1069. *The Solvolysis of γ-Phenyltetronic Acid Enol Esters. Part II.* The Methanolysis of γ-Phenyltetronic Acid Enol Acetate.*

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Methanolysis of γ-phenyltetronic acid enol acetate under basic conditions is shown to follow a second-order rate law, the rate being proportional to the concentration of ester and to the concentration of base. By using a series of methyl-substituted pyridines of different basic strengths, it is shown that the rate is determined by a balance between the basic strength and the steric hindrance of the methyl groups. This is in marked contrast to the behaviour of the benzoate, for which the basic strength was the sole factor determining the catalytic activity. It is concluded that, in the present case, the rate-determining step is the attack by the base on the neutral molecule. The catalysed methanolysis is thus an example of nucleophilic catalysis.

IN Part I * it has been shown that γ-phenyltetronic acid enol benzoate undergoes methanolysis either by a bimolecular mechanism, following a pre-equilibrium, or by a termolecular mechanism, involving ester, solvent, and base or solvent, depending on whether it is studied under initially basic or initially neutral conditions. As the phenyl group in the benzoate causes a certain degree of crowding, it was thought of interest to study the acetate, for which steric considerations might be expected to be less important.

The nature of the products was established as described in Part I. For neutral methanolysis, after ~6 hours' heating at 55° 97% of γ-phenyltetronic acid and 93·4% of methyl acetate were recovered, indicating acyl–oxygen fission. In the presence of bases, product separation yielded the results shown in Table 1. Thus under both initially neutral and initially basic conditions, acyl–oxygen fission occurs.

TABLE 1.

Product analysis: reaction at 55°.

Base	Heating (hr.)	MeOAc (%)	Acid (%)
None	6	93·4	97
Pyridine	2	—	95
2,6-Lutidine	3	104	113

The Kinetics of Neutral Methanolysis.—Neutral methanolysis was studied by the conductance technique and the results were analysed as described in Part I. Because methanolysis of the acetate is about six times faster than that of the benzoate at 55° (at which all kinetic runs were done), extrapolation for $\lambda_s°$ and $(d\lambda_s/dt)_0$ was carried out over the first ten minutes of each run. The first-order rate coefficients obtained (Table 2) are independent of the initial concentration of ester. The methanolysis is thus of the first order, the mean rate constant being $1·46 \times 10^{-4}$ sec.$^{-1}$. Comparing this value with that reported in Part I for γ-phenyltetronic acid enol benzoate, namely, $2·25 \times 10^{-5}$ sec.$^{-1}$, gives the rate ratio acetate : benzoate as 6·5 : 1. This value is close to that (10 : 1) found for ethyl acetate and ethyl benzoate in alkaline hydrolysis, which proceeds by the $B_{Ac}2$ mechanism.[1] In both cases, the results can be attributed to the steric effect of the relatively bulky phenyl group. Specific base-catalysis by the methoxide ion is eliminated

TABLE 2.

Rate coefficients for neutral methanolysis at 55°.

Concn. (mmoles l.$^{-1}$)	64·7	48·0	19·3
10^4k_1 (sec.$^{-1}$)	1·46	1·44	1·48

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* Part I, preceding paper.

[1] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953.

as a possible mechanism by the fact that the γ-phenyltetronic acid formed in the reaction does not cause a fall in the rate coefficient. The mechanism thus involves the attack of solvent upon the ester, as for the benzoate.

The Kinetics of Base-catalysed Methanolysis.—In the presence of 0·1N-sodium hydroxide, apparently instantaneous methanolysis took place. As with the benzoate, pyridine and its methyl derivatives, 2-picoline, 2,6-lutidine and 2,4,6-collidine proved to be of convenient strength for studying the catalysed reaction. In the presence of these bases, reproducible calibration curves of the concentration of γ-phenyltetronic acid against specific conductance of the solution were obtained. Use of these curves enabled the γ-phenyltetronic acid in a solution undergoing methanolysis to be determined at various stages of the reaction. A typical first-order plot [log $(c_\infty - c)$ against time] is shown in Fig. 1. The points all lie close to the line up to about 75% reaction. Observed infinity values of the concentration of γ-phenyltetronic acid (in mmoles l.$^{-1}$), together with those obtained by the Swinbourne method [2] and those from the weight of ester taken for the run (theor.), are shown in Table 3. By using a conductance cell with platinum wire electrodes of cell constant 0·671 cm.$^{-1}$ (to be compared with values of 0·03—0·06 cm.$^{-1}$ for the cells normally used), it was shown that there was no surface catalysis by platinum. The rate constants were $6{\cdot}10 \times 10^{-4}$ and $5{\cdot}56 \times 10^{-4}$ sec.$^{-1}$, for the platinum wire and normal cells, respectively, for runs in methanol containing 10 mmoles of pyridine per l. A run in the presence of lutidine and γ-phenyltetronic acid (10 and 9·4 mmoles l.$^{-1}$, respectively) gave for the first-order rate constant $3{\cdot}96 \times 10^{-4}$ sec.$^{-1}$, to be compared with a mean value of $3{\cdot}77 \times 10^{-4}$ sec.$^{-1}$ in the absence of the acid.

