A Study of the Acid Dissociation of Furan- and Thiophenedicarboxylic Acids and of the Alkaline Hydrolysis of Their Methyl Esters

By Shigeru OAE, Naomichi FURUKAWA, Takao WATANABE
Yoshio OTSUJI and Masayuki HAMADA

(Received August 15, 1964)

The physical and chemical behavior of furan- and thiophenemonocarboxylic acids and their derivatives has been investigated extensively and shown to be considerably different from that of benzoic acid.[1] Cocker et al. have suggested the formation of an intramolecular hydrogen bond in their study of the acid dissociations of four carboxylic groups and the infrared spectrum of furantetracarboxylic acid.[2] Meanwhile, a few dicarboxylic acids, such as succinic acid[3] and maleic acid,[4] have been known to form intra- or intermolecular hydrogen bondings that create substantial differences between their first and second dissociation constants.

Meanwhile, although there have been many reports on the alkaline hydrolysis of the monocarboxylic esters and the reaction mechanism of the saponification has been well elucidated,[5] only a few investigations of the hydrolyses of dicarboxylic esters have been carried out. This is perhaps due to the extreme difficulty of following the kinetics of the hydrolyses of these diesters, because they do not obey the simple second-order kinetic equation. However, a few noteworthy treatments have been made. Namely, one of the earliest treatments of the competitive consecutive second-order reaction for the alkaline saponification of diesters has been carried out by Ingold.[6] However, this graphic approximation gives by no means an accurate estimation. Meanwhile, other investigators have made many efforts to get accurate kinetic data for those dicarboxylic esters.[7] Frost and Schwemer have presented what appears to be the first legitimate method for the calculation of the consecutive competitive second-order kinetic equation of the alkaline hydrolysis of dicarboxylic esters.[8]

The present work was initiated in order to investigate the nature of the interaction between the two carboxyl groups attached to the furan and thiophene rings and the alkaline hydrolyses of the diesters of these carboxylic

---

* Preliminary results have been reported previously in *Ann. Rept. of Radiation Center Osaka Pref.*, **2**, 106 (1961).

[1] a) C. C. Price and E. A. Dudley, *J. Am. Chem. Soc.*, **78**, 68 (1956); b) S. Oae and C. C. Price, ibid., **79**, 2547 (1957); c) E. Imoto, Y. Otsuji, T. Hirai and H. Inoue, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **77**, 804, 809 (1959).

[2] W. Cocker, W. J. Oavis, T. B. H. McMurry and P. A. Start, *Tetrahedron*, **7**, 299 (1959).

[3] L. Eberson, *Acta Chem. Scand.*, **2**, 13 (1959).

[4] a) M. Shahat, *Acta Cryst.*, **5**, 763 (1962); b) H. M. E. Cardwell, J. D. Danitz and L. E. Orgel, *J. Chem. Soc.*, **1953**, 3740.

[5] a) J. Hine "Physical Organic Chemistry," McGraw-Hill Book Company, New York (1962), pp. 275—301; b) C. K. Ingold, "Organic Chemistry," Cornell University Press, Ithaca, New York (1953); c) M. L. Bender, *Chem. Revs.*, **60**, 53 (1960).

[6] C. K. Ingold, *J. Chem. Soc.*, **1931**, 2170.

[7] a) M. Ritchie, ibid., **1931**, 3112; b) F. H. Westheimer, W. A. Jones and R. A. Lad, *J. Chem. Phys.*, **10**, 478 (1942); c) D. French, *J. Am. Chem. Soc.*, **72**, 4806 (1950); **73**, 4541 (1951).

[8] A. A. Frost and W. C. Schwemer, ibid., **74**, 1268 (1952).

acids in comparison with the dissociations of phthalic acids and maleic acid and the saponification of their esters.

