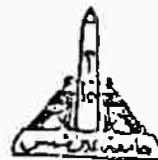


STRUCTURAL EFFECTS ON THE ACID-CATALYZED HYDROLYSIS OF
(E)-3-CARBOXY-4-ARYL-BUT-3-ENOIC ANHYDRIDES

- 28 -

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The rates of acid-catalyzed hydrolysis of (E)-3-carboxy-4-phenyl(1), 4-(1-naphthyl)(2), 4,4-diphenyl(3) and 4-methyl, 4-phenyl(4)-but-3-enoic-anhydrides are compared in dioxane-water mixtures at different temperatures and pH values and are in the sequence $1 > 2 > 3 > 4$. The rate decreases with increase of pH, reaches a minimum at about pH 3.1 then increases gradually till pH 5.7.

INTRODUCTION

Hydrolysis of carboxylic anhydrides in initially neutral solution have been studied extensively. Reaction is retarded by the addition of non-polar solvents to the water and values of energies of activation are lower, and the entropies more negative, than those observed for nucleophilic substitution at a saturated carbon atom^{1,2}. Bunton and co-workers³ have reported that bond breaking is not kinetically important in the hydrolysis of

some carboxylic anhydrides and the reaction is slower in the less aqueous solvents. The reactivities of symmetrical anhydrides of both aliphatic and aromatic carboxylic acids are increased by electron-attracting substituents^{4,5}. However, although some work on the kinetics of the hydrolysis of anhydrides has been reported, the pH-rate profile and solvent effect on the hydrolysis of unsymmetrical α,β -unsaturated carboxylic anhydrides have not been much studied. Thus it was of great interest to investigate the rate of hydrolysis of unsymmetrical anhydrides 1-4 which contain an olefinic linkage conjugated with only one carbonyl group and extended conjugation with one or two aromatic rings.

EXPERIMENTAL

The (E) anhydrides 1, m.p., 166-7°C⁶; 2, m.p., 165-6°C⁷; 3, m.p., 149-51°C⁸, and 4, m.p. 112°C⁹, were prepared and their structures confirmed.

The ¹HNMR were determined in CDCl₃ with a Bucker WH-400 instrument (TMS as internal standard).

Anhydride 2: ¹HNMR.- δ = 3.81 (d, J = 2.5 Hz; CH₂), 7.60 (dd, J = 8, 1.5 Hz; 7-H), 7.63 (mc; 2-, 3-H), 7.66 (dd, J = 8, 1.5 Hz, 4-H), 7.93, 8.11 (AA'BB' system, J = 9 Hz; 5-, 6-H), 7.99 (dd, J = 8, 1.5 Hz; 1-H), 8.57 (t, J = 2.5 Hz; 8-H).

Anhydride 4: ¹HNMR.- δ = 3.49 (q, J = 1 Hz; CH₂), 2.68 (t, J = 1 Hz; Me), 7.25 (dd, J = 8, 1.5 Hz; 1-H), 7.44 (mc; 2-, 3-H).

Kinetic Measurements

The rates of hydrolysis of dicarboxylic anhydrides(1-4) were studied in different mixtures of redistilled CO₂-free water and pure dioxane¹⁰ containing different buffers¹¹ at pH, s 1.2-5.7 and at 25-50°C. The kinetic measurements were made using 0.015^{mol} of anhydride in 100 ml buffer. The general procedure used for the hydrolysis of anhydrides by addition of aniline¹² could not be applied to the anhydrides 1-4, because the reaction with aniline was too slow. Fortunately reaction with hydroxide is also relatively slow at low temperature, so that the acids produced could be titrated directly with alkali¹³. A titrimetric procedure involving the estimation of the liberated dicarboxylic acid in the presence of diphenol purple as indicator¹¹ was followed. The structures of the dicarboxylic acid produced after complete hydrolysis were identical with that stated in the literature⁶⁻⁹.

A thermostat was used so that the temperature could be adjusted to $\pm 0.02^\circ\text{C}$. The rate constants k_1 were calculated graphically by using the integrated form of the first order rate equation and were reproducible within $\pm 1\%$.