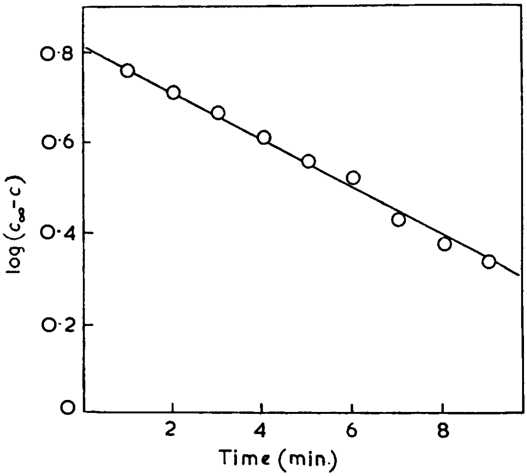

FIG. 1. A typical kinetic run in presence of 100 mmoles of 2,6-lutidine per l.

TABLE 3.

Infinity values for base-catalysed methanolysis obtained by various methods.

Base	Obs.	Swinbourne	Theor.	$10^4 k_1$ (sec.$^{-1}$)
Pyridine	13·1	13·8	13·1	17·4
α-Picoline	10·7	10·7	11·2	4·2
2,6-Lutidine	6·9	6·9	7·9	7·3

The observed first-order rate coefficients (k_1^{B}) were proportional to the concentration of added base (Fig. 2). Thus, $k_1^{\mathrm{B}} = k_1^{\mathrm{N}} + k_2^{\mathrm{B}}[\mathrm{B}]$, where k_1^{N} is the observed first-order rate constant for the neutral reaction, and k_2^{B} is the catalytic constant. Values of the catalytic constants are shown in Table 4. It will be observed that the value of k_1^{N}

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[2] Swinbourne, *J.*, 1960, 2371.

obtained from these experiments, is consistent with the value obtained from the independent study of the neutral reactions.

It is obvious (Table 4) that the Brönsted relation, $\log k_2^{\mathrm{B}} = \alpha + \beta \log K_{\mathrm{B}}$, is not followed in the case of the acetate, as it is in that of the benzoate.

TABLE 4.

The catalytic constants.

Base	10^2k_2 (mole^{-1} l. sec.$^{-1}$)	pK_{B}
Pyridine	4·45	8·78 *
2-Picoline	0·75	8·04 *
2,6-Lutidine	2·08	7·28 *
2,4,6-Collidine	3·97	6·55 †

* Andon, Cox, and Herrington, *Trans. Faraday Soc.*, 1954, **50**, 918.
† Golombic and Orchin, *J. Amer. Chem. Soc.*, 1957, **79**, 2365.

Discussion.—The rate of the base-catalysed methanolysis of γ-phenyltetronic acid enol acetate is extremely sensitive to the steric properties of the tertiary amines, as can be seen from Fig. 2 and Table 4. 2,4,6-Collidine, the strongest of the bases (pK_{B} 6·55 in water), gives a second-order rate constant of $4{\cdot}0 \times 10^{-2}$ mole^{-1} l. sec.$^{-1}$, which is lower than that for pyridine, $4{\cdot}5 \times 10^{-2}$ mole^{-1} l. sec.$^{-1}$, in which the nitrogen atom is not sterically hindered. Also 2,6-lutidine, of basic strength appreciably higher than pyridine, actually has a much lower catalytic constant, only half that of pyridine; and α-picoline, although less sterically hindered than 2,6-lutidine, is a much weaker base, which explains its very low catalytic constant.