Experimental

Materials. — *2, 3-Furandicarboxylic Acid.*⁹⁾ — 4,4-Diethoxybutyronitrile, obtained from acrolein, was condensed with diethyl oxalate, giving 2-ethoxalyl-4,4-diethoxybutyronitrile. Ethyl 3-carbamyl-2-furancarboxylate, prepared by the cyclization of the above nitrile, was hydrolyzed to 2,3-furandicarboxylic acid. Colorless crystals of the acid melted at 221—222°C, and the yield was 20% on the basis of the 2-ethoxalyl-4,4-diethoxybutyronitrile used.

The 2-Monomethyl Ester of 2,3-Furandicarboxylic Acid.—The above acid was converted to its monosilver salt by adding 1.2 mol. of silver nitrate to one mole of the monosodium salt in water. To a solution of one mole of the dried monosilver salt obtained above in benzene, one mole of methyl iodide was added, and then the mixture was refluxed for two hours and filtered to remove the silver iodide. The benzene solution was evaporated to dryness, and recrystallization from water gave the monoester in a 70% yield. M. p. 118°C.

Found: C, 49.28; H, 3.97. Calcd. for $C_7H_6O_7$: C, 49.44; H, 3.56%.

Since in 2,3-furandicarboxylic acid the 2-carboxylic group is much more acidic than the 3-carboxylic group, it is reasonable to assume that 2,3-furandicarboxylic acid is esterified first at the 2-position by the method used in this investigation. Thus the monoester obtained would have to be 2-monomethylester of 2,3-furandicarboxylic acid.

*3, 4-Furandicarboxylic Acid.*¹⁰⁾—Diethyl α-formylsuccinate was converted to its acetal, which was again formylated to diethyl 1-formyl-2-diethoxymethylsuccinate. 3,4-Furandicarboxylic acid was prepared by the cyclization of the above compound. Recrystallization from water gave colorless crystals (m. p. 214°C), and the yield was 50% on the basis of the diethyl succinate used.

The 3-Monomethyl Ester of 3, 4-Furandicarboxylic Acid.—This ester was obtained in a 76% yield by the method used for the esterification of 2,3-furandicarboxylic acid (m. p. 135—137°C).

Found: C, 49.06; H, 3.76. Calcd. for $C_7H_6O_5$: C, 49.44; H, 3.56%.

*2, 5-Furandicarboxylic Acid.*¹¹⁾ — This acid was obtained first by chloromethylating ethyl 2-furancarboxylate and then by oxidizing the resulting compound (m. p. 365°C) in a 70% yield.

*2,4-Furandicarboxylic Acid.*¹²⁾—This acid was prepared by the rearrangement of the methyl 6-bromocoumalin 5-carboxylate obtained from coumalin 5-carboxylic acid (m. p. 268–269°C) in a 48% yield.

*3,4-Thiophenedicarboxylic Acid.*¹⁰⁾—This acid was prepared from diethyl 1-formyl-2-diethoxymethylsuccinate, the method of synthesis which has been reported earlier. The cyclization of diethyl 1-formyl-2-diethoxymethylsuccinate was carried out using phosphorous pentasulfide. The diethyl 3,4-thiophenedicarboxylate thus obtained was hydrolyzed with aqueous sodium hydroxide to the acid (m. p. 225.5—226.5°C) in 20% yield.

The 3-Monomethyl Ester of 3,4-Thiophenedicarboxylic Acid.—The monoester of 3,4-thiophenedicarboxylic acid was prepared by the same method as was used for the synthesis of the 3-monomethyl ester of 3,4-furandicarboxylic acid (m. p. 115.5—116.5°C).

*2, 5-Thiophenedicarboxylic Acid.*¹³⁾—Thiophene was chloromethylated with paraformaldehyde as usual to give 2,5-dichloromethylthiophene, which was further treated with sodium acetate and subsequent hydrolysis to yield 2,5-dihydroxymethylthiophene. This alcohol was oxidized with potassium permanganate to obtain the dicarboxylic acid (m. p. 358.5°C) in a 75% yield.

p*K*-Measurements.—pK measurements of the acids were made by potentiometric titrations using a Horiba model P pH meter (glass and calomel electrodes). The acids were dissolved in an aliquot amount of carbon dioxide-free distilled water, and then carbon dioxide-free nitrogen gas was added to the solution, while the temperature was maintained constant during the measurements. The titration was carried out using a 0.100 N standard potassium hydroxide solution, and the pK's of the acids were calculated by the method described in the literature.¹⁴⁾ The graphical method using titration curves shown in Figs. 1 and 2 was also applied to the acids for which the ΔpK was small (the difference between pK_1 and pK_2).

