important in regulating the ^{19}F chemical shift,[17] the above assumption seems to us to be very tenuous.

(f) Surely the logical approach for magnetic resonance investigation of the field component of the total SCS observed in an aromatic system (whether ^{19}F or ^{13}C) is to examine a system in which the probe nucleus is still in the aromatic environment, but the substituent is contained in an attached, desirably strain-free system, so constructed that resonance and related effects are prohibited. We have seen above that in system V, dipolar substituents actually shield C_4 but in aromatic systems, the whole π system is polarized, and leads to a deshielding of the carbon probe.[18]

The data in Table I indicate wide variations for the α, β, and γ effects as a function of substituent and molecular system.[19] For the α effect there appears to be a basic correlation with substituent electronegativity within a system, but substantial differences between systems for the same substituent, e.g., for the sterically small fluoro, α effects of +68.48 (III), +49.5 (IV), and +69.92 (VI) are noted. The β effects are again positive, i.e., deshielding in nature, but the dependence on substituent electronegativity is not obvious. It would seem in fact, that more electronegative substituents may be associated in part with increased shielding at C_β, a result in accord with some theoretical work predicting alternation of charge in a σ-bonded framework.[20] Other factors, such as degree of substitution and strain, may be important, the latter particularly at the α position. Small but significant deshielding effects at C_γ are also observed, and these C_γ positions are anti to the substituent. It is not clear how well the alternating polarization hypothesis accommodates these data, but a number of factors are almost certainly operating in this region.

Experimental Section

Compounds. The maleic anhydride adducts (series IV) were prepared in the standard way by refluxing the 9-substituted anthracene with slightly more than 1 equiv of maleic anhydride in the minimum amount of *o*-xylene for 3–12 h, depending on the 9-substituent.[21] On cooling crystals of the adducts separated, in quite pure form, and one further crystallization from xylene provided analytically pure compounds.

9,10-Dideuterioanthracene was obtained by the *p*-toluenesulfonic acid catalyzed H–D exchange with anthracene. Specifically 9-deuterated anthracene resulted from lithium aluminum deuteride reduction of anthrone followed by acid (3 N HCl) induced dehydration. ^1H NMR analysis indicated ~95% deuterium incorporation. 9-Bromo-10-deuterioanthracene was synthesized by bromine addition and hydrogen bromide elimination in the reported manner.[22] Careful ^1H NMR measurements revealed ca. 50% deuterium at the 10 position indicating the absence of a significant isotope effect in the elimination. 9-Cyano-10-deuterioanthracene was obtained from the 9-bromo compound on treatment with copper(I) cyanide in *N,N*-dimethylformamide.[23]

The dimethyl acetylenedicarboxylate adducts (series V)[24] were prepared by refluxing equimolar amounts of the reagents in benzene and monitoring the reaction by ^1H NMR analysis of the $COOCH_3$ region. The benzene solvent was removed and the adducts were recrystallized from methanol. The structures of the adducts were confirmed by elemental analyses, ^1H NMR spectra (where solubility was adequate), and of course the ^{13}C spectra.

Compounds in series I, II, and III have been reported elsewhere,[2,9] while those in series VI will be described in detail in another connection.[25]

^{13}C spectra were recorded with a Bruker HX-90 spectrometer operating in the FT mode, and chemical shifts are relative to internal Me_4Si and accurate to ±0.05 ppm.

The analytical data for new compounds are assembled in Table II, and the ^1H NMR data for series V also. These adducts are generally quite soluble, and the chemical shifts ($CDCl_3$, internal Me_4Si) pertain to 5% weight/volume solutions. The maleic anhydride adducts are far less soluble, and chemical shift data for series IV, X = H, F, and $COCH_3$, only, are tabulated.