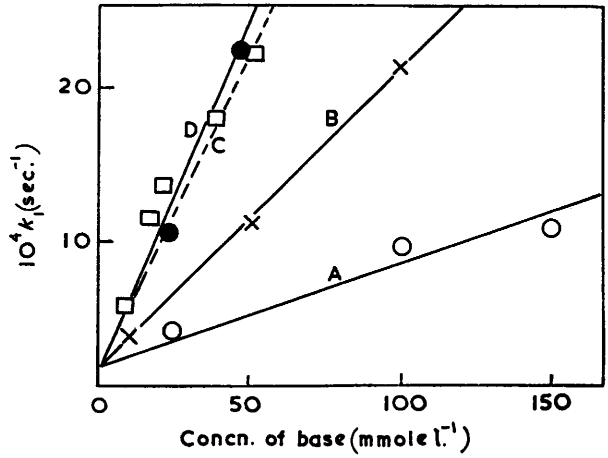
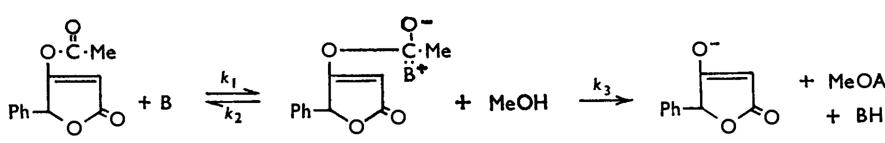


FIG. 2. Methanolysis of γ-phenyltetronic acid in presence of tertiary amines.

○, α-Picoline; ×, 2,6-lutidine; ●, 2,4,6-collidine, □, pyridine.

Mechanistically these results can be interpreted as a bimolecular nucleophilic attack of the base on the carbonyl centre, followed by the interaction of the complex so formed with the solvent:



This scheme would lead to the kinetic equation

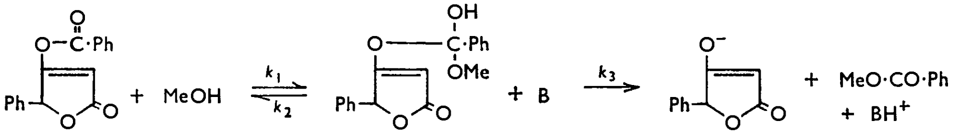
$$\frac{d[P]}{dt} = \frac{k_1k_3[A][B][S]}{k_2 + k_3[S]}$$

which for $k_3[S] \gg k_2$, reduces to

$$d[P]/dt = k_1[A][B],$$

where *P* stands for products, B is base, and A is ester. Nucleophilic attack is thus the rate-determining step and is followed by the rapid attack of the solvent on the complex, giving acyl–oxygen fission and the observed products, γ-phenyltetronic acid and methyl acetate. This scheme would predict a first-order disappearance of ester, since the concentration of base remains constant.

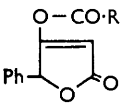
This behaviour contrasts strongly with that observed for γ-phenyltetronic acid enol benzoate. For in that case the Brönsted relation was obeyed and the kinetic behaviour was shown to be consistent with either a pre-equilibrium of solvent and ester, followed by the slow decomposition of the complex, or a termolecular mechanism, involving ester, base, and solvent. The former mechanism was written as:



which for $k_2 \gg k_3[\mathrm{B}]$ leads to the kinetic equation

$$d[\mathrm{P}]/dt = k_1k_3[\mathrm{A}][\mathrm{B}][\mathrm{S}]/k_2.$$

This suggests a critical steric effect of the group R in the ester (A) which, if too large, precludes the possibility of nucleophilic catalysis, even in the presence of unsubstituted pyridine, thus forcing either a prior or a simultaneous attack by the solvent molecule.



(A)

Gold and his co-workers [3] studied the hydrolysis of acetic anhydride in the presence of a series of tertiary amines. 2-Methyl- or 2,6-dimethyl-pyridine showed a kinetic steric effect, while non-sterically hindered tertiary bases at low concentration obeyed the Brönsted law, the value of β being about 0·9. These results were interpreted in terms of the rate-determining transfer of the acetyl ion Ac⁺ from the anhydride to the catalyst, followed by rapid hydrolysis of the resulting cation.* The same was shown to be true in the case of acetic formic anhydride.

Koskillalio [4] studied the methanolysis of acetic anhydride in the presence of pyridine. The catalytic effect of pyridine was not greatly different from that of acetate ions. Changing the solvent to water gives a 10^5-fold increase in rate, pointing to a highly polar transition state. This suggested that the rate-determining step was addition of the catalyst to the anhydride molecule, a mechanism similar to that suggested for γ-phenyltetronic acid enol acetate. The rate constants for attack by pyridine and by methanol were $6{\cdot}5 \times 10^{-7}$ and $9{\cdot}9 \times 10^{-4}$ mole^{-2} l. sec.$^{-1}$, giving a ratio ~1500. The corresponding ratio in the case of γ-phenyltetronic acid enol acetate was 7400.