RESULTS AND DISCUSSION

The specific rates of the acid-catalyzed hydrolysis of the dicarboxylic anhydrides1-4 in different buffer solutions at pH,s 1.2-5.7 in 50% aqueous dioxane (v/v) were presented in Table 1 at the given temperatures. Fig 1 shows the inverted bell-shaped rate-pH profile with a minimum at about pH 3.5. This indicates

that acid catalysis is considerably less effective than base catalysis. At the minimum in the pH-rate profile $k_b/k_a=10^7$, where k_a and k_b are the catalytic coefficients of acid and base, respectively¹⁴.

A statistical least squares treatment¹⁵ of the Arrhenius equation was used to calculate the activation energy E^\ddagger based on the rate constant k_1 at pH values 1.2 and 5.7 in 50% aqueous dioxane. The enthalpies (ΔH^\ddagger), entropies (ΔS^\ddagger) and free energies (ΔG^\ddagger) of activation and also the Arrhenius frequency factor (A) were calculated using the absolute rate equation¹⁶ and are given in Table 2. However, although the values of ΔH^\ddagger and ΔS^\ddagger for anhydrides 1-4 somewhat change as the structures are changed, the compensation effect between ΔH^\ddagger and $T\Delta S^\ddagger$ plays a part in keeping ΔG^\ddagger more or less constant. This is ascertained by the linear relationship between them with slope unity.

Enhancement of the rate of hydrolysis with the increase of the dielectric constant of the medium (D) can be attributed to the high polarity and greater solvation of the transition state. The linear relationship between $\log k_1$ and $D-1/2D+1$ with positive slope indicates the dipolar interaction¹⁷. The dielectric constants of the dioxane-water mixtures were obtained from data of Akerlof¹⁸. The results are presented in Table 3. The linear relationship between $\log k_1$ and $\log [H_2O]$ with slope equals to unity at pH, s 1.2 and 5.7 indicate that a water molecule acts as a strong nucleophile and is involved in the rate-determining step¹⁹. Thus, from the given results and rate profile the

hydrolysis seems to take place by $A_{AC}2$, and the reaction is catalyzed by both acid and by base but catalysis by base is rather more effective since it becomes dominant while the solution is still acidic¹⁴. The bimolecular mechanism is substantiated by the values of E^\ddagger , ΔS^\ddagger and the Arrhenius frequency factor $\log A$. The large negative value of entropy of activation indicates that initial protonation is followed by synchronous displacement of the carboxylate group (A_2 or S_N2) with no discrete tetrahedral intermediate^{20,21}.

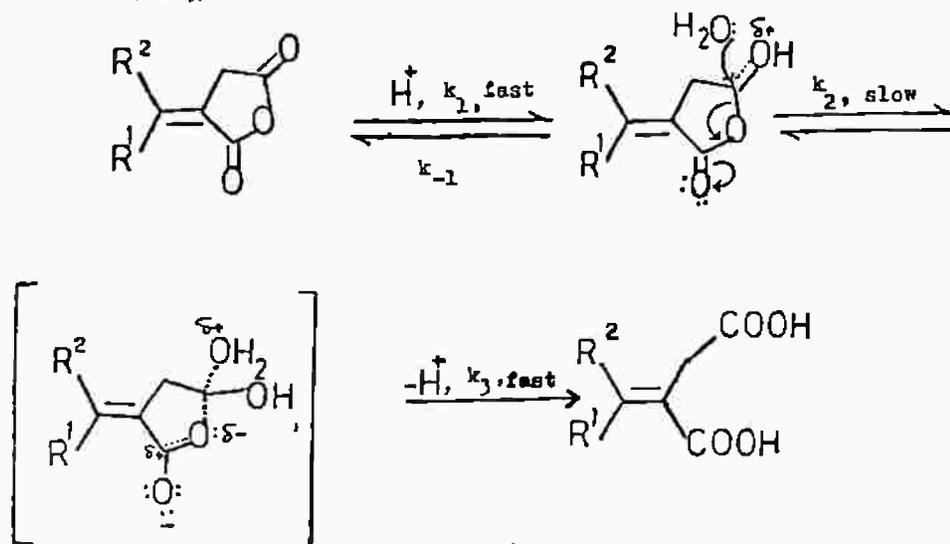
The low sensitivity of the reaction to substituent effect is in accord with the $A_{AC}2$ mechanism.