Infrared Spectrum.—The infrared spectra of the acids were taken in their potassium bromide disks. In the case of 3,4-furandicarboxylic acid, carboxylic hydrogen was exchanged with deuterium by repeated recrystallization from D_2O, and this deuterated dicarboxylic acid was examined similarly.

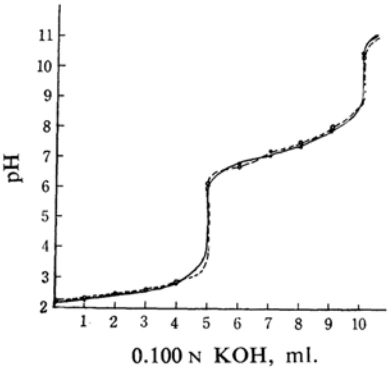


Fig. 1

—— 2,3-Furandicarboxylic acid
---- 3,4-Furandicarboxylic acid

---

9) R. G. Jones, ibid., **77**, 4069 (1955).

10) E. C. Kornfeld and R. G. Jones, *J. Org. Chem.*, **19**, 1617 (1954).

11) Y. Shono and Y. Hachihama, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zassi*), **57**, 836 (1954).

12) H. Gilman and R. Burther, *J. Am. Chem. Soc.*, **55**, 2903 (1933).

13) J. M. Griffing and L. F. Salisburg, ibid., **70**, 3416 (1948).

14) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley & Sons, New York (1962).

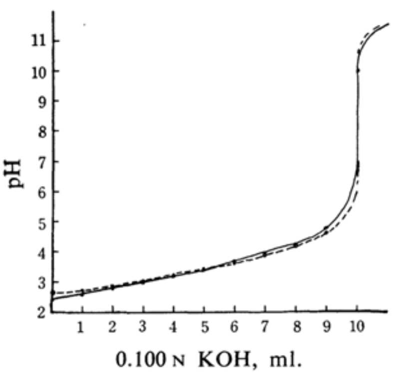


Fig. 2

—— 2, 4-Furandicarboxylic acid
---- 2, 5-Furandicarboxylic acid

X-Ray Diffraction. — The X-ray diffraction of 3, 4-furandicarboxylic acid and its analysis[15] were carried out by Williams and Rundle at Iowa State University.

Kinetics.—*Dimethyl Esters.* — All the dimethyl esters except dimethyl terephthalate were synthesized in the following manner (dimethyl terephthalate was a commercially-available product which was purified just before use). Dicarboxylic acid (0.064 mol.) was refluxed with 10 ml. of anhydrous methanol in a benzene solution with one or two drops of concentrated sulfuric acid for several hours. After the removal of the excess methanol, the residual dimethyl ester was recrystallized from a suitable solvent several times to give the correct melting point.

By this method the following compounds were obtained :

Ester	Solvent for recryst.	M. p. °C	Yield %
Dimethyl 2, 5-furan-dicarboxylate	H_2O - MeOH	112	68.7
Dimethyl 3, 4-furan-dicarboxylate	Ether - *n*-Hexane	47.5	77.2
Dimethyl 2, 5-thiophene-dicarboxylate	Benzene	150—150.5	74.3
Diemthyl 3, 4-thiophene-dicarboxylate	Ether - *n*-Hexane	60—61	81.5

Monomethyl Terephthalate.—Dimethyl terephthalate (20 g.) was dissolved in 50 ml. of an alcoholic aqueous solution containing 5.6 g. of potassium hydroxide and refluxed for several hours; then the unreacted dimethyl ester was filtered off. The aqueous alcoholic solution was acidified with concentrated hydrochloric acid. The precipitated monoester was recrystallized several times from water. The yield was 5.0 g. (25%), (m. p. 216.5—217°C).