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Registry No.—III (X = H), 280-33-1; III (X = Br), 7697-09-8; III (X = F), 20277-22-9; IV (X = H), 5443-16-3; IV (X = Br), 58802-01-0; IV (X = F), 26306-24-1; IV (X = CN), 58802-02-1; IV (X = Me), 58802-03-2; IV (X = $COCH_3$), 17478-86-3; V (X = H), 1625-82-7; V (X = Br), 58802-04-3; V (X = CN), 58802-05-4; V (X = NO_2), 58802-06-5; V (X = CH_3), 58802-07-6; V (X = $C(CH_3)_3$), 33740-56-6; VI (X = H), 23062-62-6; VI (X = OMe), 6555-88-0; VI (X = OH), 2001-62-9; VI (X = OCOMe), 54986-35-5; VI (X = F), 22947-58-6; VI (X = Cl), 33732-68-2.

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A Method for Relating Esterification Rates and Structures of Alkyl-Substituted Acetic Acids

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The relationship between the esterification rate and structure of aliphatic acids has been investigated since the latter part of the 19th century.[1] The collection of data by Loening, Garrett, and Newman[2] for hydrogen chloride catalyzed esterifications in methanol is commonly used in relating structure and rate. By including additional data, some recent studies have suggested that there are relationships between rate and structure not previously disclosed.[3] The purpose of the present study is to further examine the problem of rate and structure by the use of an expanded collection of comparable esterification data.

In the original method the determination of rate coefficients of slow-reacting acids was seriously limited since during the extended esterification time a substantial amount of the hydrogen chloride catalyst reacted with the methanol.[2] In the present study, pairs of acids are allowed to react together and the ratios of the rate coefficients are determined by gas–liquid

Table I. Source and Purity of the Acids and Experimental Results

Registry no.	Acid no.	Structure	Source of acid or precursor	NE$_{calcd}$ − NE$_{found}$	GLC % area	"Known" acid	$k_{known}/k_{unknown}$ ± std dev
503-74-2	1[a]	$(CH_3)_2CHCH_2COOH$	Eastman Organic	−0.5	98.3		
105-43-1	2	$CH_3CH_2CH(CH_3)CH_2COOH$	K & K	0.3	98.1	1	1.2360 ± 0.0218
97-61-0	3	$CH_3CH_2CH_2CH(CH_3)COOH$	K & K	−0.5	98.5	1	1.4950 ± 0.1422
1070-83-3	4	$(CH_3)_3CCH_2COOH$	Aldrich	1.0	99.0	14	0.3840 ± 0.0520
88-09-5	5	$(CH_3CH_2)_2CHCOOH$	Eastman Organic	−0.9	99.1	14	0.7994 ± 0.0200
14287-61-7	6	$(CH_3)_2CHCH(CH_3)COOH$	K & K	−1.5	96.7	14	0.6773 ± 0.0259
595-37-9	7	$CH_3CH_2C(CH_3)_2COOH$	K & K	−1.3	98.6	14	1.3263 ± 0.1168
32444-32-9	8[a–c]	$(CH_3)_2CHCH(C_2H_5)COOH$	Eastman Organic	1.2	98.1		
19889-37-3	9	$CH_3CH_2C(C_2H_5)(CH_3)COOH$	Chemical Samples	−0.4	99.8	8	1.7825 ± 0.1805
3302-09-8	10[c,d]	$(CH_3)_3CCH_2CH(CH_3)COOH$	Pfautz and Bauer	−0.5	99.6	14	0.2942 ± 0.0137
						14	0.2980 ± 0.0071[e]
149-57-5	11	$CH_3CH_2CH_2CH_2CH(C_2H_5)COOH$	Baker Chemical	−0.4	99.6	15	0.3461 ± 0.0162[f]
813-72-9	12[g]	$CH_3CH_2CH_2CH_2C(CH_3)_2COOH$	K & K	−0.9	95.7	14	1.3456 ± 0.0208
108-81-6	13	$(CH_3)_2CHCH_2CH(C_2H_5)COOH$	Pfautz and Bauer	−0.6	99.1	14	1.1261 ± 0.0924
99-66-1	14[a]	$(CH_3CH_2CH_2)_2CHCOOH$	K & K	−0.5	99.3		
866-72-8	15[g]	$(CH_3)_2CHCH_2C(CH_3)_2COOH$	Pfautz and Bauer	−2.3	98.6	14	2.4691 ± 0.2055
813-58-1	16[c]	$(CH_3CH_2)_3CCOOH$	K & K	−2.4	99.3	9	14.20 ± 4.10
						8	25.61 ± 1.48[e]
						8	25.0[h]
32118-53-9	17[i]	$[(CH_3)_2CH]_2CHCOOH$	Pfautz and Bauer	0.2	94.5	16	2.053 ± 0.031[e,f]
						18	0.827 ± 0.043[e,f]
6967-84-6	18[c]	$(CH_3)_3CCH(C_2H_5)COOH$	Dow Chemical	0.0	99.7	16	2.385 ± 0.431
						16	2.551 ± 0.144[e]