EXPERIMENTAL

γ-Phenyltetronic acid was prepared from *O*-acetylmandeloyl chloride and diethyl malonate.[5] A typical sample had m. p. 127°. The acetate was prepared by treating γ-phenyltetronic acid with an excess of acetic anhydride in the presence of a few drops of concentrated sulphuric acid; the solution was then diluted with chloroform and washed with ice-cold aqueous sodium hydrogen carbonate; the chloroform layer was dried (Na_2SO_4) and evaporated under reduced pressure; the oily brown residue crystallised and was recrystallised from light petroleum (b. p. 60—80°), having m. p. 79° (Found: C, 65·9; H, 4·65. Calc. for $C_{12}H_{10}O_4$: C, 66·1; H, 4·6%). Equivalent-weight determination, by titration of a methanolic solution with Thymol Blue–Cresol Red as indicator showed $\not>$ 0·8% of non-acid impurities.

Pyridine was purified by recrystallisation of its zinc chloride salt; [6] other bases were distilled.

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* Bunton *et al* (*Tetrahedron Letters*, 1961, 458) have shown by isotopic studies that the rate-determining step is the hydrolysis of acylpyridinium ions (cf. Butler and Gold, *Proc. Chem. Soc.*, 1960, 15).

[3] Gold and Bafra, *J.*, 1953, 1406; Gold and Jefferson, *J.*, 1953, 1409, 1416.

[4] Koskillalio, *Suomen Kem.*, 1959, **32**, *B*, 41.

[5] Haynes, Plimmer, and Stanners, *J.*, 1956, 4661.

[6] Vogel, " Practical Organic Chemistry," Longmans, Green & Co., London, 1948.

The conductance cells used were of conventional design, with bright platinum electrodes and all had constants in the range 0·03—0·06 cm.$^{-1}$. The conductance measurements were done with a Pye bridge, the accuracy of the readings being $\pm 0{\cdot}2\%$. The thermostat temperature was 54·95° ± 0·01°.

The solutions of bases were prepared by weighing the base and making up the solution to a standard volume. The solutions of ester were made up by adding a known weight of ester to the pre-heated solvent. The solution was then added to the pre-heated conductance cell, and readings of λ_s were made at the appropriate times. Points observed for the first few minutes were neglected, to allow for the attainment of thermal equilibrium. From the appropriate calibration curve, the concentration of γ-phenyltetronic acid was found as a function of time, and first-order rate constants were calculated in the conventional manner.

The rate constants tabulated refer to concentrations in moles l.$^{-1}$, k_1 in sec.$^{-1}$, and k_2 in mmole^{-1} l. sec.$^{-1}$.

	[Pyridine] 10·1			[Pyridine] 19·7				[Pyridine] 24·4			
[Ester]	20·0	21·5	29·6	11·3	12·4	16·7	22·7	8·3	18·7	20·0	26·3
10^4k_1	5·38	5·56	5·75	10·8	11·5	10·3	10·3	14·1	13·1	13·5	13·0
10^5k_2	4·05			4·69				4·90			

	[Pyridine] 39·5				[Pyridine] 57·7					
[Ester]	10·3	13·8	16·0	22·3	10·7	11·2	14·6	16·0	26·5	36·6
10^4k_1	17·4	18·4	17·4	18·0	23·0	26·0	21·6	19·3	19·3	23·0
10^5k_2	4·15				3·97					

[α-Picoline]	25·0		100	150
[Ester]	7·7	11·2	7·48	7·2
10^4k_1	3·64	4·21	9·60	10·2
10^5k_2	0·87		0·81	0·58

[2,4,6-Collidine]	24·5	49·0
[Ester]	73·8	8·39
10^4k_1	10·5	22·3
10^5k_2	3·70	4·25

[2,6-Lutidine]	10·0				50			100
[Ester]	9·58	12·6	14·4 *	23·1	6·46	8·64	10·0	7·53
10^4k_1	3·26	3·62	3·96	4·25	10·4	11·0	11·1	21·2
10^5k_2	2·31				1·87			1·97

* In presence of 9·4 mmoles of γ-phenyltetronic acid per l.

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