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ACID DISSOCIATION, UV SPECTRA AND HYDROLYSES OF SEVERAL α-MERCAPTO- AND α-ALKOXYACETIC ACIDS AND THEIR ETHYL ESTERS[†] [‡]

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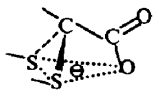
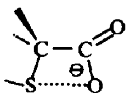
Abstract—New σ^* values of some α-mercapto and α-alkoxy groups have been obtained from the kinetic measurements of acidic and alkaline hydrolyses of ethyl α-substituted carboxylates. The acid dissociation constants and UV spectra of these carboxylic acids are discussed using these newly obtained σ^* values. The relative dissociation constants of α-substituted carboxylic acids cannot be accounted for by the polar effects only since the steric inhibition of solvation around the carboxylate ion by α-substituents plays an important role. In addition, the non-bonding interaction between the α-mercapto group and the carboxylate ion appears to be significant.

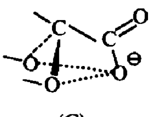
In connection with recent work on the 3d-orbital resonance in divalent sulphides, many mono-, di- and tri-substituted carboxylic acids and their ethyl esters have been synthesized and the dissociation constants of these acids and the rate constants of the hydrolyses of their ethyl esters determined. The object of the investigation was, (1) to estimate the new σ^* values of α-mercapto groups; (2) to examine the principle of additivity of the polar substituent constant σ^* in the dissociation of the poly-substituted acetic acids; and (3) to determine the extent of the non-bonding interaction between α-heteroatoms and carboxylate oxygen like (A), (B) and (C) in the acid dissociation equilibrium.



(A)



(B)



(C)

RESULTS AND DISCUSSION

Estimation of σ^* and Es values of α-mercapto and alkoxy groups

In order to discuss quantitatively the effect of α-mercapto and other related groups on the acid dissociation equilibrium of α-substituted carboxylic acids, it was necessary to determine σ^* values of the α-substituents. The kinetic data obtained from the acidic and alkaline hydrolyses of various ethyl carboxylates furnished a new set of σ^* and *Es* values for α-mercapto and alkoxy groups.

Acid catalysed hydrolyses were carried out in 70% v/v acetone–water containing

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[‡] 3d-Orbital Resonance in Divalent Sulphides—XI.

0·1N HCl and the alkaline hydrolyses were performed in 80% v/v ethanol–water solution at 10°. The estimation of σ^* and *Es* values was according to the method of Taft.[1]

The kinetic data obtained from the experimental procedure are listed in Tables 2 and 3. Table 2 indicates that in the alkaline hydrolyses of ethyl α-substituted carboxylates, ethoxy and phenoxy groups accelerate the reaction more than the corresponding ethylmercapto and phenylmercapto groups, and the additional substitution of ethoxy groups in ethylethoxyacetate increases the reaction rate, while ethylmercapto groups decrease the rate. The cyclic compounds react much faster than the corresponding open chain compounds. Table 1 shows a new set of the σ^* and *Es* values.

The σ^* values obtained for EtO and Ph groups are 0·57 and 0·23, both of which agree with the reported values for MeO and Ph groups of 0·52 and 0·215 respectively. The σ^* value obtained for the phenoxy group (0·95) is greater than the value (0·85) reported by Taft.[1] This is probably due to the difference in the experimental conditions used or/and a higher estimated *Es* value ($Es = -0{\cdot}62$ as compared with $-0{\cdot}33$ reported[1]). We believe that the steric effect of the phenoxy group should be greater than that reported since the *Es* value of the Ph group is $-0{\cdot}38$ and the difference of *Es* values between phenylmercapto ($-0{\cdot}79$) and ethylmercapto ($-0{\cdot}47$) is $-0{\cdot}32$; therefore the estimated *Es* value for the phenoxy group is nearly equal to $-0{\cdot}57$, which was calculated by adding $-0{\cdot}32$ to the *Es* value of EtO group ($-0{\cdot}25$).

A comparison of the polar effect of a α-mercapto with that of a α-alkoxy group shows that the σ^* value of the ethylmercapto group is nearly equal to that of EtO group and larger than that of the Ph group, while the phenylmercapto group ($\sigma^* = 0{\cdot}77$) is less electronegative than the phenoxy group ($\sigma^* = 0{\cdot}95$, reported value 0·85). These values are in accord with the greater electronegativity of the O atom attached to a conjugated system.

The *Es* values of α-mercapto and related substituents are listed in Table 1 together with those already reported. The *Es* values of ethylmercapto and phenylmercapto groups are greater than those of the corresponding oxygen analogues. The steric effect of a divalent S atom is estimated to be greater than that of a methylene group despite the fact that the van der Waals radii of a S atom (1·85 Å) is smaller than that of methylene (2·00 Å).[2]

Acid dissociation equilibria of α-substituted carboxylic acids

The observed p*Ka* values in 50% v/v ethanol–water and in water are summarized in Table 1. In order to determine the effect of α-heteroatoms on the acid dissociation of carboxylic acids bearing one or more heteroatoms in the α-position, the observed p*Ka* values were plotted against σ^*. Figure 1 indicates that all the points cannot possibly lie on a single straight line, but appear to lie on three different straight lines for mono-, di- and tri-substituted carboxylic acids, having ρ values of $-1{\cdot}76$, $-1{\cdot}07$ and $-0{\cdot}91$ respectively. A few substituent groups such as ethoxy, diethoxy, diethylmercapto and dichloro gave points which departed from linearity. Other workers[3–5] have also found scattered correlations between σ^* and p*Ka* values for α-substituted carboxylic acids and the reason is a subject for investigation. Our results indicate that the degree of acid dissociation is not only determined by the polar effect of α-substituents, but also by other factors, including steric hindrance, non-bonding

