356. *Mechanism of, and Constitutional Factors controlling, the Hydro-
lysis of Carboxylic Esters. Part VII. cycloPentanedicarboxylic
Esters. Attempted Check on the Calculation of Molecular Dimensions.*

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IT has been suggested in previous parts of this series that the velocity coefficients of the
hydrolysis of carboxylic esters are connected with the spatial configuration of the esters in
such a way as to permit the calculation of molecular dimensions on the following basis.
Two esters are compared which differ only in the circumstance that one contains a polar
group not possessed by the other. This constitutional difference creates a difference with
respect to the potential energy of the same polar reagent at the moment of its reaction with
each ester. In certain circumstances this potential-energy difference can be calculated.
If it can, the assumption may be made that, owing to the similarity of the two esters, the
non-exponential factor of reaction velocity is the same for both.* It follows that the differ-
ence of potential energy will merely produce a corresponding difference of critical energy,
which can then be simply related to the ratio of the reaction velocities at any given
temperature.

The possibility of calculating the potential-energy difference due to the polar substituent
depends on a knowledge of (*a*) the electrical specification of the reagent, and (*b*) the polar
field of the substituent, at the seat of the reaction. With regard to (*a*), the important
quantities concerning the reagent are its ionic charge and electric moment. The latter,
however, is not the same at the instant of reaction as at any earlier time, because the
individuality of the reagent has become lost in the formation of the critical complex. The
ionic charge is the only electrical constant of the reagent which can be considered known at
the moment of reaction, because it is the only one which the reagent carries unchanged into
the critical complex.† Therefore attention is confined to ionic reagents, for which the
potential energy is controlled mainly by the ionic charge. Concerning (*b*), the field of the
substituent, whether this be an ionic charge or a dipole, can in first approximation be treated

* It should be recognised that this is an assumption without strict foundation, and is unlikely to
be *exactly* true.

† This restriction on the validity of electrostatic calculations of polar effects on reaction velocity
seems to us of great importance, but it has not always been recognised.

by Coulomb's law; thus does the distance between the polar substituent and seat of reaction obtain connexion with the measured velocities. This approximation, however, neglects certain more or less serious disturbances. The chief of these arise from (i) the propagation of electrical effects through the bonds of the ester molecule itself, and (ii) local variations in the dielectric properties of the medium. These difficulties are also encountered in the calculation of molecular dimensions from the dissociation constants of dibasic acids; for here the distance between the ionic charges in the dibasic anion would enter through Coulomb's law into relation with the measured quantities were it not for the same two disturbances. Concerning this problem, Gane and Ingold showed that disturbance (i) was practically limited to certain types of structure the use of which could easily be avoided. They found, on the other hand, that disturbance (ii) was general, but that an allowance for it could be made by means of an approximate theoretical calculation (J., 1931, 2153, 2179). In Part VI (J., 1931, 2170) these conceptions were applied to the problem of calculating molecular dimensions from reaction velocities in the field of ester hydrolysis : disturbance (i) was obviated by a proper choice of structure, whilst (ii) was allowed for theoretically. However, since the calculation concerning local effects in the dielectric applies only to the field of a free ionic charge, it was necessary that the polar substituent should be an ionic centre, and therefore the comparison instituted was between the rates of the first and second stages of the alkaline hydrolysis of symmetrical dicarboxylic esters : the ionic charge produced in the first stage was the " polar substituent " for the second, and the reagent for both stages was the hydroxide ion.

It was considered desirable to control these methods of calculation as far as possible by application to molecules the relevant dimensions of which could be considered known. In a recent paper, we applied such a check to Gane and Ingold's treatment of the calculation of molecular dimensions from acid strengths (this vol., p. 949). The symmetrical dibasic acids chosen for the purpose were the *cis*- and *trans-cyclo*pentane-1 : 2- and 1 : 3-dicarboxylic acids, since these acids, besides largely avoiding disturbance (i), can be considered more justly than most others to possess a fixed configuration involving known valency angles. In this paper we attempt a similar check on Ingold's treatment of molecular dimensions in relation to ester hydrolysis. For this purpose we employ the methyl esters of the same four *cyclo*pentane acids for identical reasons.

In the model employed to determine what the dimensions should be, we assume as before (1) rigidity, (2) C–C distances equal to 1·54 Å., (3) extracyclic valency angles equal to 109·5°, (4) that the ends of the determined distance are situated on the symmetry axis of each carboxylate ion at a distance of 1·00 Å. from the corresponding carbon nucleus. All these assumptions except (2), which is certain to within 2%, involve definite approximations. Assumption (4), although originally indicated by Gane and Ingold, is necessarily arbitrary in the present connexion.

The observed rate constants for the two stages of hydrolysis of the *cyclo*pentane esters by hydroxide ions are given in a later section. The solvent was water, since the calculation of the local dielectric disturbance has been performed only for this medium. The measurements were made in very dilute solution in order to minimise complications attributable to finite ionic strength.