[a] Used as a "known" acid having the value given in ref 2. [b] Prepared by alkaline permanganate oxidation of the aldehyde. [c] The nmr spectra is in agreement with the designated structure. [d] Prepared by periodate–permanganate oxidation of 3,5,5-trimethyl-1-hexene. [e] GLC analysis of both acids and esters. [f] Esterification experiment carried out with each acid in a separate container. [g] Prepared by alkaline permanganate oxidation of the alcohol. [h] Esterification experiment carried out under the conditions given in ref 2. [i] Prepared from isobutyroin, A. A. Sacks and J. G. Aston, *J. Am. Chem. Soc.*, **73**, 3902 (1951).

chromatographic analysis. This method should not be influenced by change in concentration of the catalyst.

The experimental results giving the relative esterification rates of the various pairs of acids are shown in Table I. In determining these relative rates, one of the acids in each pair is considered to have a known rate. Therefore, the value for the "unknown" acid can be calculated. Several acids were used as "knowns" having the rate values given in the collected data of Loening, Garrett, and Newman.

For an examination of the relationship between structure and esterification rates, it was found extremely useful to represent the structure of an acid as a series of digits to be called the "carbon–carbon bond number pattern". Each digit represents the position of a carbon atom in relation to the number of carbon–carbon bonds to the carboxyl group. For example, the carbon–carbon bond number pattern for structure $CH_3CH_2C(CH_3)_2COOH$ is 32221. There are cases, of course, where several acid isomers have the same pattern. All rate data are given as relative to that of butanoic acid and the higher molecular weight normal acids. This is convenient because these acids have essentially the same rate. Examination of the relative rates and the carbon–carbon bond number patterns of acids from the collected data of ref 2 and from this study has led to the proposal of five simple rules for ranking the rate of the acids:

1. If the patterns are the same, the rates are approximately the same.
2. If the patterns for two isomers differ in the value of only one digit, the acid with the lower digit has the slower rate.
3. The acid with the greater combined number of "2's" and "3's" has the slower rate.
4. An acid has a faster or equal rate if its pattern is included in that of another.
5. For acids that cannot be ranked by these rules, the one with the greater number of "2's" has the slower rate.

Although some of these "rules" may seem quite simple, together they form a powerful tool for ranking the rates of the acids. In Table II, the acids have been ranked according to these five rules. The excellent agreement between the ranking by the patterns and experimentally determined values is obvious from inspection of the first two columns. A rank correlation of 0.99 is obtained from this data. Members of a group of acids with the same pattern (five pairs) or undifferentiated by any of the rules (one pair) are given the mean value of the ranks. Values determined in this study are given precedence over those of the collected data. A serious discrepancy occurs in the values for 2,2-diethylbutanoic acid, the last entry in Table II, where the value determined in the present study is only one-seventh of that previously reported. Therefore, several rate coefficients were determined by the method used

Table II. Aliphatic Acids Ranked with Respect to the Carbon–Carbon Bond Number Pattern Rules and the Experimentally Determined Relative Esterification Rates

