0·530

VI. ISOBUTYRIC ACID.

1					2				
A = 0·0988 N. B = 0·0677 N.			C = 0·0215 N. a = 29·2.		A = 0·0983 N. B = 0·0677 N.			C = 0·0206 N. a = 29·05.	
1	2	3	4	5	1	2	3	4	5
0	29·2	...	...	...	0	29·05	...	...	...
0·5	26·1	10·6	0·0976	0·0349	1	23·50	19·1	0·0920	0·0336
1·0	23·55	19·4	0·0934	0·0320	2	19·50	34·3	0·0866	0·0334
1·5	21·40	26·7	0·0900	0·0340	3	46·40	43·5	0·0828	0·0331
2·0	19·5	33·2	0·0877	0·0339	4	14·00	51·8	0·0793	0·0326
2·5	17·85	38·9	0·0852	0·0334	5	12·05	58·5	0·0764	0·0322
3·0	16·45	43·7	0·0831	0·0333	6	10·40	64·2	0·0744	0·0321
3·5	15·25	47·8	0·0806	0·0328	7	9·00	69·0	0·0727	0·0319
4·0	14·15	51·6	0·0787	0·0324	8	7·90	72·8	0·0707	0·0318
5·0	12·15	58·4	0·0762	0·0321					

Mean value of K = 0·0331 = 0·0326

Mean value calculated for 0·1 N. catalyst = 0·156 = 0·156

3					4				
A=0·1002 N. B=0·0677 N.			C=0·0208 N. a=29·60.		A=0·1002 N. B=0·0677 N.			C=0·0208 N. a=29·60.	
1	2	3	4	5	1	2	3	4	5
1	27·65	6·6	...	...	2	25·15	15·0	0·0354	[0·0396]
3	23·00	22·3	0·0365	0·0342	3	23·30	21·3	0·0346	[0·0305]
4	21·35	27·9	0·0330	0·0331	4	21·60	27·0	0·0342	0·0322
5	19·75	33·3	0·0351	0·0335	5	20·10	32·1	0·0336	0·0318
7	17·00	42·6	0·0344	0·0331	6	18·70	36·8	0·0333	0·0318
9	14·65	50·5	0·0339	0·0330	8	16·20	45·3	0·0327	0·0316
10	13·65	53·9	0·0336	0·0329	10	14·15	52·2	0·0321	0·0313
11	12·75	56·9	0·0333	0·0327					
20	7·00	76·3	0·0313	0·0318					

Mean value of K=0·0330 =0·0317.

Mean value calculated for 0·1N. catalyst =0·160 =0·152.

VII. METHYLETHYLACETIC ACID.

1					2				
A=0·0907 N. B=0·0677 N.			C=0·0508. N. a=26·8.		A=0·0880 N. B=0·0677 N.			C=0·0508 N. a=26·0.	
1	2	3	4	5	1	2	3	4	5
2·5	18·90	29·5	0·0636	0·0237	2·5	19·40	25·4	0·0636	0·0237
3·5	16·80	37·3	0·0619	0·0234	3·5	18·20	30·0	0·0619	0·0234
4·5	15·05	43·9	0·0587	0·0227	4·5	16·20	37·7	0·0587	0·0227
6·0	12·90	51·9	0·0560	0·0221	6·0	14·55	44·0	0·0560	0·0221
7·0	11·70	56·3	0·0533	0·0216	7·0	12·45	52·1	0·0533	0·0216
8·0	10·70	61·1	0·0520	0·0214	9·0	11·25	56·7	0·0520	0·0214
10·0	9·00	66·4	0·0481	0·0202	10·0	9·60	63·1	0·0481	0·0202
12·0	7·55	71·8	0·0466	0·0198	12·0	8·90	65·8	0·0466	0·0198
24·5	3·80	88·7	0·0445	...	24·5	7·60	70·8	0·0445	...