TABLE 1. IONIZATION CONSTANTS AT 25° IN 50% (v/v) EtOH–H_2O AND IN H_2O AND σ^* AND *Es* VALUE

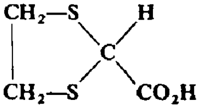
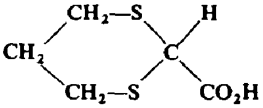
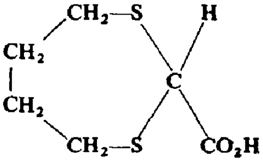
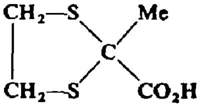
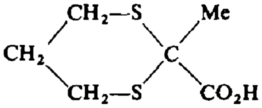
	Carboxylic acid	p*Ka* in 50% (v/v)	in water	σ^*	*Es*[j]
RCH_2CO_2H *type*					
I	$EtOCH_2CO_2H$	4·92 ± 0·03	(3·84 ± 0·03)	0·57†	−0·25†
II	$EtSCH_2$—	4·75 ± 0·02	(4·11 ± 0·05)	0·56†	−0·47
III	$PhOCH_2$—	4·16 ± 0·04[a]		0·95[h]†	−0·62[h]†
IV	$PhSCH_2$—	4·44 ± 0·05[a]		0·77†	−0·79†
V	Me	5·69 ± 0·05[b]	(4·74 ± 0·02)[d]	0	0
VI	$ClCH_2$—	3·77 ± 0·04[b]	(2·83 ± 0·03)[e]	1·05	−0·24
VII	Et—	5·97 ± 0·03[b]	(4·86 ± 0·03)[f]	−0·10	−0·07
XXVI	$PhCH_2$—	5·30 ± 0·04		0·23[i]†	−0·45[i]†
$RR'CHCO_2H$ *type*					
VIII	$(EtO)_2CH$—	4·82 ± 0·06		1·14	(−1·18)
IX	$(EtS)_2CH$—	4·52 ± 0·05		0·94†	−2·31†
X	$(PhO)_2CH$—	3·64 ± 0·03		1·90	
XI	$(PhS)_2CH$—	4·12 ± 0·04		1·54	(−3·29)
XII	EtS·CH(Me)—	5·28 ± 0·03		0·49†	−1·53†
XIII	PhSCH(Me)—	5·05 ± 0·03		0·67	(−1·76)
XIV	PhSCH(Ph)—	4·70 ± 0·03		1·00	
XV	Cl_2CH—	2·51 ± 0·04[b]		2·10	−1·54
XVI		4·46 ± 0·04		1·02†	−1·02†
XVII		4·27 ± 0·05		0·92†	−1·69†
XVIII		4·27 ± 0·04		1·00†	−1·69†
$RR'R''CCO_2H$ *type*[g]					
XIX	$(EtS)_2C(Me)$—	4·96 ± 0·03		0·84	
XX	$(PhS)_2C(Me)$—	4·59 ± 0·04		1·44	
XXI	$(EtS)_2C(Ph)$—	4·57[c]		1·17	
XXII	$(PhS)_2C(Ph)$—	4·23 ± 0·02		1·77	
XXIII	Cl_3C—	2·05 ± 0·06		3·15	
XXIV		4·70 ± 0·05		0·92	

TABLE 1—*continued*

	Carboxylic acid	p*Ka* in 50% (v/v)	in water	σ^*	Es^j
XXV		4·83 ± 0·04		0·82	

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† Newly obtained values in these experiments.

[a] Reported values of III and IV, 4·20 and 4·67 respectively (D. J. Pasto and R. Kent, *J. Org. Chem* 30, 2684 (1965).

[b] Reported values 5·5 for V, 3·5 for VI and 2·3 for XV (J. Hine and O. B. Ramsay, *J. Am. Chem. Soc.* 84, 973 (1962). The p*Ka*'s were determined from the pH values at the half-equivalent points, at which the ionic strength was 0·004M.

[c] From only one run.

[d] Reported value 4·756, D. A. MacInnes and T. Shedlousky, *J. Am. Chem. Soc.* 54, 1429 (1932).

[e] 2·85 (20°), 2·87 (25°), D. J. G. Ives and J. H. Pryor, *J. Chem. Soc.*, 2104 (1955).

[f] Reported value 4·874, H. S. Harned and R. W. Ehlers, *J. Am. Chem. Soc.* 54, 1350 (1932).

[g] σ^* Values were caluclated on an additive basis.

[h] 0·85 (σ^*), −0·33 (*Es*) R. W. Taft, Jr., see Ref. 3.

[i] 0·215 ± 0·04 (σ^*), −0·38 (*Es*), see Ref. 3.

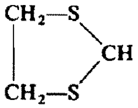
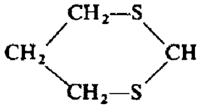
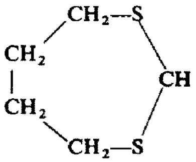
[j] Values in parentheses were calculated from substituting σ^* and $\log (k/k_0)_B$ into Eq. (2).

interactions such as (A), (B) and (C) and neighbouring group participation like (D), etc. Since the steric effect is significant in acid dissociation, recalculation of p*Ka* values has been tried using Eq. (1), taking into account the steric effects of α-substituents in the same way as the Taft–Ingold treatment in the alkaline hydrolyses of α-substituted carboxylic acid esters.

$$\Delta pKa = \rho \cdot \sigma^* - \gamma \cdot Es \qquad (1)$$

The Δp*Ka* is the p*Ka* of a substituted carboxylic acid in relation to that of acetic acid, and γ is the constant which gives the degree of steric effect of a α-substituent and should be smaller than unity, since in acid dissociation equilibrium, the reaction centre (carboxylate ion) is further away from the α-substituent than in the hydrolysis reaction. Trial and error gave the best. line $\Delta pKa = -1{\cdot}97\sigma^* - 0{\cdot}35 \cdot Es$ with correlation coefficient $r = 0{\cdot}999$ as shown in Fig. 2. This Fig. 2 shows that the above treatment allows all the points of these di-substituted carboxylic acids to fall satisfactorily on a single straight line. Consequently, the above results show that the solvation of the carboxylate ion is an important factor controlling dissociation and that α-substituents reduce the solvation of the dissociated carboxylate ion and decrease the dissociation. The importance of solvation for the stabilization of anions by protic solvents has been proposed by other workers[6] and recently it was suggested that the acid dissociation equilibria of a few *ortho*-substituted phenols in water were depressed by *ortho* substituents causing steric hindrance of solvation around the phenolate ion.[7] Hall,[8] also has suggested a possible steric inhibition of solvation in the acid dissociation equilibria of various ammonium salts in water. Thus, it is reasonable to expect that the carboxylate ion formed in the dissociation should be solvated by hydrogen-bonding with a protic solvent. This hydrogen-bonding can only take place if the protic solvent molecules, namely, water or ethanol in this case,