Rank according to C–C bond no. pattern rules	Rank according to Exptl detd rel rates	Structure	Carbon–carbon bond no. pattern	Rel esterification rate, 40 °C: Coll data (ref 2)	Rel esterification rate, 40 °C: This report
1	1	CH_3COOH	1	2.02	
2	2	CH_3CH_2COOH	21	1.70	
3	3	$H(CH_2)_nCOOH$ ($n > 2$)	*n*. .321	1.00	
4	4	$(CH_3)_2CHCH_2CH_2COOH$	44321	0.972	
5.5	5	$(CH_3)_3CCH_2CH_2COOH$	444321	0.937	
5.5	8	$(CH_3)_3CCH(C_2H_5)CH_2CH_2COOH$	555544321	0.206	
7	6	$(CH_3)_2CHCOOH$	221	0.675	
8	7	$(CH_3)_2CHCH_2COOH$	3321	0.236	(0.236)
9	10	$CH_3CH_2CH(CH_3)CH_2COOH$	43321		0.191
10	9	$CH_3CH_2CH(CH_3)COOH$	3221	0.201	
11	11	$CH_3CH_2CH_2CH(CH_3)COOH$	43221		0.158
12	13	$(CH_3)_3CCH_2CH(CH_3)COOH$	4443221	0.0311	0.0632
13	12	$(CH_3)_3CCOOH$	2221	0.0756	
14	14	$(CH_3)_3CCH_2COOH$	33321	0.0474	0.0487
15.5	15	$(CH_3)_2CHCH(CH_3)COOH$	33221		0.0276
15.5	16	$(CH_3CH_2)_2CHCOOH$	33221	0.0202	0.0234
17	17	$CH_3CH_2CH_2CH_2CH(C_2H_5)$-$COOH$	5433221		0.0219
18.5	18	$(CH_3CH_2CH_2)_2CHCOOH$	4433221	0.0187	(0.0187)
18.5	20	$(CH_3)_2CHCH_2CH(C_2H_5)COOH$	4433221		0.0166
20	19	$(n\text{-}C_4H_9)_2CHCOOH$	554433221	0.0169	
21	23	$[(CH_3)_2CHCH_2]_2CHCOOH$	444433221	0.00839	
22	26	$[(CH_3)_3CCH_2]_2CHCOOH$	44444433221	0.00176	
23	21	$CH_3CH_2C(CH_3)_2COOH$	32221		0.0141
24	22	$CH_3CH_2CH_2CH_2C(CH_3)_2COOH$	5432221		0.0139
25	24	$(CH_3)_2CHCH_2C(CH_3)_2COOH$	4432221		0.00758
26	25	$(CH_3)_3CCH_2C(CH_3)_2COOH$	44432221	0.00667	
27.5	27	$(CH_3)_3CCH(CH_3)COOH$	333221	0.00125	
27.5	28	$(CH_3)_2CHCH(C_2H_5)COOH$	333221	0.00120	(0.00120)
29	29	$CH_3CH_2C(C_2H_5)(CH_3)COOH$	332221		0.000673
30.5	32	$[(CH_3)_2CH]_2CHCOOH$	3333221	Too slow	0.0000232
30.5	33	$(CH_3)_3CCH(C_2H_5)COOH$	3333221	Too slow	0.0000192
32.5	30	$(CH_3)_3CC(CH_3)_2COOH$	3332221	0.000261	
32.5	31	$(CH_3CH_2)_3CCOOH$	3332221	0.000328	0.0000474

to derive the previously reported data. The excellent agreement of these determinations with the GLC analyses gives strong support to this smaller value.

This method of ranking the expected relative esterification rates according to the carbon–carbon bond number patterns is, of course, based on the simple idea that the closer to the carboxyl group, the more effective is a group in retarding the rate. The scheme could not have been previously set forth because until quite recently[3b] it was generally accepted that a more distant β-substitution, a "3" in this case, would have more effect in retarding esterification than a nearer α-substitution, a "2". Only in cases of the extremely hindered acids, the last four entries in Table II, does it seem that this previously accepted concept holds true.