However, in the unsymmetrical anhydrides, 1-4, the only reactive centre of nucleophilic attack is the nonconjugated carbonyl group where conjugation of the other carbonyl group with the olefinic linkage and its extension to aryl group lowers its susceptibility toward nucleophilic attack (Scheme 1). The sequence of reactivity $1 > 2 > 3 > 4$ reveals that the important effect which influences hydrolysis, similar to cyclization of acids to anhydrides, is steric in origin²¹. It appears that the larger the substituent, the lower is the rate of hydrolysis. Table 2 shows that both enthalpy and entropy changes become less favorable to hydrolysis.

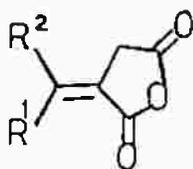
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REFERENCES

1. Gold, Trans. Faraday Soc., 44, 506, (1948).
2. Koskikallio, Ann. Acad. Sci. Fennicae, A II, 57, 1, (1954).
3. C.A. Bunton, N.A., Fuller, S.G. Perry and V.J. Shiner; J. Chem. Soc. 2918 (1963).
4. Rivet and Sidgwick, J. Chem. Soc. 97, 1677, (1910); Wildson and Sidgwick, J. Chem. Soc., 103, 1959, (1913); Kilpatrick, J. Amer. Chem. Soc., 52, 1410, (1930).
5. Berliner and Alschul, J. Amer. Chem. Soc., 74, 4110, (1952).
6. L.S. El-Assal and A.M. El-abbady, J. Chem. Soc., 1024, (1959); Ber., Part 2, 4350, (1908).
7. S.M. Abdel Wahhab, L.S. El-Assal and N.G. Ramses, J. Chem. Soc., 863, (1968).
8. W.S. Johnson, J.W. Peterson and W.P. Scheider, J. Amer. Chem. Soc., 69, 74 (1947); H. Stobbe, Annalen, 308, 89, (1899).
9. S.M. Abdel Wahhab, L.S. El Assal and S.M. Abdel Aziz, Egypt J. Chem., 11, 293, (1968).
10. A.I. Vogel, "Practical Organic Chemistry", Longmanns Green Co., London, New York, Toronto, 1957.
11. F.G. Baddar, S.M. Abdel Wahhab, B.M. Awad, and N.M. Gindy, J. Org. Chem., (B), 739, (1970).
12. Vlès, Rec. Trav. Chem., 52, 809, (1933), Kappelmeier and van Goor, Analyt. Chem. Acta, 2, 146, (1948).
13. C.A. Bunton and S.G. Perry, J. Chem. Soc., 3070, (1960).
14. R.A.Y. Jones "Physical and Mechanistic Organic Chemistry", 2nd Ed., p.269, Cambridge University Press, Cambridge London, New Rochelle, Melbourne, Sidney, 1984.
15. E.S. Swinbourne, "Analysis of Kinetic Data", Thomas Nelson and Sons, Ltd., London, 1971.
16. S. Glasstone, K.J. Laidler and H. Eyring, "The Theory of Rate Processes" McGraw Hill, New York, 1941.
17. K.J. Laidler and C.A. Landskroener, Trans. Faraday. 52, 200, (1956).
18. G. Akerlof, J. Amer. Chem. Soc., 58, 1241, (1936).
19. J.F. Bunnett, J. Amer. Chem. Soc., 83, 4956, (1961).
20. J.F. Bunnett, Acc. Chem. Res. 6, 41, (1973).
21. N.S. Isaacs, "Physical Organic Chemistry", Longman Group, U.K., p. 488, 1987.