TABLE 2. RATE CONSTANTS AND ACTIVATION PARAMETERS OF ALKALINE HYDROLYSES OF ETHYL ESTERS

R in RCO_2Et	$k \times 10 (l \cdot mol^{-1} \cdot min^{-1})$ at 10·0°	$\log (k/k_0)$	*Ea* (Kcal/mol)	S (e.u) at 10·0°
Me	1·77	0	14·4	−23·8
Et	0·889	−0·30		
$PhCH_2$	2·42	0·13		
$EtOCH_2$	25·6	1·16		
$EtSCH_2$	14·4	0·91	13·8	−21·6
$PhOCH_2$	78·9	1·65		
$PhSCH_2$	22·8	1·11		
$ClCH_2$	490[a]	2·84[b]		
$(EtO)_2CH$	77·1	1·64	11·0	−28·3
$(EtS)_2CH$	1·83	0·013	11·3	−34·6
$(Ph)S_2CH$	5·75	0·51		
EtSCH(Me)	0·861	−0·31		
PhSCH(Me)	1·42	−0·10		
	59·7	1·53	13·3	−20·6
	6·85	0·59	14·7	−20·8
	11·0	0·59		

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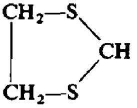
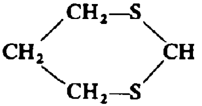
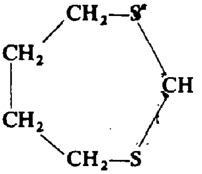
[a] Rate at 0·4°.

[b] Relative rate at 0·4°, calculated from extrapolation of rate constant of ethyl acetate using activation energy.

Ea = 14·4 Kcal/mol.

are suitably oriented around the carboxylate ion to be solvated. Bulky α-substituents will undoubtedly inhibit the orientation of these protic solvent molecules around the carboxylate ion, thus reducing the solvation and the stability of the ion. The slight departures from linearity by points on the graph are produced by groups such as the mercapto group which apparently has an acid strengthening effect or the EtO group which has an acid weakening effect in α-substituted acetic acids. This departure from linearity is also found in the free energy relation between acid dissociation of these carboxylic acids and the rates of alkaline hydrolysis of the corresponding ethyl carboxylates (Fig. 3). Thus, it seems that the combination of polar and steric effects alone is not enough to account for all the facts in the dissociation of these

TABLE 3. ACID-CATALYSED HYDROLYSES OF ETHYL ESTERS

Ester R in $RCO_2C_2H_5$	Experimental temp[a] (°C)	Ea (Kcal/mol)	$k(25°) \times 10^5$ $(l \cdot mol^{-1} \cdot sec^{-1})$[b]
Me	39·5, 49·9, 60·1	16·3 (16·2)[c]	4·30
$ClCH_2$	39·1, 60·1, 65·7	15·9	2·65
$PhCH_2$	55·0, 65·7, 78·5	15·9	1·50
$PhOCH_2$	51·2, 60·0, 73·4	17·7	1·20
$EtOCH_2$	40·0, 50·0, 30·0	16·9	2·57
$EtSCH_2$	40·0, 50·0, 30·0	15·8	1·42
$PhSCH_2$	30·0, 50·0, 60·0	16·7	0·73
$(EtS)_2CH$	60·0, 79·3, 90·6	18·3	0·0257
EtSCH(Me)	73·4, 78·5, 89·5	17·5	0·142
	40·0, 60·0	18·3	0·50
	60·0, 79·3, 90·6	17·7	0·10
	90·5		0·10[d]

[a] Temp was controlled within the maximum deviation of 0·05°.

[b] Extrapolated values from Arrhenius plot.

[c] Hilton A. Smith and R. R. Myers, *J. Am. Chem. Soc.* **64**, 2362 (1942).

[d] The calculated value k (25°) was obtained assuming the activation energy to be 18·0 Kcal/mol, average value of the 5- and 6-membered compounds.

α-heteroatom substituted carboxylic acids. The exceptions may be due to non-bonding interactions like (A), (B) and (C), intramolecular hydrogen-bonding such as (E) and neighbouring group participation like (D). Further, if the dissociated carboxylate ion is sufficiently stabilized by an effective ionizing solvent, such as water,[6] then the dissociation may be controlled mainly by the inductive effect, and ethoxyacetic acid would be a stronger acid than the sulphur analogue in the same solvent. And if ethanol, which is a less effective ionizing solvent, is added to the water, the dissociated ion from ethoxyacetic acid should become less stable due to the non-bonding repulsion between carboxylate oxygen and the EtO group like (C) especially in the case of diethoxyacetic acid. On the other hand, intramolecular hydrogen-bonding like (E) in the undissociated carboxylic acid may be stronger in a less polar medium than in an ionizing medium, i.e. water, thus reducing the dissocation. If the double bond–no bond resonance[9] such as (F) operates, then diethoxyacetic acid should be more acidic than the sulphur analogue, but this is not the case. Neighbouring group