Kinetic Procedure. — A detailed procedure for kinetic determination is described in the literature.[1a,b,8] The solvent used was 70% aqueous dioxane, which was made by diluting 30 ml. of carbon dioxide-free water with dioxane to 100 ml. of the solution. The rate measurements were carried out by mixing equal volumes of sodium hydroxide and ester solutions of the same concentration at the desired temperature, and then pipeting an aliquot into an excess of standard hydrochloric acid from time to time, it was then back titrated with a standard sodium hydroxide solution, using phenolphthalein as the indicator.

The Calculation of Consecutive Competitive Rate Constants.—The calculation of the consecutive competitive rate constants for the saponification of the diesters was carried out using the following Frost equation[8] :

$$A + B \xrightarrow{k_1} C + E, \qquad A + C \xrightarrow{k_2} D + E$$

$$dA/dt = -k_1AB - k_2AC, \qquad dB/dt = -k_1AB,$$

$$dC/dt = k_1AB - k_2AC$$

where A, B and C represent the molar concentrations of the corresponding chemical species. Then the above equations were expressed as follws, by

TABLE I. THE SAPONIFICATION RATE OF DIMETHYL 3, 4-FURANDICARBOXYLATE WITH SODIUM HYDROXIDE IN A 70% DIOXANE - WATER - 0.200 N POTASSIUM CHLORIDE SOLUTION

Time sec.	NaOH ml. in titration	OH^-, N	$\alpha = [OH^-]/[OH^-]_0$
0	0	0.009738	1.000
98	5.55	0.00881	0.905
439	6.06	0.00778	0.799
797	6.48	0.00694	0.713
1079	6.79	0.00633	0.650
1458	7.04	0.00581	0.597
1833	7.19	0.00551	0.566
2411	7.55	0.00478	0.491
2762	7.67	0.00454	0.466
3194	7.78	0.00432	0.433
3789	7.97	0.00393	0.403
4139	8.04	0.00379	0.389

Run : Initial concentration of reactants, 0.00974 N ; normality of sodium hydroxide for titration, 0.02016 N ; normality of hydrochloric acid, 0.0200 N ; temperature at 20±0.01°C.

TABLE II. CALCULATIONS OF RATE CONSTANTS FOR DIMETHYL 3, 4-FURANDICARBOXYLATE

% Rx.	*t*, sec.	Percentages compared	*t*, ratio	$1/\kappa$
20	436	60/20	8.862	5.779
30	855	60/30	4.519	4.789
40	1437	60/40	2.689	4.578
50	2342	60/50	1.650	4.446
60	3864	50/20	5.371	7.010
		50/30	2.739	5.101
			Aver.	4.728

% Rx.	τ	k_1
20	0.2684	0.126
30	0.4835	0.116
40	0.8014	0.114
50	1.305	0.114
60	2.175	0.115
	Aver.	0.115

$k_1 = 0.115 \text{ l.mol}^{-1}\text{sec}^{-1}$

$k_2 = 0.115 \times (1/4.728)$

$= 0.0243 \text{ l.mol}^{-1}\text{sec}^{-1}$

---

[15] D. Williams and R. E. Rundle, *J. Am. Chem. Soc.*, **86**, 1660 (1964).

introducing the dimensionless variables, α, β, τ and κ:

$$\alpha=A/A_0,\quad \beta=B/B_0,\quad \tau=B_0k_1t,\quad \kappa=k_2/k_1$$

A_0, B_0; initial concentrations of A and B.

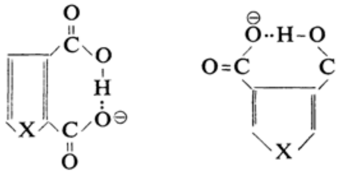
A typical run is shown in Tables I and II.

The rate constants of the monomethyl esters were calculated as usual.