3					4				
A=0·0906 N. B=0·0684 N.			C=0·1460 N. a=26·5		A=0·0906 N. B=0·0684 N.			C=0·1460 N. a=26·5	
1	2	3	4	5	1	2	3	4	5
1	18·60	29·8	0·1537	0·582	0·5	21·80	17·7	0·1654	0·0616
2	13·80	47·9	0·1417	0·568	2·5	11·90	55·1	0·1399	0·0570
3	10·50	60·4	0·1340	0·560	3·5	9·20	65·3	0·1316	0·0560
4	8·20	69·1	0·1274	0·550	4·5	7·10	73·2	0·1270	0·0556
5	3·40	87·2	0·1115	0·520	8·0	3·30	87·5	0·1131	0·0528

	1	2	3	4
Mean value of K	=0·0218	0·0222	0·0565	0·0551
Mean value calculated for 0·1 N. catalyst	=0·0429	0·0437	0·0387	0·0380

VIII. DIETHYLACETIC ACID.

1

A = 0·1005 N. B = 0·0677 N. C = 0·0194 N. a = 29·7.

1	2	3	4	5
2	29·16	...	...	...
8	28·21	...	...	...
24	26·36	11·2	0·00215	0·000771
48	23·86	19·8	0·00198	0·000729
72	21·76	26·7	0·00188	0·000710
120	18·51	37·7	0·00171	0·000678

2

A = 0·1005 N. B = 0·0677 N. C = 0·0194 N. a = 29·7.

1	2	3	4	5
0	29·70	...	...	...
2	29·31	...	...	...
8	28·60	...	...	...
24	26·36	11·2	0·00215	0·000778
48	23·86	19·8	0·00198	0·000729
72	21·66	27·1	0·00190	0·000718
120	18·16	38·9	0·00178	0·000702
168	15·41	48·1	0·00169	0·000707
264	11·51	61·2	0·00156	0·000667

3

A = 0·1153 N. B = 0·0677 N. C = 0·0508 N. a = 34·05.

1	2	3	4	5
12	29·70	16·7	0·00494	0·00179
24	25·85	24·1	0·00498	0·00188
36	23·50	31·0	0·00447	0·00174
48	21·10	38·0	0·00433	0·00173
60	19·10	43·8	0·00419	0·00172
72	17·60	49·3	0·00398	0·00166
84	15·85	53·5	0·00395	0·00177
108	13·15	61·4	0·00383	0·00168

4

A = 0·0869 N. B = 0·0684 N. C = 0 1460 N. a = 25·40.

1	2	3	4	5
5	21·70	14·4	0·0135	0·00488
22	14·50	42·9	0·0111	0·00437
33	19·75	57·7	0·0113	0·00466
45·5	8·15	67·2	0·0108	0·00457
71	4·70	81·5	0·0101	0·00452

5

A, B, C and a as in No. 4.

1	2	3	4	5
9	19·60	22·8	0·0125	0·00462
22	14·5	42·9	0·0111	0·00437
33	10·80	57·5	0·0113	0·00466
46	8·00	68·6	0·0109	0·00467
71	4·90	80·3	0·0103	0·00464

	1	2	3	4	5
Mean value of K =	0·000722	0·000725	0·00175	0·00453	0·00459
Mean value calculated for 0·1 N. catalyst =	0·00372	0·00374	0·00344	0·00312	0·00314

IX. ETHYLPROPYLACETIC ACID.

1					2				
A=0·1136 N. B=0·0684 N.			C=0·1105 N. a=33·20.		A=0·1136 N. B=0·0684 N.			C=0·1069 N. a=33·20.	
1	2	3	4	5	1	2	3	4	5
24	20·70	37·6	0·00855	0·00341	16	23·95	27·8	0·00887	0·00290
48	14·00	57·7	0·00781	0·00333	31	18·55	44·1	0·00815	0·00353
67	10·60	68·1	0·00740	0·00334	48	14·45	57·4	0·00772	0·00332
81	8·70	73·8	0·00718	0·00333	73	9·70	71·8	0·00732	0·00334
119·25	6·80	81·6	0·00617	0·00297	117·5	4·95	85·1	0·00703	0·00344