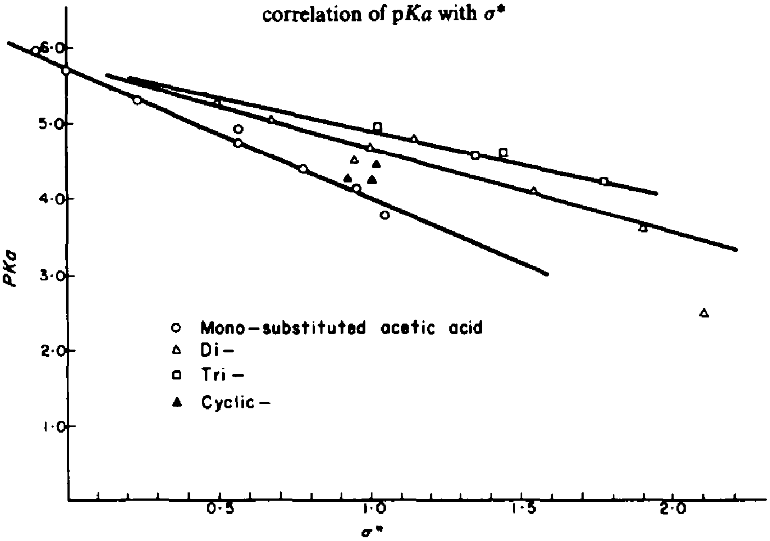


FIG. 1

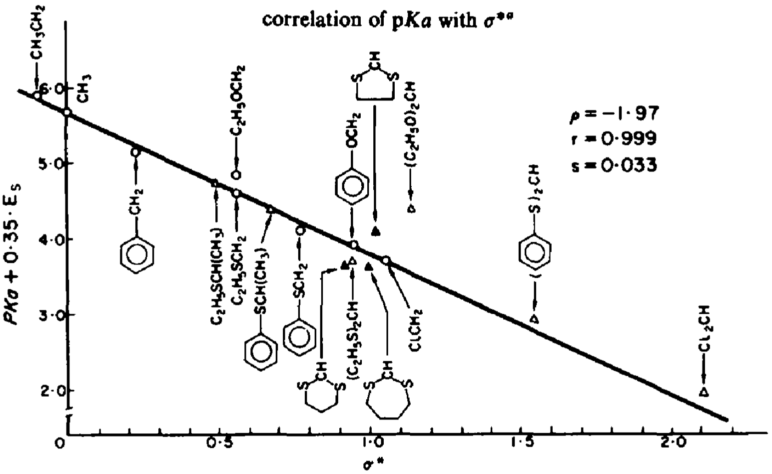
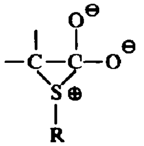


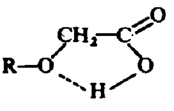
FIG. 2

[a] Ethoxy, diethoxy, dichloro and cyclicmercapto cartoxylic acids are omitted from the calculation of ζ

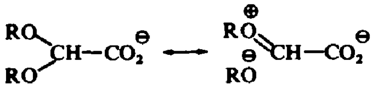
participation between the α-heteroatoms and the carbonyl carbon like (D) should, if operative, destabilize the dissociated carboxylate ion due to the repulsion between lone pair electrons on both carbonyl oxygens, thus reducing the dissociation of the sulphur compounds. But again this was not found to be the case although such a participation is quite conceivable in the photoexcited state.[10]



(D)



(E)



(F)

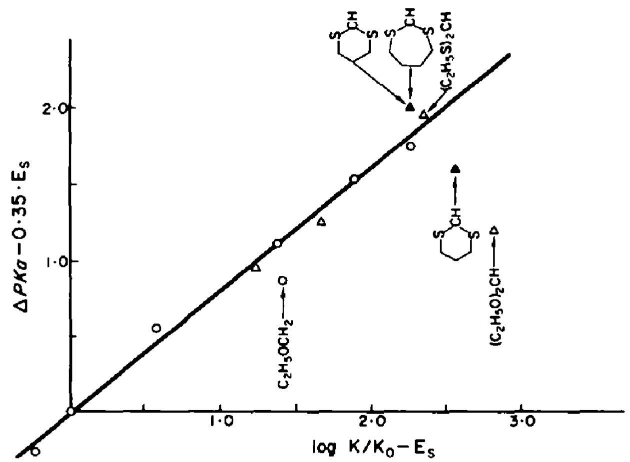


Fig. 3 Linear Free Energy Relationship between p*Ka*[a] and Alkaline Hydrolysis[b]

[a] p*Ka* in 50% v/v ethanol–water at 25° (see Table 1)

[b] Alkaline hydrolyses of corresponding ethyl esters (see Table 2).

In the case of sulphur analogues, such non-bonding repulsion in the dissociated ion would be very small or even suppressed by the attraction due to the overlapping of a 2p-orbital of the carbonyl oxygen and one of the empty 3d-orbitals of the S atom like (A) and (B), while the undissociated acid cannot be stabilized by hydrogen-bonding to the α-S atom as in the oxygen analogues, thus increasing the acid dissociation. Consequently, as seen in Table 1, ethylmercapto- and diethylmercapto-acetic acids are more acidic than the corresponding oxygen acids in 50% v/v ethanol–water.

Ring effect

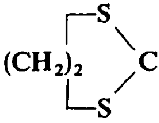
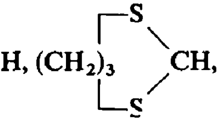
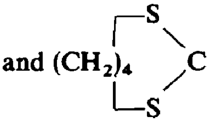
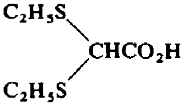
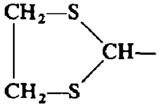
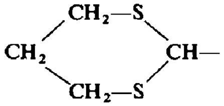
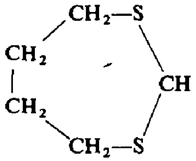
Comparison of the p*Ka* values of the open chain dimercapto substituted acids with those of the series of cyclic acids shows that the open chain compounds (IX and XIX) are slightly less acidic than the corresponding cyclic compounds (XVI, XVII, XVIII, XXIV and XXV). A possible explanation is that non-bonding interaction like (A) is presumably more effective in the cyclic compounds than the corresponding open chain compounds. Another explanation is that the carboxylate ion from the open chain compounds would be less solvated due to the relatively larger steric inhibition of solvation than in the cyclic acids. In fact, *Es* values of $(EtS)_2CH$,  ,  and  are −2·31, −1·02, −1·69 and −1·69, respectively. Figure 2 indicates that the open chain, 6- and 7-membered cyclic compounds lie below the straight line (acid strengthening), but the 5-membered compound alone is located above the line (acid weakening). Meanwhile, the chemical shifts of α-methyne protons of these four carboxylate compounds were correlated by the newly obtained σ^* values. (See Table 4.)

TABLE 4. THE σ^* AND KINETIC DATA OF CYCLIC CARBOXYLIC ACIDS

Compound	σ^*	Chem. shift[a]	pK_a[b]	Rate constant of alkaline hydrolysis[c]
	0·94	4·19	4·52	1·83
	1·02	4·68	4·46	59·7
	0·92	3·92	4·27	6·85
	1·00	4·44	4·27	11·0

[a] Chemical Shift (ppm) of α-methyne proton of its ethyl ester in 10% CCl_4 soln at 25°. TMS was used as an internal standard.
[b] In 50% v/v ethanol–water at 25°.
[c] $k \times 10\,(\text{l-mol}^{-1}\ \text{min}^{-1})$ at 10°

We believe that non-bonding interaction is significant in controlling the acid dissociation of these cyclic carboxylic acid but does not offer an explanation for the departure of the 5-membered carboxylic acid. Perhaps a slightly different configuration around the carboxyl group in this acid reduces the non-bonding interaction, but this cannot be confirmed until the exact configuration of this acid has been determined.