Results and Discussion

The titration curves of the acids are shown in Figs. 1 and 2. The pK's of the acids are summarized in Table III. The rate constants of the esters are also tabulated in Table IV.

The pK's for the furan- and thiophene-dicarboxylic acids change considerably with the change in the location of two carboxyl groups in the furan or thiophene ring. The acids in which two carboxyl groups are at adjacent carbon atom, e. g., 2, 3- and 3, 4-furan- or thiophene-dicarboxylic acids, have large ΔpK values, while the other acids (2, 4- and 2, 5-acids) have relatively small ΔpK values. The relatively large ΔpK values found for the former acids are undoubtedly caused by the formation of strong intramolecular hydrogen bonds in the resulting acid ions, as is shown below:



X; O or S

Therefore, the acids which would from a strong intramolecular hydrogen bond increase the first dissociation of a dicarboxylic acid and decrease the second one, eventually giving rise to a large ΔpK value.

In contrast, those acids in which the two carboxyl groups are separated by extra CH groups in the furan or thiophene ring and cannot form intramolecular hydrogen bonding,

TABLE III. THE DISSOCIATION CONSTANTS OF ACIDS

	pK_1	pK_2	ΔpK	pK_e	ΔpK_e
2, 3-Furan	2.45	7.25	4.80	3.09	0.64
3, 4-Furan	2.51	7.43	4.92	3.75	1.24
2, 4-Furan	2.63	3.77	1.14		
2, 5-Furan	2.60 (2.95*)	3.55 (4.13*)	0.95		
2-Furan[1c]	3.12				
3-Furan[14]	3.95				
3, 4-Thiophene	2.81	6.93	4.02	3.57*	(0.76)
2, 5-Thiophene	(3.18*)	(4.28*)	1.10		
Phthalic[a]	2.98	5.28	2.30	3.32	0.34
Isophthalic[a]	3.46	4.46	1.00		
Terephthalic[a]	3.51	4.82	1.31		
Benzoic[a]	4.20				
Maleic[a]	1.92	6.23	4.31		1.03

* 30 wt.% of EtOH–H_2O

a) The pK's of these compounds are taken from H. C. Brown, D. H. McDaniel and O. Hafligen, "Dissociation Constants," Chapter 14, "Determination of Organic Structure by Physical Method," Academic Press, New York (1955).

pK_1, pK_2: first and second dissociation constants respectively.

ΔpK: the difference between pK_1 and pK_2.

pK_e: the dissociation constants of monoesters.

ΔpK_e: the difference between pK_1 and pK_e.

TABLE IV. THE RATE CONSTANTS OF THE ESTERS AT 20±0.01°C IN 70% DIOXANE SOLUTIONS

Ester	K_1 l. mol^{-1} sec^{-1}	K_2 l. mol^{-1} sec^{-1}	$1/\kappa$ $=K_1/K_2$
Dimethyl 2, 5-furandicarboxylate	1.48	0.553	2.67
Dimethyl 3, 4-furandicarboxylate	0.115	0.0243	4.73
Dimethyl 2, 5-thiophenedicarboxylate	0.228	0.03	7.36
Dimethyl 3, 4-thiophenedicarboxylate	0.0260	0.005	5.17
Dimethyl terephthalate	0.0886	0.0113	7.84
Monomethyl 3, 4-furandicarboxylate	0.0469		
Monomethyl 3, 4-thiophenedicarboxylate	0.0134		
Monomethyl terephthalate	0.0208		

have small ΔpK values. Symmetrical dicarboxylic acids usually have a small statistical ΔpK value (ca. 0.1).

A substantially larger value of ΔpK than the statistical value must result from a specific interaction between the functional groups in a dicarboxylic acid. In the case of furan and thiophene dicarboxylic acids, small deviations from the statistical ΔpK value are considered to be due to the polar interaction between the two carboxyl groups.