In Table I we compare intramolecular distances (Å.) calculated from the ionisation equilibria of the four *cyclo*pentane acids, those deduced from the rates of saponification of their methyl esters, and those given by the model specified above. The distances in the top three lines are calculated without the correction for local dielectric effects, the basis of the calculations being, in order : ˙(i) Wassermann's data for the ionisation constants of the acids (*Helv. Chim. Acta*, 1930, **13**, 207, 223), (ii) our results for these equilibria (*loc. cit.*), and (iii) the results recorded in this paper on the rates of hydrolysis of the esters. The next three lines of the table exactly correspond except that now the correction for local dielectric variations is applied. The last line contains the distances given by the model.

These figures confirm the general validity of the correction for local electrical effects in the aqueous medium; but deviations remain, the causes of which cannot be traced in detail. The most probable causes would, however, appear to be the following : (1) Inadequate treatment has been accorded to the essentially discontinuous character of the

TABLE I.

Inter-carboxyl Distances of cis- *and* trans-cyclo*Pentane*-1 : 2- *and* 1 : 3-*dicarboxylic Acids, as deduced from Ionisation Constants, and of their Methyl Esters, as deduced from Rates of Alkaline Hydrolysis.*

	cis-1 : 2-.	*trans*-1 : 2-.	*cis*-1 : 3-.	*trans*-1 : 3-.
Without dielectric correction :				
K's of acids (Wassermann)	2·0	2·2	4·5	6·9
,, ,, (I. and M.)	2·0	2·4	4·8	6·2
k's of hydrolysis of esters	1·6	3·2	6·4	6·6
With dielectric correction :				
K's of acids (Wassermann)	3·9	4·1	5·5	7·4
,, ,, (I. and M.)	3·9	4·2	5·7	6·8
k's of hydrolysis of esters	3·6	4·6	7·0	7·1
Model	3·3	5·2	5·3	6·7

medium in the region in which the potential field varies strongly (cf. Gane and Ingold, *loc· cit.*). (2) We have calculated the disturbance caused by the field of the polar substituent to the properties of a medium which, it is supposed, would otherwise have been normal; we should have calculated the *further* abnormality conferred by the field of the substituent on a medium which is already disturbed by the reacting group : the departure of the two disturbances from additivity has therefore been neglected. (3) The validity of our model is doubtful in many respects, but especially with regard to the location of the points between which the determined distance lies; in the ester problem, at any rate, these points might not even lie on the carboxylate symmetry axes; and in this case the preference of the carbomethoxy-groups for particular rotatory orientations would certainly modify the measured distances. (4) We have neglected the internally propagated electric effect of the polar substituent. (5) The electrostatic theory takes account of interaction between poles, but neglects the contributions of dipoles and higher multipoles to that part of the potential energy of the collision complex which depends on the ionic substituent. (6) The theory also neglects those solvation differences of which the electrostatic description would refer to changes in the pressure field of the solvent surrounding the collision complex.

Of all these possible causes of deviation, numbers (1), (2), and (3) are likely to be the most serious. There are reasons of analogy for believing that disturbance (4) is usually small, although possibly not always negligible (Part VI, *loc. cit.*); and disturbances (5) and (6) have been shown by calculation to be small (J., 1931, 2187 *et seq.*). Concerning (6), the discussion in the paper cited was incomplete in one respect and the omission may now be remedied. The inhomogeneous pressure field around an ion will exert a compressional as well as a translational force both on the dissolved reagent and on its equivalent in terms of (displaced) solvent : the energy of compression, as well as that of position, due to the press-ure field should have been taken into account. A short calculation shows that the order of magnitude of the compression term does not exceed that of the position term; and accordingly, the whole effect of the pressure field is small in comparison with the main part of the electrostatic effect.

EXPERIMENTAL.

Materials.—Methyl cis-cyclo*pentane*-1 : 2-*dicarboxylate* was prepared from the corresponding acid (12·6 g.) through the silver salt, which, after thorough drying over phosphoric oxide in a vacuum, was boiled with methyl iodide (50 g.) in benzene (60 c.c.) for 3·5 hrs. The ester after a first distillation was treated in ether with a little lime to remove a trace of acidity, and re-distilled several times. It had b. p. 116—117°/12 mm. ·(Found : C, 58·0; H, 7·5. $C_9H_{14}O_4$ requires C, 58·0; H, 7·6%); yield 10·4 g.