Studies of UV spectra of α-mercaptocarboxylic acids

In connection with the acid dissociation equilibrium and the base-catalysed decarboxylation reaction, UV spectra of α-mercaptocarboxylic acids were measured in ethanol, cyclohexane, 0·1N NaOH and 0·1N HCl and the data were compared with that of previous work on α-mercaptoles.[11] The observed λ_{max} and intensities of all these compounds are listed in Table 5.

Dialkyl sulphides absorb in the region of 210 mμ with intensities near log ε = 3, while the substitution of one additional mercapto group or carbonyl group[10, 11] at the α-carbon results in a marked red shift. These shifts in α-mercaptoles were explained in terms of non-bonding interaction between two geminal S atoms like (G), while those of α-ketosulphides were ascribed to the neighbouring group participation of a S atom to the carbonyl group like (H) and (I), in the photoexcited state.

α,α′-Diethylmercaptoacetic acid and related compounds bearing another potential chromophore, i.e. a CO group were examined. The spectra of diethylmercaptoacetic

TABLE 5. ABSORPTION MAXIMA AND MOLAR EXTINCTION COEFFICIENTS IN THE NEAR UV REGION

Compound	in 0·1N HClaq		in 0·1N NaOHaq		in ethanol		Corresponding mercaptal[b] in EtOH	Corresponding mercaptal[b] in cyclohexane	
	λ_{max} (mμ)	ε	λ_{max} (mμ)	ε	λ_{max} (mμ)	ε	λ_{max} (mμ) ε	λ_{max} (mμ)	ε
II	246	167	‡	‡	248	195			
IX	244†	885	244†	836	242†	955	237 (553)		
	302	414	288	310	297	171			
IXa[a]					243†	982		242†	1094
XIX	246†	518	242†	855	240†	604	239 (707)		
XXI					249	2140			
XVI	252†	431	240	414	251†	456	246 (285)		
					224†	826			
XVIa[a]					253†	511		254†	587
					223†	933		224†	962
XXIV	249†	493	247†	383	250	491	246 (314)		
XVII	240†	675	248†	608	233	1245	250 (469)		
XVIIa[a]					233	1410		237	1507
XXV	232†	1063	225	1076	234	1121	252 (449)		
	251†	497	251†	452	‡	‡			
XVIII	241†	780	‡	‡	237†	930	230–250 (500)		
XVIIIa					238†	956		238	1046
XI					261	7913			
					272†	4505			
XXII					286†	3251			
IV					253	6325			
XIII					256	4139			
XIV					255	4697			
XXVII[c]					254	9912			
XXVIII[d]					259	12300			
X					262†	1415			
					268	1778			
					274	1406			

† Shoulder.

‡ There are no maxima and shoulders in the region between 220 mμ and 360 mμ.

[a] Its ethyl ester.

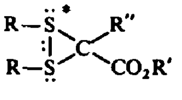
[b] See Ref. 11.

[c] Thioanisole.

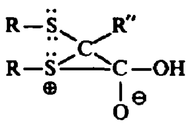
[d] Diphenylmercaptoformal.

acid and cyclic compounds are shown in Fig. 4. As these spectra are complicated and only the 6-membered compound has a clear absorption maximum, very little can be deduced from the analyses as follows.

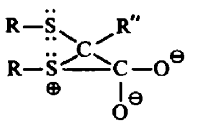
(1) The intensities of absorption of these α-alkylmercapto carboxylic acids are generally higher than those of the corresponding mercaptals previously observed[11] (Table 5). (2) The shapes of the spectra are similar to those of the corresponding



(G)



(H)



(I)

ethyl esters, which have slightly higher intensities. (3) A change of solvent from ethanol to cyclohexane does not change the spectra. (4) The absorption maxima of the α,α′-diethylmercaptoacetic acid derivatives in ethanol are 240–243 mμ for the open chain, 250–251 mμ for the 5-membered, 233–234 mμ for the 6-membered and 237–238 mμ for the 7-membered compounds and a α-Me group does not change the maxima. (5) All these compounds show lower intensities of absorption at shorter wavelength in the acidic medium and higher intensities at longer wavelength as compared to those in the alkaline medium (Fig. 5). This is typical for the acid-base equilibrium systems and the intersecting points may correspond to the isobestic points. Since all the mercapto acids studied have the p*Ka* around 4·5 in 50% ethanol–water, they are almost completely dissociated in dilute sodium hydroxide solution, while they are largely undissociated in dilute hydrochloric acid. Therefore the increase of absorption at a longer wavelength in the acidic medium may be due to the increased contribution of the structure (H), at the photoexcited state. The excited state for the dissociated anion would be represented by the structure (I), which would have a higher energy than that of (H) because of the dianion structure, thus absorbing at shorter wavelength. These results suggest that in diethylmercaptoacetic acid and cyclic compounds, the chromophoric contribution of (G), (H) and (I) may be superimposed to one another in the photoexcited state to give complicated spectra. The Ph group of α,α′-diethylmercaptophenylacetic acid caused a bathochromic shift of 7 mμ together with a higher intensity as compared to that of diethylmercaptoacetic

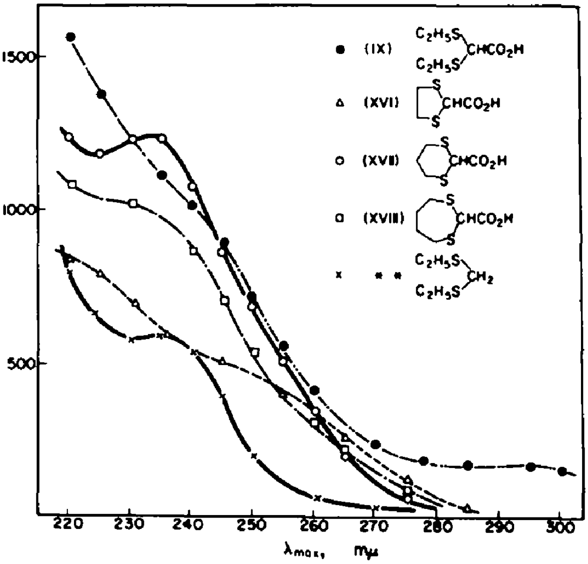
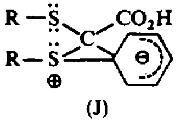


Fig. 4 Absorption Spectra of Diethylmercaptoacetic Acid and Cyclic Acids in Ethanol.
** See Refs. 10 and 11.

acid. This effect of a α-Ph group may be attributed to the additional chromophoric interaction shown by (J), but this effect apparently does not operate in the photo-