3					4				
A=0·1368 N. B=0·0684 N.			C=0·3256 N. a=10·00.		A=0·2121 N. B=0·0684 N.			C=0·3256 N. a=15·50 .	
1	2	3	4	5	1	2	3	4	5
9·5	6·10	39·0	0·0226	0·0093	9	9·70	37·4	0·0226	0·0100
22	3·40	66·0	0·0217	0·0102	22	6·60	63·9	0·0201	0·0106
28·25	2·50	75·0	0·0213	0·0104	28	4·30	73·3	0·0198	0·0110
47	1·10	89·0	0·0204	0·0108	47	1·90	87·7	0·0196	0·0123

	1	2	3	4
Mean value of K=	0·00335	0·00341	0·0105	0·0105.
Mean value calculated for 0·1 N. catalyst=	0·00303	0·00319	0·00322	0·00322.

X. CYCLOPROPANE-1-CARBOXYLIC ACID.

1					2				
A=0·0962 N. B=0·0677 N.			C=0·0202 N. a= 28·40.		A, B, C, and a as in No. 1.				
1	2	3	4	5	1	2	3	4	5
0·5	27·72	2·4	0·0210	...	1	27·07	4·7	0·0208	0·00729
1	27·12	4·5	0·0201	0·00707	3	24·82	11·5	0·0195	0·00701
3	24·87	11·4	0·0192	0·00690	5	22·87	19·5	0·0188	0·00692
5	22·87	19·5	0·0188	0·00692	8	20·38	28·2	0·0180	0·00682
8	20·28	28·6	0·0183	0·00695	11	18·22	35·8	0·0175	0·00680
11	18·22	35·8	0·0175	0·00680	14	16·42	42·2	0·0170	0·00675
14	16·37	42·4	0·0170	0·00675	17	14·87	47·6	0·0165	0·00673
17	14·82	47·8	0·0166	0·00673	24	11·92	58·0	0·0157	0·00670
24	11·87	58·2	0·0158	0·00663	36	8·37	70·5	0·0147	...
36	8·52	70·0	0·0145	...	...	...	...	...	...

3

A = 0·0990 N.
B = 0·0684 N.

C = 0·1094 N.
α = 28·95.

1	2	3	4	5
1·0	23·55	18·7	0·0897	0·0330
2·0	19·55	32·5	0·0853	0·0353
3·0	16·25	43·9	0·0836	0·0338
4·0	13·65	52·9	0·0817	0·0335
5·0	11·60	59·9	0·0794	0·0337
6.0	9·85	66·0	0·0781	0·0339
7·0	7·45	74·3	0·0786	0·0340
9·5	5·35	81·5	0·0772	0·0357
11·5	4·30	85·2	0·0720	0·0340

4

A = 0·0739 N.
B = 0·0684 N.

C = 0·1061 N.
α = 21·6.

1	2	3	4	5
0·5	18·60	13·9	0·1300	0·0464
1·5	15·50	28·3	0·0960	0·0356
2·5	12·80	40·7	0·0910	0·0356
3·5	10·60	52·9	0·0884	0·0348
6·0	6·80	68·5	0·0837	0·0347

5

A, B, C and α same as in No. 4.

1	2	3	4	5
1	16·80	22·2	0·1092	0·0399
2	13·90	35·7	0·0958	0·0362
3	11·55	46·5	0·0906	0·0353
4	9·65	55·3	0·0875	0·0349
6	6·80	68·5	0·0837	0·0347

	1	2	3	4	5
Mean value of K =	0·00684	0·00680	0·0341	0·0352	0·0353.
Mean value calculated for 0·1 N catalyst =	0·0339	0·0337	0·0324	0·0332	0·0332.

XI. CYCLOBUTANE-1-CARBOXYLIC ACID.

1

A = 0·1005 N.
B = 0·0677 N.

C = 0·0193 N.
α = 29·68.

1	2	3	4	5
1·0	16·10	45·8	0·2657	0·107
1·25	14·20	52·2	0·2552	0·105
1·5	12·50	57·9	0·2504	0·106
1·75	11·00	63·0	0·2460	0·106
2·0	9·85	66·8	0·2396	0·105
2·5	7·90	73·4	0·2299	0·103
3·0	6·30	78·3	0·2244	0·103
4·0	4·75	84·0	0·1989	0·094
5·0	2·85	90·4	0·2015	0·098

2

A = 0·1041 N.
B = 0·0677 N.