Methyl *trans*-cyclo*pentane*-1 : 2-dicarboxylate was prepared by treating a solution of the acid (10 g.) in anhydrous methyl alcohol (10 c.c.) and sulphuric acid (0·5 c.c.) at 81° with the vapour of methyl alcohol (from 225 c.c. of liquid) for 6 hrs., during which the volume was maintained approximately constant. The ester, isolated by the use of ice and sodium carbonate, and purified by distillation and freezing, had m. p. — 3·5°, b. p. 119—120°/16 mm.; yield 10·2 g. (Found : C, 58·0; H, 7·7%). Östling gives b. p. 118·5—119°/17 mm. (J., 1912, **101**, 475).

Methyl *cis-cyclo*pentane-1 : 3-dicarboxylate, prepared through the silver salt of the acid as described for the *cis*-1 : 2-isomeride, had b. p. 140°/25 mm., 124—126°/12 mm. (Found : C, 57·9; H, 7·6%). Pospischill gives b. p. 138—138·5°/25 mm. (*Ber.*, 1898, **31**, 1950), and Diels, Blom, and Koll give b. p. 124—125°/13 mm. (*Annalen*, 1925, **443**, 242). On saponification with aqueous sodium hydroxide, it yielded the *cis*-1 : 3-acid free from any of the *trans*-iso-meride.

Methyl *trans-cyclo*pentane-1 : 3-dicarboxylate was prepared by adding an ethereal solution of diazomethane to an ethereal solution of the acid (2·0 g.) until a distinct yellow colour remained. After 1·5 hrs. the ether was removed and the ester distilled. It has b. p. 132°/*ca.* 30 mm., and the yield was 1·95 g. Semmler and Bartelt give b. p. 118—120°/9 mm. (*Ber.*, 1908, **41**, 385).

Measurements.—The general method was that described by Ingold (*loc. cit.*). The temper-ature of the measurements was 20·00° ± 0·05°. The hydrolyses and titrations were done with carbonate-free aqueous sodium hydroxide, which was obtained by centrifuging a solution prepared from equal weights of sodium hydroxide and water, and diluting the clear liquid with carbon dioxide-free distilled water of good quality. Freedom from carbonate was proved by titra-tion with sulphuric acid with the differential use of phenolphthalein and bromophenol-blue as indicators. The hydroxide solutions were preserved in waxed bottles with rubber stoppers fitted with the usual syphons and soda-lime tubes.

For the determination of the rate constant of the first stage of hydrolysis, 0·002*M*-solutions of reactants were employed. An aqueous solution of the ester (usually about 0·37 g.) was made up to 500 c.c. in the thermostat, and then poured into a large dry flask also in the thermostat. An equivalent of sodium hydroxide was also made up to 500 c.c. in the thermostat, and, after temperature equilibrium had been attained, was poured into the solution of the ester, the mean time of the addition being accepted as the time of commencement of the reaction. The portions withdrawn (50 c.c.) were run into 0·01*N*-hydrochloric acid (10 c.c.), the mean time of mixing being taken as the time of arrest of hydrolysis. Near the end-point in the succeeding titration with 0·01*N*-sodium hydroxide, the cresol-red indicator turned blue for a moment with each additional drop of the alkali, and the end-point was taken as that point at which the blue colour became much more stable. This method was found to give consistent results, and the curves obtained by plotting the fall in alkalinity against the time passed through the origin. In the measurements of the second stage of hydrolysis the solutions were 0·002*M* with respect to the sodium salt of the acid ester, except for the *cis*-1 : 2-compound, the hydrolysis of which was so slow that the initial concentration was increased to 0·006*M*. The titrations were considerably easier than for the first stage of hydrolysis owing to the greater constancy of the indicator colour near the end-point. In titrating to the theoretical p_H, which for the second-stage experi-ments lay in the range 8·0—8·6, it was, as before, found advantageous to use colour standards prepared from the indicator and suitable buffers (*loc. cit.*). The times over which the hydrolyses were followed varied from less than ½ hour, for the first stages of three of the esters, to a week or more, for the second stage of the *cis*-1 : 2-compound.

Solutions of the sodium salt of the acid ester were prepared for measurements on the second stage of hydrolysis by half-saponifying the neutral ester with 1 mol. of sodium hydroxide, or, in some cases, with a 5% excess. After removal of the neutral ester by repeated extraction with chloroform and light petroleum, traces of emulsified solvent were rendered by means of a stream of carbon dioxide-free air. The hydrolysis frequently carried the p_H of the solution into the acid region. Any such acidity was determined by titration of a sample, which was subsequently used for the estimation of the concentration of acid ester by means of its saponification value. These determinations were always carried out at least in duplicate, and a further sample of the same half-hydrolysed and extracted solution was used for the velocity measurement.

Results.—In the following tables, a_1 is the initial concentration of neutral ester, a_2 that of sodium salt of acid ester, and b that of hydroxide ions; u is the fall in the concentration of hydr-oxide ions after a time t from the commencement of reaction; and k_1 and k_2 are the velocity constants for the first and second stages of hydrolysis. Concentrations are in mols./litre, time in mins., and velocity constants in litres/mol./min.