(J)

excitation of α,α′-diphenylmercaptophenylacetic acid (XXII). In the case of α-phenylmercapto substituted carboxylic acids, well separated absorption maxima are usually observed and the shapes of the spectra are similar to those of the corresponding sulphides; thus, λ_{max} of phenylmercapto- and diphenylmercaptoacetic acids (IV and XI) are 253 mμ and 261 mμ in ethanol, comparable with 254 mμ for thioanisole and 259 mμ for diphenylmercaptoformal, respectively, while their intensities are even lower than those of the corresponding sulphides (Fig. 6). The chromophore of the phenylmercapto group absorbs near 254 mμ and is independent of the nature of α-substituent (compare the UV spectra of IV, XIII, XIV and XXVII). This shows that the neighbouring group participation of the α-S atom to the CO group like (H) and (I) does not operate in these phenylmercapto derivatives because of the lower electron-donating ability of the S atom attached to the Ph ring. Moreover, it is noticeable that the substitution of one additional phenylmercapto group at the α-C of either phenylmercaptoacetic acid or thioanisole causes a red shift of 8 mμ for diphenylmercaptoacetic acid and 5 mμ for diphenylmercaptoformal.

As a large red shifts of 25–40 mμ was observed in diethylmercaptoformal and cyclic dimercaptals,[11] these results indicate that the non-bonding interaction of the type (G) between the two geminal S atoms of diphenylmercapto compounds is much

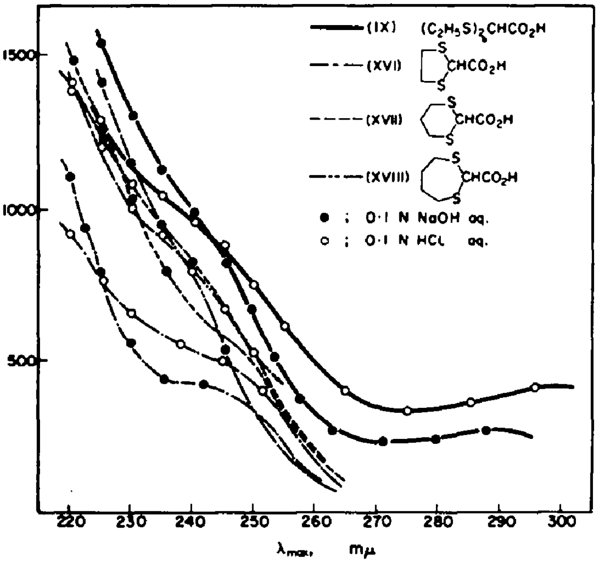


Fig. 5 Absorption Spectra of Mercapto-Substituted Acids in Alkaline and Acidic aq. Soln.

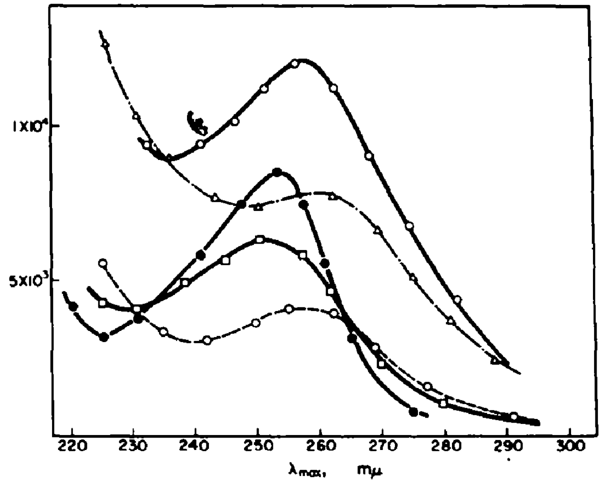


FIG. 6. Absorption Spectra of Phenylmercapto substituted Carboxylic Acids and related compound in EtOH.

—○— (PhS)$_2$CH$_2$ —●— PhSCH$_3$
—△— (PhS)$_2$CHCO$_2$H —○— PhSCH(CH$_3$)CO$_2$H
—□— PhSCH$_2$CO$_2$H

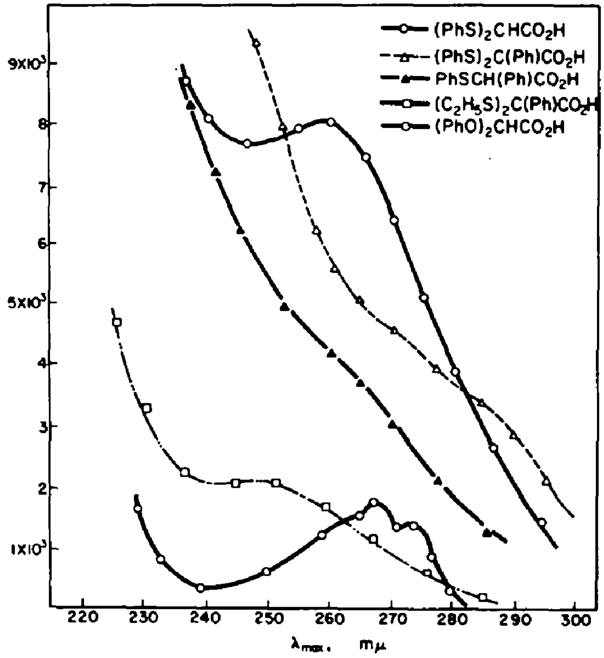


FIG. 7 Absorption Spectra of Phenylmercapto and Phenoxy substituted Carboxylic Acids in EtOH.

smaller than in diethylmercapto compounds in the photoexcited state. Therefore, the phenylmercapto group is considered to be the only principal chromophore in phenylmercapto substituted compounds.

EXPERIMENTAL

Preparation of materials

2-Methyl-1,3-dithiolan-2-carboxylic acid (XXIV). Into 7·0 g (0·08 moles) pyruvic acid dissolved in 30 ml abs ether, 7·5 g 0·08 moles) ethanedithiol (obtained from ethylene dibromide) dissolved in 30 ml abs ether was dropped portionwise within a minute at room temp and into this reaction mixture, dry HCl was bubbled with stirring. After keeping the mixture at room temp for 3 hr, the ether was removed on a water bath and the remaining crystals were recrystallized twice from n-hexane–EtOAc to give colourless crystals, m.p. 100·5–103, yield 50%. The 6-membered cyclic XXV was synthesized in the same way yielding 40% colourless crystals, m.p. 132–134°.)