Scheme I

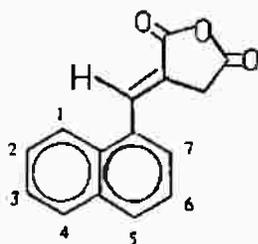


1, $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{H}$

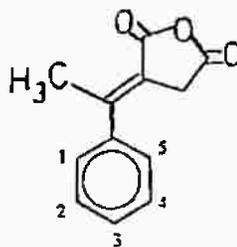
3, $\text{R}^1 = \text{R}^2 = \text{Ph}$

2, $\text{R}^1 = 1\text{-Naphthyl}$, $\text{R}^2 = \text{H}$

4, $\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{Me}$



2



4

TABLE 1

RELATION BETWEEN pH VALUES AND VELOCITY CONSTANTS AT DIFFERENT TEMPERATURES IN 50% AQUEOUS DIOXANE

pH ^a	t°C	10 ⁴ x k ₁ sec ⁻¹			
		Anhydride			
		1	2	3	4
1.2	25	3.327	2.851	1.203	0.770
	30	5.246	4.467	1.919	1.279
	35	7.805	6.998	3.071	2.047
	40	11.643	10.619	4.734	3.199
	45	17.912	16.032	7.423	5.118
	50	25.845	24.266	11.515	7.933
2.1	40	7.293	6.397	2.687	2.175
3.1	40	5.374	4.989	2.303	1.791
4.8	40	8.700	8.316	4.094	2.303
5.7	25	4.222	3.838	2.047	0.870
	30	6.525	5.757	3.071	1.407
	35	9.852	8.700	4.862	2.239
	40	14.840	12.794	7.293	3.455
	45	22.134	18.936	10.747	5.374
	50	31.986	27.764	15.737	8.316

^aThe buffers used are reported in literature¹¹. The buffer solutions were prepared in large batches in order to give reproducible media.

TABLE 2
ACTIVATION PARAMETERS FOR THE HYDROLYSIS OF ANHYDRIDES (1-4)
IN 50% AQUEOUS DIOXANE

Anhydride	pH value	E^{\ddagger} K cal mol ⁻¹	$\Delta H_{400}^{\ddagger}$ K cal mol ⁻¹	$-\Delta S_{400}^{\ddagger}$ cal deg ⁻¹ mol ⁻¹	$\Delta G_{400}^{\ddagger}$ K. cal mol ⁻¹	log A_{400}
1	1.2	16.581	15.955	21.562	22.704	8.5693
	5.7	15.670	15.044	23.987	22.552	8.0427
2	1.2	17.042	16.416	20.273	22.761	8.8491
	5.7	16.121	15.495	22.843	22.645	8.2911
3	1.2	17.963	17.337	18.947	23.267	9.1373
	5.7	17.042	16.416	21.065	22.997	8.6859
4	1.2	18.424	17.798	18.259	23.513	9.2869
	5.7	17.503	16.877	21.047	23.465	8.6814

TABLE 3
RELATION BETWEEN VELOCITY CONSTANTS AND DIELECTRIC CONSTANTS
OF THE MEDIUM AT pH 1.2 AND 5.7

Anhydride	D-W mixture (v/v)	D_{400}	4 + log k_1	
			pH 1.2	pH 5.7
1	60:40	35.39	0.9763	1.0847
	50:50	37.41	1.0661	1.1715
	40:60	39.45	1.1444	1.2500
	30:70	41.80	1.2108	1.3056
	20:80	44.19	1.2625	1.3671
2	60:40	35.39	0.9132	1.0266
	50:50	37.41	1.0261	1.1070
	40:60	39.45	1.0937	1.1714
	30:70	41.80	1.1562	1.2406
	20:80	44.19	1.2108	1.2970
3	60:40	35.39	0.5840	0.7602
	50:50	37.41	0.6752	0.8629
	40:60	39.45	0.7405	0.9395
	30:70	41.80	0.8059	0.9991
	20:80	44.19	0.8552	1.0612
4	60:40	35.39	0.4081	0.4494
	50:50	37.41	0.5049	0.5383
	40:60	39.45	0.5840	0.6122
	30:70	41.80	0.6511	0.6868
	20:80	44.19	0.7198	0.7504