2, 3- and 3, 4-Furan- or thiophenedicarboxylic acids were found to give large ΔpK values. A similar large ΔpK value has also been observed for maleic acid (Table III), where the difference has been explained in terms of the formation of an intramolecular hydrogen bond of the resulted acid anion. Recently evidence for the existence of hydrogen bonding in maleic acid in the crystalline state has been given by Schahat and by others from their investigations of the acid by X-ray and infrared analyses.[4a)] Phthalic acid is also considered to form a fairly strong intramolecular hydrogen bond, but the ΔpK value is found to be much smaller than those of 2, 3- and 3, 4-furan or thiophene-dicarboxylic acids. Hydrogen bonding is obviously involved as one of the important factors in determining these ΔpK values, and a heterocyclic aromatic ring such as furan or thiophene must also play a significant role in favoring the formation of a relatively stable acid ion from the furan- or thiophene-dicarboxylic acids than that from phthalic acid. One conceivable reason for this differences is the difference in geometry between the monohydrogen phthalate ion and the monohydrogen furan or thiophene dicarboxylate ion. The

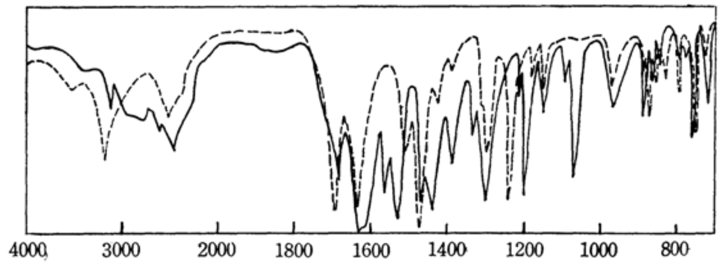


Fig. 3

—— 3, 4-Furandicarboxylic acid
---- 3, 4-Thiophenedicarboxylic acid

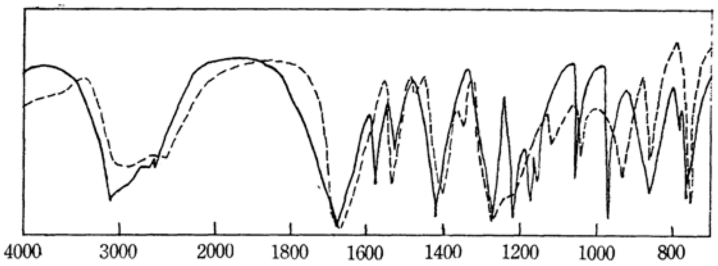


Fig. 4

—— 2, 5-Furandicarboxylic acid
---- 2, 5-Thiophenedicarboxylic acid

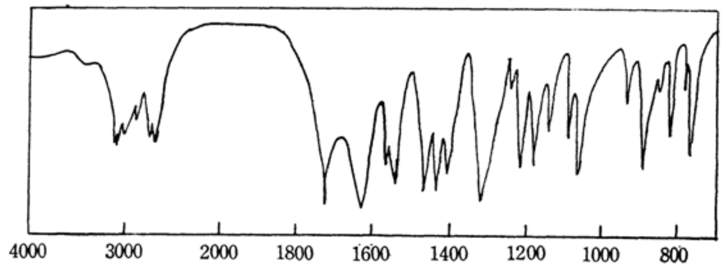


Fig. 5

Monomethyl ester of 3, 4-furandicarboxylic acid latter hydrogen-bonded ions are of 5- and 7-membered binuclear condensed rings, like an azulene ring, which are known to be quite stable. In the case of the monohydrogen phthalate ion, the structure is composed of 6- and 7-membered rings, which may not provide a very stable arrangement for an intramolecular hydrogen bond formation. It is also interesting to note that the ΔpK_a value for 3, 4-furandicarboxylic acid is larger than that for the corresponding thiophene counterpart. It may be that the furan ring is geometrically more favored for the hydrogen bond formation because of the smaller size of the oxygen atom than that of the sulfur atom of the thiophene ring.