C = 0·0193 N.
α = 30·78.

1	2	3	4	5
0·25	25·85	16·0	0·3028	0·110
0·5	22·20	27·9	0·2836	0·108
0·75	19·35	37·1	0·2687	0·108
1·0	17·00	43·5	0·2578	0·105
1·5	13·10	57·4	0·2472	0·105
2·0	10·40	66·2	0·2356	0·103
2·5	8·35	72·9	0·2266	0·103
3·0	6·75	78·1	0·2196	0·101
6·0	2·15	92·8	0·1900	0·095

3

A=0·0809 N. B=0·0684 N.			C= 0·1069 N. a=23·65.	
1	2	3	4	5
0·1	16·65	29·6	1·524	0·570
0·3	8·95	62·1	1·407	0·580
0·5	5·10	78·4	1·332	0·582
0·6	3·85	83·7	1·313	0·585
0·7	2·95	87·5	1·291	0·586
1·0	1·35	94·3	1·244	0·587

	1	2	3
Mean value of K=0·105		0·105	0·582.
Mean value calculated for 0·1 N. catalyst=0·544		0·544	0·544.

XII. CYCLOPENTANE-I-CARBOXYLIC ACID.

1

A=0·0811 N. B=0·0684 N.			C= 0·0192 N. a=23·70.	
1	2	3	4	5
1	18·00	24·0	0·1194	0·0441
2	14·20	40·1	0·1112	0 0430
4	9·30	60·8	0·1015	0·0418
7	5·20	78·1	0·0941	0·0388

2

A, B, C and a as in No. 1				
1	2	3	4	5
1	18·20	23·2	0·1146	0·0436
2	14·40	39·2	0·1082	0·0427
3	11·60	51·0	0·1034	0·0422
4	9·50	59·9	0·0992	0·0416

3

A=0·0960 N. B=0·0684 N.			C= 0·1105N. a=28·05.	
1	2	3	4	5
0·25	20·25	27·8	0·5660	0·216
0·5	15·20	45·8	0·5324	0·215
0·75	11·45	59·2	0·5192	0·214
1·25	6·90	75·4	0·4872	0·218

4

A, B, C and a as in No. 3.				
1	2	3	4	5
0·25	20·10	28·3	0·5792	0·219
0·5	15·20	45·8	0·5324	0·215
0·75	11·60	58·6	0·5112	0·214
1	8·95	68·3	0·4986	0·217

	1	2	3	4
Mean value of K=0·0429		0·0425	0·216	0·216.
Mean value calculated for 0·1 N. catalyst=0·223		0·222	0·196	0·196.

XIII. CYCLOHEXANE-I-CARBOXYLIC ACID.

1

A = 0·0954 N. B = 0·0677 N. C = 0·0212 N. α = 28·20.

1	2	3	4	5
1	24·74	12·3	0·0568	0·0204
2	22·14	21·5	0·0525	0·0195
3	19·89	29·5	0·0505	0·0192
4	18·04	36·0	0·0485	0·0188
6	14·94	47·0	0·0459	0·0182
8	12·54	55·5	0·0440	0·0182
10	10·59	62·4	0·0425	0·0181

2

A = 0·0963 N. B = 0·0677 N. C = 0·0209 N. α = 28·45.

1	2	3	4	5
2	22·70	21·2	0·0490	0·0186
4	18·65	34·5	0·0459	0·0181
6	15·55	45·4	0·0437	0·0177
8	13·20	53·6	0·0417	0·0174
10	11·20	60·6	0·0419	0·0181
12	9·60	66·3	0·0406	0·0178
14	8·40	71·5	0·0382	0·0170

3

A = 0·1039 N. B = 0·0677 N. C = 0·1054 N. α = 30·70.