Rule 3 is in accord with the findings of Smith and Burn,[4] who reported that the esterification rates of various types of aliphatic acids tend to fall into classes according to the number of α and β substitutions (the number of "2's" and "3's" in the case of the carbon–carbon bond number patterns). However, this observation apparently was not used in any sort of predictive scheme. Instead, Newman's rule of six[2] is still commonly used to correlate rates with structures.[5] Although determined differently, the six-number of an acid amounts to three times the number of "3's" in the pattern. The greater the six-number the slower the predicted rate. Results would be much improved if consideration were given to the sum of the "2's" and "3's", designated here as the "steric hindrance number". For the acids in Table II with molecular weights above that of propionic, the logarithm of the relative rate is plotted vs. the steric hindrance number. The line determined by the least squares method is

$$\log \text{relative rate} = 2.21 - 1.05\ (\text{steric hindrance number})$$

With the value of 0.36 for the standard error of estimate for the log of the relative rate, accurate predictions are, of course, not expected. However, since the esterification rate tends to be decreased by a factor of 10 when the steric hindrance number is increased by a unit, a rough estimate can be obtained from the following:

$$\text{estimated rate compared to butanoic acid} = 10^{(2\,-\,\text{steric hindrance number})}$$

Two-thirds of the acids in Table II have relative rate values that are within a factor of 2 of the estimated values.

What has been accomplished here is the development of a method whereby aliphatic acids are ranked according to expected relative esterification rates by a simple inspection of the structures. The demonstrated success of this scheme indicates that it is far superior to any presently available.

Experimental Section

Of the 18 acids used in this study, five were synthesized by methods referred to in Table I. Purity is indicated from neutralization equivalents and GLC analysis. Designated structures of several of the acids were substantiated by NMR spectra obtained on a Varian HA-100 spectrometer modified for carbon-13 pulsed Fourier transform operation. The analytical gas–liquid chromatography was carried out on a Beckman GC-4 gas chromatograph equipped with a flame ionization detector which was interfaced with a Perkin-Elmer PEP-1 data processor. The 6 ft × 0.125 in. stainless steel chromatographic column was packed with 20% diethylene glycol adipate polyester and 3% phosphoric acid on 60/80 mesh Gas-Chrom P.

Experimental Procedures. The reaction mixture containing 5 ml of methanol, approximately 0.05 g of each of the two acids, and 0.01 ml of concentrated hydrochloric acid was esterified at 40 ± 0.04 °C. Reaction times ranged from less than 1 h to more than 1 month. The calculation of r, the relative rate, is based on the equation

$$k_1/k_2 = \ln A/\ln B = r$$

where A is the fraction of acid 1 and B the fraction of acid 2 remaining after the partial esterification. Two GLC methods of analysis were used to determine A and B. In the first method, the analyses were carried out with the column at 160 °C. The reaction mixture also contained 0.05 g of methyl myristate as an internal standard. Determinations of A and B are based on the results of two chromatograms, one taken before and one after the partial esterification; for example

$$A = [\text{final acid 1}][\text{initial standard}]/[\text{initial acid 1}][\text{final standard}]$$

where the items in brackets refer to the GLC areas of the components in the chromatograms. Neither hydrolysis of the internal standard nor esterification occurring in the chromatographic system during analysis was found to be significant. For the second GLC analytical method, in which case the acids and esters are analyzed, the temperature of the column was held at 100 °C for 4 min and then programmed to 160 °C over an 8-min period. No internal standard is needed for this method and only the chromatogram of the partly esterified mixture is used to determine A and B; for example

$$A = (\text{acid 1})/[(\text{acid 1}) + c\ (\text{ester 1})]$$

where c is the mole-area correction factor for the acid–ester pair. The correction factor of 0.92, determined for 2-ethylhexanoic acid and methyl 2-ethylhexanoate, was assumed to hold for the five octanoate entries in Table I.

In two cases, as indicated in Table I, the esterification was carried out with each acid in a separate container because the GLC separation of the mixture was not adequate for good analysis. This means that the esterification environment was not exactly the same for each acid because of different amounts of water produced during the reaction. However, the results should not be particularly affected since under the experimental conditions the "wetness" of the alcohol does not greatly increase during the esterification.