A comparison of the strengths of the half esters of the dicarboxylic acids with these of the corresponding free acids, gives further support to the postulate that the internal hydrogen bonding in the carboxylate acid ions is an important factor. There is considerable evidence that the polar effect of carboalkoxyl group is similar to that of a carboxyl group. Consequently, in the absence of specific interactions, such as hydrogen bonding between the two functional groups, it may be expected that ΔpK_e (the difference between pK_1 and pK_e for the monoester of the dicarboxylic acid) would have the value of 0.3, corresponding to the statistical value for the dicarboxylic acids. Phthalic acid has a value close to 0.3. Other acids for which a strong intramolecular hydrogen bonding is proposed exhibit considerably larger values: 2, 3-furandicarboxylic acid, 0.64; 3, 4-furandicarboxylic acid, 1.24; 3, 4-thiophenedicarboxylic acid, 0.76; maleic acid, 1.03. These values are consistent with the discussion above.

Other support for the existence of an intramolecular hydrogen bonding in 2, 3- and 3, 4-furan- or thiophene-dicarboxylic acids is given by the infrared data for the acids (Figs. 3, 4, and 5) and by the X-ray analysis for 3, 4-furandicarboxylic acid (Figs. 6 and 7).

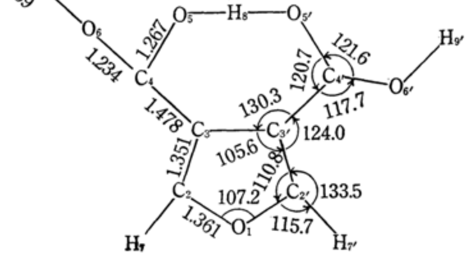


Fig. 6. Intramolecular distances and angles.

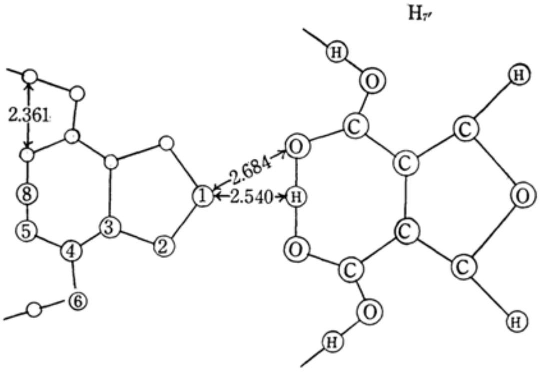


Fig. 7. The structure projected onto the ring square plane.

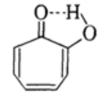
From the infrared spectra taken as KBr disks, the hydroxyl bands for all the acids investigated appear as broad absorption bands with many submaxima between 3000 cm^{-1} and 2000 cm^{-1} instead of the normal hydroxyl band near 3500 cm^{-1}. This fact is consistent with the existence of the intramolecular hydrogen bonding. Also, it has been proposed that the acids which are capable of forming an intramolecular hydrogen bonding give the carbonyl absorption between 1670 cm^{-1} and 1650 cm^{-1} 16) (the normal carboxylic acid C=O band appears near 1700 cm^{-1}) when examined in the solid or liquid state, while the normal aromatic acids absorb at 1700 cm^{-1}. Phthalic acid is normal in this regard, showing a simple C=O band at 1690 cm^{-1}, 2, 4- and 2, 5-furan- or thiophenedicarboxylic acids were also found to give a single intense carbonyl band between 1680 cm^{-1} and 1700 cm^{-1}, indicating that these acids are normal. On the other hand, 2, 3- and 3, 4-furan- or thiophenedicarboxylic acids have double carbonyl bands (Fig. 3), one of which is near 1700 cm^{-1} and the other between 1650 cm^{-1} and 1620 cm^{-1}. The latter bands are fairly intense as compared to the normal carbonyl absorption band. All these observation are consistent with the assumption that these acids are intramolecularly hydrogen-bonded, even in undissociated forms. When hydroxyl hydrogen was replaced by deuterium, the absorption bands due to the -OH stretching shifted towards longer wavelengths. However, no remarkable effect appeared in the C=O stretching region. For example, acetic acid, which generally forms a dimer which absorbs at 3125 cm^{-1} due to OH stretching, changes its band to 2299 cm^{-1} upon deuterium substitution.16) A better example would be tropolone, which forms a strong intramolecular

---

16) See, for example, L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley & Sons, New York (1958), pp. 161—176.