The open chain XIX was synthesized as follows. Pyruvic acid 8·8 g (0·1 mole) and 25 g (0·4 moles) ethylmercaptan were dissolved in 80 ml abs ether and the soln was saturated with dry HCl with stirring at room temp. After 3 hr, water which separated from the ether layer was decanted and additional 8·8 g (0·1 mole) ethylmercaptan was added to the ether with stirring for 1 hr. Ether, unreacted mercaptan and HCl were removed under reduced press, and the residual oil was poured into 5% NaOHaq followed by ether extraction. The water layer was acidified with HCl and also extracted with ether. The ether layers were washed twice with water and dried (Na_2SO_4). After removal of the ether on a water bath the residual oil was vacuum distilled to give a colourless oil, b.p. 98–100/0·1 mmHg; yield 60%. Similar treatment of pyruvic acid with thiophenol gave colourless crystals of α,α′-diphenylmercaptopropionic acid, m.p. 114–116°.

1,3-Dithiolan-2-carboxylic acid (XVI). A benzene soln of 48 g ethyl diethoxyacetate and 31 g ethanedithiol containing 25 ml BF_3–Et_2O was refluxed for 7·5 hr and the reaction soln then poured into ice water, and extracted with ether. The ether was evaporated and the residual oil distilled under a reduced press to give a colourless oil, b.p. 96·0–96·4/2 mmHg. The esters of XVII, b.p. 132–133/4 mmHg, XVIII, b.p. 115–117/1·8 mmHg, and IX, b.p. 98·0–98·5/2 mmHg, were prepared by a similar procedure, using trimethylene dithiol, tetramethylene dithiol and ethylmercaptan, respectively. The corresponding carboxylic acids of these esters were prepared by hydrolysis in 5% by weight KOH–MeOH soln. The 5- and 6-membered compounds were recrystallized from water and the 7-membered compound from n-hexane–EtOAc. The open chain compound was distilled under reduced press under N_2. The properties of these carboxylic acids are shown in Table 6.

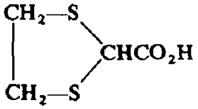
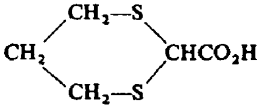
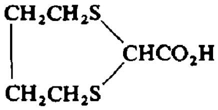
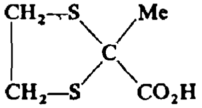
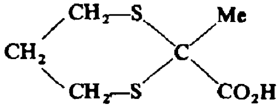
Mono-substituted carboxylic acids. The ethoxy-I, phenoxy-III, ethylmercapto-II and XII, phenylmercaptoacetic acids IV and XIII were synthesized by hydrolysis of the corresponding esters, which were obtained by the substitution reaction of ethyl chloroacetate and ethyl α-chloropropionate with sodium alkoxides and mercaptides in ethanol.

Diethoxy-VIII *and diphenoxy*-X *acetic acids.* Ethyl α,α′-diethoxyacetate was prepared by the Moffett method[14] and hydrolysis was carried out at room temp. Ethyl α,α′-diphenoxyacetate was prepared as follows. Metallic Na (2·7 g) was dissolved in 80 g abs EtOH in a 200 ml 3-necked flask and then 11 g phenol was added. To this reaction mixture 10 g ethyl dichloroacetate dissolved in 20 ml abs EtOH was added portionwise with stirring and the mixture refluxed for 20 hr. The mixture was then concentrated by evaporation of EtOH under reduced press and 50 ml of the remaining residual oil was poured into 150 ml ice water containing an equal volume of ether. The ether extraction was once again carried out with an additional 100 ml ether. The ether layers were washed with water, dried (Na_2SO_4), concentrated and finally distilled under reduced press to give a colourless liquid, b.p. 208/28 mmHg. The above ester was hydrolysed and recrystallized first from water and then from n-hexane–ethyl acetate to give colourless needle crystals, m.p. 92–92·5; total yield 40%.

α-Phenylmercapto-phenyl-XIV, *α,α′-diphenylmercapto*-XI, *α-phenyl-α,α′-diethylmercapto*-XXI *and α-phenyl-α,α′-diphenylmercapto*-XXII *acetic acids.* The syntheses and the properties of these carboxylic acids have been reported previously.[13] The monochloroacetic, dichloroacetic, acetic and propionic acids used in these experiments, were prepared by careful fractionation of the commercial materials. Purities and identifications of these above sample compounds were checked by IR, NMR spectra and elemental analyses. The properties of these carboxylic acids are all listed in Table 6.

Solvent. Water used for the p*Ka* measurements was purified by first refluxing with $KMnO_4$ for a day and then by distillation twice before final use. Abs EtOH was prepared by refluxing the commercial grade with NaOH for a few hr in order to remove aldehydes, followed by distillation, then refluxing over CaO for a day to exclude water and finally by distilling twice through an efficient column. The 50% aqueous EtOH soln was prepared by mixing an equal volume of water and EtOH. The 0·100M titrant alkaline soln was prepared by dissolving KOH into the above EtOH–water soln under N_2, followed by standardization

TABLE 6. THE BOILING AND MELTING POINTS AND ELEMENTAL ANALYSES OF CARBOXYLIC ACIDS

Compound	b.p. °C/mmHg (m.p. °C)	Its ethyl ester b.p. °C/mmHg	Found[f]		Calc	
			C%	H%	C%	H%
$EtOCH_2CO_2H$	110–110·5/22	109–110/22				
$EtSCH_2CO_2H$	145/30	98/34				
$PhOCH_2CO_2H$	(97–98)[a]	151/27				
$PhSCH_2CO_2H$	(61–62)[b]	118/1·0				
$(EtO)_2CHCO_2H$	95–96·5/11	91/23	48·68	8·39	48·64	8·16
$(EtS)_2CHCO_2H$	131–132/1·8	93–93·5/2	39·75	6·78	39·96	6·71
$(PhO)_2CHCO_2H$	(92–92·5)		69·13	5·07	68·84	4·95
$(PhS)_2CHCO_2H$	(104–105)	165–167/1	60·86	4·55	60·84	4·38
$EtSCH(CH_3)CO_2H$	94/4	65/2·5	44·87	7·58	44·75	7·51
$PhSCH(CH_3)CO_2H$	134/2	159–161/23·5				
$PhSCH(Ph)CO_2H$	(100–101)		68·89	5·26	68·83	4·95
	(91–92)	96–96·4/2	32·41	4·32	31·98	4·02
	(116–117)	132–133/4	36·59	5·18	36·56	4·90
	(85–86)	115–117/1·8	40·63	5·82	40·42	5·65
$(EtS)_2C(Me)CO_2H$	98–100/0·1		43·27	7·26	43·58	7·68
$(PhS)_2C(Me)CO_2H$	(114–116)[c]		62·27	5·06	62·04	4·86
$(EtS)_2C(Ph)CO_2H$	(79–81)		56·60	6·29	56·21	6·29
$(PhS)_2C(Ph)CO_2H$	(140–141)[d]		68·20	4·72	68·15	4·58
	(100·5–103)[e]		36·10	5·55	36·56	4·91
	(132–134)		40·43	5·72	40·42	5·65

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[a] 98·5–99·5° (D. J. Pasto and R. Kent, *J. Org. Chem.* **30**, 2684 (1965)).