1	2	3	4	5
0·5	23·75	22·6	0·2230	0·0836
0·75	21·05	31·4	0·2184	0·0846
1·0	18·70	39·1	0·2153	0·0855
1·5	14·85	51·6	0·2102	0·0868
2·0	12·15	60·5	0·2013	0·0866
2·5	9·85	67·9	0·1974	0·0874
3·5	6·85	77·7	0·1861	0·0861
5·0	4·25	86·2	0·1718	0·0828
7·0	2·55	91·7	0·1720	0·0872

	1	2	3
Mean value of K =	0·0183	0·0178	0·0856.
Mean value calculated for 0·1 N. catalyst =	0·0863	0·0852	0·0812.

Table XIV gives the mean values of K calculated for 0·1N. catalyst and using approximately 0·1N. catalyst for the reaction for the different acids as calculated by Goldschmidt and Udby's formula and arranged in descending order of magnitude. In the same table are given the values for the dissociation constants of the acids multiplied by 10^5.

TABLE XIV.

Acid	Velocity Constant K	Dissociation Constant × 10^5
Cyclobutane-1-carboxylic acid	0·544	1·82 [1]
Cyclopentane-1-carboxylic acid	0·196	...
Isobutyric acid	0·156	1·62 [2]
Cyclohexane-1-carboxylic acid	0·0812	1·26 [3]
Methylethylacetic acid	0·0384	1·68 [2]
Cyclopropane-1-carboxylic acid	0·0324	1·44 [4]
Diethylacetic acid	0·00313	2·02 [2]
Ethylpropylacetic acid	0·00311	...

DISCUSSION OF RESULTS.

1. The values for propionic acid prove that the values given in this paper are directly comparable with those given by Goldschmidt and Udby.

2. The values recorded in the Tables V—XIII confirm Goldschmidt and Udby's conclusion that when their equation

$$K = {}^1/_{ct}\,[(n+r+a)\,\log a/a\text{-}x - x]$$

is used, the results vary somewhat with the concentration of the hydrogen chloride used as catalyst. With 0·02 N. hydrogen chloride the values for K tend to diminish as the time increases; with 0·1 N. catalyst the values are fairly constant or slightly irregular, but with more concentrated hydrogen chloride, e.g. above 0·2 N., the tendency is for the values of K to increase with the time.

3. They also confirm another conclusion drawn by Goldschmidt and Udby, viz. that the constant is not absolutely proportional to the concentration of the catalyst. With lower concentrations of catalyst, e.g. 0·02 N., the constants are relatively higher than with 0·1 N. solution.

[1] Walker, *J. Chem. Soc.*, 1892, **61**, 705.
[2] Billitzer, *Zeitsch. physikal. Chem.*, 1902, **40**, 542.
[3] Lumsden, *J. Chem. Soc.*, 1905, **87**, 90.
[4] Dalle, *Bull. Acad. roy. Belg.*, 1902, 36.

4. It will be noted, however, that in the case of an acid which esterifies rapidly the constants obtained with a 0·02 N. catalyst do not tend to fall to the same extent as in the slower reactions. It is, therefore, probable that the increase or decrease of the values of K with the time is rather a question of time than of concentration of the catalyst.

A diminution with an increase in the time might be due to a diminution of the concentration of the catalyst due to the formation of ethyl chloride and water, but blank experiments made at 25° with ethyl alcohol and hydrogen chloride showed no diminution in acidity even after several days.

5. In the case of the disubstituted acetic acids examined, isobutyric acid is esterified most readily and diethyl and ethylpropyl least readily. Apparently the methyl group has the smallest inhibiting effect and the ethyl and *n*-propyl groups have practically the same effect. This is in harmony with the fact previously established that in the case of the normal fatty acids an ethyl or *n*-propyl or any longer normal chain produces the same lowering of the rate of esterification of acetic acid.

We intend determining the esterification constants of the following series of acids in order to make quite sure that the same generalisation applies to the disubstituted acetic acid

Methylpropyl, dipropyl, methylhexyl.

6. The constants for the cyclic acids and those of the corresponding disubstituted acetic acids provide several interesting comparisons.