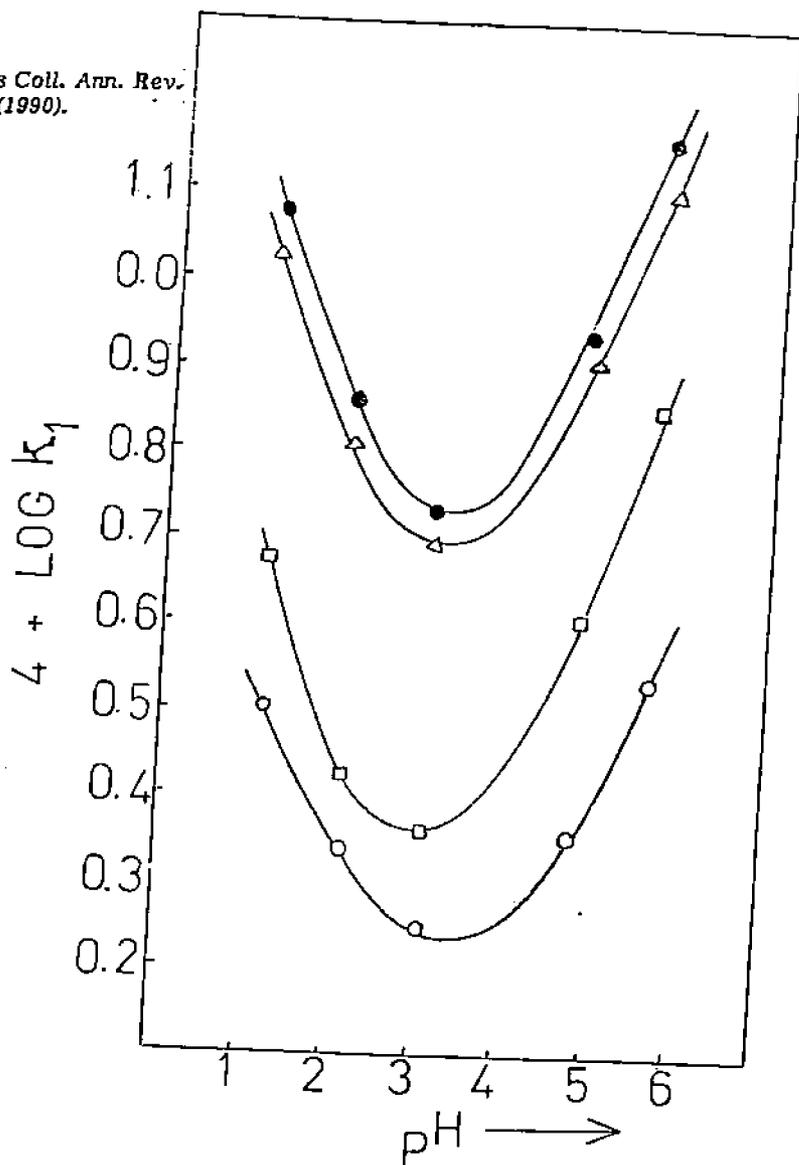


FIGURE (1)

Fig. 1: pH-rate profile for the hydrolysis of anhydride 1
●—●, 2 △—△, 3 □—□ and 4 ○—○ at 40°C in
50% aqueous dioxane.

ملخص عربي

تأثير التركيب البنائي على معدل التحلل المائي في وسط حمض لانهيدرات
(E)-3- كركيوكس -E- ارييل - بيوت -3- إينوك

شادية محمود عبدالله

قسم الكيمياء - كلية البنات - جامعة عين شمس - مصر الجديدة
القاهرة

تم مقارنة معدلات التحلل المائي في وسط حمض لانهيدرات (E)-3-
كركيوكس -E- فينيل (1) ، E- (1-نفتيل) (2) ، E-داي فينيل (3) و E-ميثيل-
E- فينيل (4) - بيوت -3- إينوك في مخاليط من الديوكسان والماء عند درجات
حراره مختلفه وان هيدروجيني مختلف .

وقد وجد ان هذه المعدلات تتبع التوالى الاتى $1 < 2 < 3 < 4$.
وقد وجد ايضا أن معدل التحلل المائي ينخفض بزيادة الأس الهيدروجيني ليصل
إدناه عند أس هيدروجيني 3 ثم يزداد تدريجياً حتى أس هيدروجيني 5.7 .