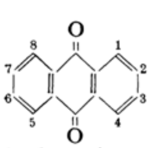
hydrogen bond[17] and the hydrogen-bonding structure of which is somewhat similar to that of 3, 4-furan- or thiophenedicarboxylic acid.

The -OH band is also shifted to a longer wavelength when -OH is changed to -OD, but no effect is observed in C=O stretching. Hadzi and Sheppard[18] have reported that the substituted anthraquinones show a remarkable shift of -OH upon deuterium substitution, as is shown in Table V.



Tropolone

TABLE V

		(OH) or (OD) cm^{-1}	(C=O) cm^{-1}
	1, 4-diOH	2860	1626
	1, 4-diOD	2260	1626
	1, 5-diOH	2950	1637
Anthraquinone	1, 5-diOD	2280	1637

In the case of 3, 4-furandicarboxylic acid, in which carboxyl -OH was exchanged with -OD, a similar effect was observed; the band due to the -O···H stretching at 2500—2800 cm^{-1} disappeared and a new broad band was observed near 1980 cm^{-1}, a band which is assumed to be that of the intramolecular hydrogen-bonded -OD.

The X-ray analysis of 3, 4-furandicarboxylic acid in Figs. 6 and 7 gives fairly good proof for our suggestion of the existence of a strong intramolecular hydrogen bonding in 2, 3- and 3, 4-furan or thiophenedicarboxylic acids. The analysis of 3, 4-furandicarboxylic acid shows that because of the intramolecular hydrogen bonding hydrogen atom lies just in the middle of the two adjacent carboxyl oxygens. The distance of the O-H-O hydrogen bond reveals a marked shortening of O-H-O linkage as compared to the acetic acid dimer or other hydrogen-bonded acids.[19]

In Table II one can see substantial fluctuations in the rate constants obtained. The main reason for the deviations is that the determination of the end point with phenolphthalein is not sharp because of the facile hydrolysis of the second ester groups in the diesters during the hydrolysis. Therefore, each of the rates, actually observed and summarized in Table III, may contain a substantial margin of inherent error. However, even at its greatest the error is not so large as to lead to a wrong conclusion.

Despite the inherent errors, one can draw a few interesting conclusions from the data. First, the order of reactivity in the hydrolysis of the diesters is furan>thiophene>benzene. This is in accord with that of the alkaline hydrolysis of the ethyl esters of monocarboxylic acids in the same solvent[1] and also is to be expected from the magnitudes of the acidity constants of these mono or dicarboxylic acids. Here again, it was confirmed that the thiophene ring is more electron-attracting than the benzene ring, but less so than the furan ring. The fact that the first hydrolysis rate constant, k_1, for dimethyl 2, 5-furandicarboxylate is of an especially high value, is to be expected from the calculation by the Hammett equation using the data for the hydrolysis rate constants of furoic acid.[1]

Another interesting fact is that the rates of the hydrolyses of the diesters in which the two ester groups are attached to adjacent carbon atoms are substantially lower than those of the esters in which the carboxyl groups are separated by CH groups. One reason for this may be that the nucleophilic attack with the hydroxyl ion on the first carbonyl carbon is retarded by the charge repulsion with the adjacent carboxyl oxygen.

Department of Applied Chemistry
Faculty of Engineering
Osaka City University
(S. O., N. F. & T. W.)

Department of Applied Chemistry
College of Engineering
The University of Osaka Prefecture
Sakai, Osaka (Y. O.)

Department of Chemistry
Radiation Center of Osaka Prefecture
Sakai, Osaka (M. H.)

---

[17] V. von Keussler and G. Rosomy, *Z. Electrochem.*, **60**, 136 (1956).

[18] D. Hadzi and N. Sheppard, *Trans. Faraday Soc.*, **50**, 911 (1956).

[19] R. Hofstadter, *J. Chem. Phys.*, **6**, 540 (1938).