[b] 62·5–63·5° (D. J. Pasto and R. Kent, *J. Org. Chem.* **30**, 2684 (1965)).

[c] 116–117° (R. Escales and E. Baumman, *Ber. Dtsch. Chem. Ges* **19**, 1787 (1886)).

[d] 143° (R. Escales and E. Baumman, *Ber. Dtsch. Chem. Ges.* **19**, 1787 (1886)).

[e] 102° (H. Fasbenden, *Ber. Dtsch. Chem. Ges.* **21**, 1477 (1888)).

[f] Elemental analysis of carboxylic acid.

with a standard aqueous potassium hydrogen phthalate soln. A standard reference buffer, pH 4·01 ± 0·02 at 25°, was prepared by diluting Horiba concentrated pH standard solution, No. 110-4, Horiba Instruments Inc.

Determination of the ionization constants.[14] The ionization constants were determined by potentiometric titrations, employing a pH-meter, model-p, No. 17317, Horiba Instruments Inc. with a scale measurable down to 0·005 pH unit. The electrodes were 2310-04T calomel and 1325-04T glass electrodes. The electrodes were standardized both before and after each run. The concentration of each sample was chosen so as to give 0·01M at the half-neutralization point. A sample 5×10^{-4} mole dissolved in 47·5 ml of 50% v/v $EtOH{-}H_2O$ was kept at 25° ± 0·1 in 100 ml vessel, into which each 0·5 ml of 0·100M alkaline KOH soln was added successively through 5 ml microburette. The pH measurement of the soln was made just after each addition of 0·5 ml alkaline soln. From 9 points of pH measurement, the p*Ka* value was calculated by the following Eq.[15]

$$\mathrm{pH} = \mathrm{p}Ka + \log \frac{[\mathrm{salt}] + [\mathrm{H}^+]}{[\mathrm{Acid}] + [\mathrm{H}^+]}$$

The hydronium ion activity was taken as the negative antilog of the pH. The p*Ka* values are listed in Table 1.

Measurement of the UV spectra. Absorption spectra were recorded at 20° using Hitachi Photoelectric Spectrophotometer Model F-PS-2. Solvents used for measurement were abs EtOH, water, cyclohexane, 0·1N NaOH and 0·1N HCl.

Concentrations of samples were changed for the range of 5×10^{-3} to 5×10^{-5}M for each compound so as to give a suitable optical density. Intensities were calculated using Beer–Lambert equation. Observed λ_{max} and intensities are listed up in Table 5.

Acidic and alkaline hydrolyses of ethyl esters. Preparations of all the ethyl esters were carried out by an usual sulphuric acid catalysed esterification of the corresponding carboxylic acids in benzene. Purities and identifications of these compounds were checked by IR, NMR spectra and gas-chromatographies. Their b.ps were listed in Table 6. Acetone used for kinetic experiments was prepared by refluxing with repeated additions of permanganate until the violet colour persisted, then drying by K_2CO_3 and finally distilling through an efficient column.

Kinetic procedure

Alkaline hydrolysis. A sample ester was dissolved in 100 ml of 80% v/v $EtOH{-}H_2O$ to make the concentration ranged from 0·5 to 5×10^{-2}M of each ester. The alkaline soln for hydrolysis was prepared by dissolving KOH into 80% v/v $EtOH{-}H_2O$ to make an initial concentration equal to that of an ester. A kinetic run was started by mixing the ester soln with the alkaline soln, both of which were kept in a thermostated bath for 10 min before use. Then, 10 ml of the reaction soln was taken out at suitable intervals and quickly quenched into excess HCl aq. By titrating the residual HCl with a standard KOH soln the amount of the sample reacted was estimated. We obtained straight lines for second order reaction and from the slopes the second-order rate constants were obtained. The kinetic runs were performed at least twice for each ester. The results are illustrated in Table 2.

Acid catalyzed hydrolysis. Each ester (5×10^{-3} mole) was dissolved in the mixture of 35 ml acetone and 5 ml 1·0N HCl and water was quickly added to keep the total volume 50 ml. Then each 5 ml of this reaction soln was quickly pipetted into a 10 ml ampoule at room temp. Seven ampoules were set in a thermostated bath. The first run was taken 30 min after the ampoules were put in the bath. Standard 0·05M KOH was used for titrating the carboxylic acid produced during the reaction. Kinetic rates were followed from 20% to 50% completion of the reaction.

Estimation of σ and Es values.* The σ^* and *Es* values of α-mercapto and α-alkoxy groups were determined the Ingold–Taft equation,[16]

$$\begin{aligned} \sigma^* &= \frac{1}{2{\cdot}48}\left[\log (k/k_0)_B - \log (k/k_0)_A\right] \\ Es &= \log (k/k_0)_A \end{aligned} \tag{2}$$

where k and k_0 are rate constants for hydrolyses of the ethyl esters of α-substituted carboxylic and acetic acids, respectively and the subscripts A and B indicate acid and base catalysed reactions. Most of the ethyl esters in these experiments were hydrolysed in the alkaline medium at 10°. Some compounds which reacted too fast to be kinetically followed at 10°, were carried out at another suitable temp and their rate constants at 10° were obtained from extrapolation by using the Arrhenius equation. The acid catalysed hydrolyses of these esters were so slow at the room temp that each sample was hydrolysed at higher temp. Hence the rate constants were extrapolated to 10°. The rate constants of the alkaline and acid catalysed hydrolyses are listed in Tables 2 and 3 and newly estimated σ^* and *Es* values were given in Table 1.

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