A table is subjoined—

Saturated Acid		Corresponding Cyclic Acid	
$CH_3 \diagdown CH \cdot CO_2H$ $CH_3 \diagup$	0·156	$CH_2 \diagdown CH \cdot CO_2H$ $CH_2 \diagup$	0·032
$CH_3 \diagup CH_2 \diagdown CH \cdot CO_2H$ $CH_3 \diagup$	0·038	$CH_2 \diagup CH_2 \diagdown CH \cdot CO_2H$ $CH_2 \diagup$	0·544
$CH_3 \cdot CH_2 \diagdown CH \cdot CO_2H$ $CH_3 \cdot CH_2 \diagup$	0·0031	$CH_2 \cdot CH_2 \diagdown CH \cdot CO_2H$ $CH_2 \cdot CH_2 \diagup$	0·196
$CH_3 \diagup CH_2 \cdot CH_2 \diagdown CH \cdot CO_2H$ $CH_3 \cdot CH_2 \diagup$	0·0031	$CH_2 \diagup CH_2 \cdot CH_2 \diagdown CH \cdot CO_2H$ $CH_2 \cdot CH_2 \diagup$	0·081

These give the ratios—

		Cyclic acid		*Corresponding saturated acid*
Tri-ring	...	0·25	:	1
Tetra ,,	...	13	:	1
Penta ,,	...	80	:	1
Hexa ,,	...	28	:	1

These results are in harmony with Menschutkin's on the acetylation of alcohols in so far as the greatest increase in the constants is noticed in the pentamethylene series and decreases in the hexamethylene. In our series there is also a diminution in the increase on passing to the cyclobutane series, but no comparison is possible with the results of acetylation of alcohols as Menschutkin examined no cyclobutane derivatives.

The most marked case is that of the cyclopropane series where the closing of the ring has actually produced a diminution in the rate of esterification.

7. If the cyclic acids alone are considered the ratios are as follows:—

Cyclopropane-carboxylic		acid	....	1
,, butane-	,,	,,	....	16
,, pentane-	,,	,,	....	7
,, hexane-	,,	,,	....	3

In other words the cyclobutane acid has the highest constant followed in order by the cyclopentane and hexane and propane acid.

It would be extremely interesting to extend the reactions examined by Menschutkin in the case of cyclopentane, cyclohexane and cycloheptane derivatives to the corresponding cyclic butane and propane compounds, in order to ascertain whether in these cases also the cyclopropane compounds occupy an anomalous position.

It is known that a 1 : 2-olefine linking has a marked effect on reducing the rate of esterification of a carboxylic acid, but as the unsaturated acids corresponding with cyclopropane-carboxylic acid, viz. vinylacetic acid, $CH_2{:}CH{\cdot}CH_2{\cdot}CO_2H$ and the crotonic acids $CH_3{\cdot}CH{:}CH{\cdot}CO_2H$ are well known, the possibility of the four having an unsaturated structure appears to be out of the question.

According to Thorpe and Deshapande,[1] Ingold, Perren and Thorpe[2] and also Power and Barrowcliff[3] certain cyclopropane

[1] *J. Chem. Soc.*, 1922, **121**, 1430. [2] *Ibid.*, p. 1767.
[3] *Ibid.*, 1905, **87**, 884; 1907, **91**, 557.

derivatives exist as tautomerides and it is possible that the low value for the esterification constant of cyclopropane-1-carboxylic acid may be attributed to tautomeric change of this type.

The abnormal esterification constant for the cyclopropane acid induced us to determine the constants of two different samples of the acid prepared by two different methods, viz. Perkin's and Henry's, but both, when carefully fractionated, gave the same results.

8. In Table VI, 3 and 4, an alcohol was used, the density of which $D_4^{25}=0{\cdot}78631$, indicated the presence of 99·45 per cent. of alcohol and 0·55 per cent. of water or 0·24 mols. per litre. The values of k obtained by using the ordinary equation for a unimolecular reaction are only about one-third of those obtained when absolute (100 per cent.) alcohol is used. The results also show that as the reaction proceeds the value of k does not decrease so rapidly as when absolute alcohol is employed.

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