Table II records a typical experiment for the determination of k_1, and Table III one for the measurement of k_2. The calculation of the latter constant from the data is straightforward. The calculation of k_1 involves the use of the approximation formula (*loc. cit.*), *viz.*,

$$t = \frac{u}{k_1 a_1^2}\left[1 + \frac{u}{a_1}\left\{1 - \frac{k_2}{2k_1}\right\} + \frac{u^2}{a_1^2}\left\{1 - \frac{7k_2}{6k_1} + \frac{2k_2^2}{3k_1^2}\right\}\right]$$

which is deduced for the special case in which $b = a_1$, and can be applied with accuracy to the first 30—40% of reaction.   An approximate value of k_1 (estimated by inspection) and the determined value of k_2 are substituted in the right-hand side of the equation along with the initial concentration a_1 and the readings u.   The t's thus calculated are compared with the observed t's; and the mean ratio of the observed and calculated t's, if not too far from unity (*i.e.*, if the original estimate of k_1 is a good one), gives the factor by which the provisional k_1 must be corrected.   Table IV summarises the constants, and also gives the values of the expression log $(k_1/2k_2)$, from which the distances in Table I have been calculated.

<div align="center">TABLE II.</div>

First Stage of the Hydrolysis of Methyl trans-cyclo*Pentane-*1 : 2-*dicarboxylate by Sodium Hydroxide in Water at* 20·0°.

<div align="center">$10^3a_1 = 10^3b = 2·00$.   Observed $k_2 = 0·948$.   Provisionally assumed $k_1 = 19·0$.</div>

t (obs.).	10^3u.	t (calc.).	t (calc.)/t (obs.).	t (obs.).	10^3u.	t (calc.).	t (calc.)/t (obs.).
2·05	0·144	2·03	0·99	11·23	0·602	10·87	0·97
4·05	0·272	4·10	1·01	12·30	0·638	11·75	0·96
5·18	0·336	5·24	1·01	13·55	0·694	13·20	0·97
6·17	0·390	6·24	1·01	14·72	0·726	14·04	0·96
7·20	0·438	7·22	1·00	15·80	0·762	15·04	0·95
8·13	0·480	8·09	1·00	17·00	0·804	16·25	0·96
9·13	0·528	9·15	1·00	18·42	0·818	16·68	0·90
10·25	0·570	10·10	0·99		Mean of first 12 values		0·989

<div align="center">$k_1 = 19·0 \times 0·989 = 18·79$.</div>

<div align="center">TABLE III.</div>

Second Stage of the Hydrolysis of Methyl cis-cyclo*Pentane-*1 : 2-*dicarboxylate by Sodium Hydroxide in Water at* 20·0°.

<div align="center">$10^3a_2 = 2·411$; $10^3b = 2·411$.</div>

t.	10^3u.	k_2.	t.	10^3u.	k_2.	t.	10^3u.	k_2.
25·0	0·435	3·65	89·0	0·941	2·98	160·0	1·351	3·30
36·0	0·538	3·31	99·0	1·088	3·44	171·0	1·391	3·31
49·0	0·713	3·55	111·0	1·152	3·42	186·0	1·415	3·17
61·0	0·805	3·41	134·0	1·232	3·23	238·5	1·470	3·72
73·0	0·905	3·41	146·0	1·287	3·23		Mean	3·29

<div align="center">TABLE IV.</div>

Summary of Rate Constants for the First and Second Stage of Hydrolysis of the Methyl cyclo-*Pentanedicarboxylates with Hydroxide Ions in Dilute Aqueous Solution at* 20·0°.

Ester.	1st Stage.		2nd Stage.			Mean values.		
	$10^3a_1 = 10^3b$.	k_1.	10^3a_2.	10^3b.	k_2.	k_1.	k_2.	$\log(k_1/2k_2)$.
cis-1 : 2-	1·967	3·32	5·594	5·594	0·0173	3·33	0·0171	1·99
	1·981	3·34	5·869	11·09	0·0167			
			5·868	13·47	0·0172			
			5·916	10·83	0·0170			
trans-1 : 2-	2·010	18·6	2·720	4·606	0·966	18·7	0·967	0·98
			1·685	1·685	0·979			
	2·004	18·8	2·891	2·891	0·953			
			2·776	2·776	0·961			
			3·228	3·228	0·977			
cis-1 : 3-	1·995	19·2	2·685	2·685	3·26	19·4	3·21	0·48
	1·857	19·5	2·411	2·411	3·29			
	1·841	19·3	2·338	2·338	3·16			
	2·024	19·6	2·192	2·192	3·33			
			2·182	2·182	3·03			
trans-1 : 3-	1·936	19·5	2·194	2·194	3·33	19·9	3·35	0·47
	1·733	20·2	2·427	2·427	3·37			

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