How errors in measuring A and B affect the computation of r has been previously considered.[6] In the present case the relative standard deviation in reproducing the chromatographic peaks was found to be about 3%. Although in the first GLC analytical method, the error in r decreases the further the esterification proceeds, data cannot be used where the hydrolysis reaction becomes significant. Therefore acid pairs were chosen with somewhat similar rates and data was taken when the faster reacting component had esterified from 50 to 80%. For the second method of analysis, based on the relative amounts of each acid and its ester in the partly esterified mixture, the extent of esterification has little influence in the computational error of r. Data can therefore be taken during the early stages of the reaction. This advantage over the first method is somewhat offset by the more complex analytical procedure. Most of the esterification experiments were carried out by the first method described. The values of r in Table I are averages from at least four determinations. The relative standard deviation for r averaged 8%.

Esterification rate coefficients for 2-ethyl-3-methylbutanoic acid and 2,2-diethylbutanoic acid were determined by the procedures used in obtaining the data in ref 2. Samples containing 0.5 M carboxylic acid and 0.005 M hydrogen chloride in dry methanol were sealed in glass ampules and kept at 40 ± 0.04 °C for 413 h. Analysis was carried out by acid titrations. The value of k in liters per mole per second for 2-ethyl-3-methylbutanoic acid was 7.47×10^{-5} (7.80×10^{-5} previously reported) and for 2,2-diethylbutanoic acid was 2.99×10^{-6} (21.4×10^{-6} previously reported). The ratio of the two rates as entered in Table I is $7.47 \times 10^{-5}/2.99 \times 10^{-6} = 25.0$.

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Oxidation of Thiols and Disulfides to Sulfonic Acids by Dimethyl Sulfoxide

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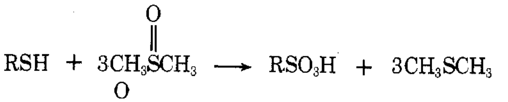
The oxidizing ability of dimethyl sulfoxide (Me_2SO) is well known;[1] still, its ability to oxidize organic sulfur compounds to sulfonic acids has received little recognition. Such oxidations would include certain decompositions of Me_2SO in the presence of bromine, hydrogen bromide, or iodine giving, among other products, methanesulfonic acid or its trimethylsulfonium salt.[2] Methanethiol[2a] and the corresponding sulfenic and sulfinic acids[2d] and sulfinyl halides[2b,c] have been suggested as intermediates.

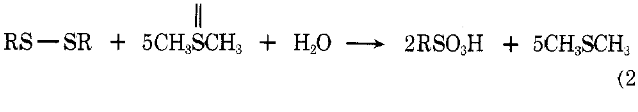
As for specific examples of the oxidation of thiols and disulfides, Toland[3] has described the oxidation of dodecanethiol to dodecanesulfonic acid in the presence of ammonium bromide at temperatures approaching 170 °C; yet, a similar, preparative decomposition of Me_2SO to methanesulfonic acid at 175 °C is also described. Further, Lipton and Bodwell[4] have reported that cystine is oxidized to cysteic acid by minor amounts of Me_2SO under conditions used for the acid-catalyzed hydrolysis of proteins.

The above Me_2SO decompositions also produce paraformaldehyde and dimethyl sulfide (DMS) and may be hazardous.[2a,5] Thus, application of Me_2SO to oxidation of thiols and disulfides has the disadvantage of both hazard and contamination of product sulfonic acid with methanesulfonic acid.

I have now found that, in the presence of a catalytic amount of bromine or iodine or their hydrogen halide, thiols and disulfides may conveniently be oxidized to the corresponding sulfonic acid with little Me_2SO decomposition through the simple expedient of having water present during the oxidation of thiols (eq 1) and excess water present during the oxidation of disulfides (eq 2). With such presence of water, the characteristic deposit of paraformaldehyde in the upper reaches of the reaction vessel is much reduced or absent and reaction occurs in good agreement



$$RSH + 3CH_3\overset{O}{\overset{\|}{S}}CH_3 \longrightarrow RSO_3H + 3CH_3SCH_3 \qquad (1)$$



$$RS{-}SR + 5CH_3\overset{O}{\overset{\|}{S}}CH_3 + H_2O \longrightarrow 2RSO_3H + 5CH_3SCH_3 \qquad (2)$$