cedure.[11] After recrystallization from hexane, it melted at 63.5–64.5°.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.84; H, 6.99.

4-Isopropylphenoxyacetic acid was made in the same way as the 3-isomer and melted at 83.5–84.5°.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.93; H, 7.34.

3-Methylthioacetophenone.—In 50 ml. of methanol was dissolved 10 g. of 3-acetylthiophenol.[12] To this solution was added 9 g. of potassium hydroxide dissolved in the minimum amount of water. Dimethyl sulfate (23 g.) was then added slowly to the stirred mixture. At this point 10 ml. of 50% potassium hydroxide and 10 g. of dimethyl sulfate were added. After a few minutes stirring, the methanol was removed *in vacuo* and the residual oil extracted with ether. Distillation yielded 7.5 g. of product, b.p. 107–108° (1 mm.).

Anal. Calcd. for $C_9H_{10}OS$: C, 65.00; H, 6.06. Found: C, 65.33; H, 6.24.

3-Methylsulfonylacetophenone.—The above methylthioacetophenone (5 g.) was dissolved in 12.5 ml. of glacial acetic acid and heated to 40°. To this warm solution was added dropwise 6.5 g. of potassium permanganate in 250 ml. of water. After the addition was complete, a small amount of sodium bisulfite was added to decompose the excess permanganate and the temperature was

(11) N. V. Hayes and G. E. K. Branch, *J. Am. Chem. Soc.*, **65**, 1555 (1943).
(12) G. Schwarzenbach and E. Rudin, *Helv. Chim. Acta*, **22**, 360 (1939).

raised until all of the crystals which had separated during the oxidation dissolved. The hot solution was filtered to remove the manganese dioxide. Upon cooling, 6 g. of colorless crystals separated. After recrystallization from water the melting point of the product was 105–106°.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.50; H, 5.08. Found: C, 54.68: H, 4.93.

3-Methylsulfonylphenylacetic Acid.—The methylsulfonylacetophenone (4 g.) was added to 2 g. of morpholine and 0.6 g. of sulfur and the mixture heated on an oil bath at 130–140 for 5 hr. The thick oil so obtained was leached with ethyl acetate and the 5 g. of morpholide crystals which were left were hydrolyzed with 100 ml. of 2 N potassium hydroxide for 18 hr. Upon acidification, 1 g. of the phenylacetic acid separated. After recrystallization from ethyl acetate–hexane, the product melted at 101–102°.

Anal. Calcd. for $C_9H_{10}O_4S$: C, 50.40; H, 4.70. Found: C, 50.48; H, 4.64.

3-Ureidophenoxyacetic acid.—Potassium cyanate (0.5 g.) was added to a solution of 1 g. of 3-aminophenoxyacetic acid in 7 ml. of 1 N hydrochloric acid at room temperature. After a few minutes, 1.2 g. of product separated. It was purified by recrystallization from ethanol, m.p. 198° dec.

Anal. Calcd. for $C_9H_{10}N_2O_4$: C, 51.42; H, 4.77. Found; C, 51.44; H, 5.05.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KENT STATE UNIVERSITY, KENT, OHIO]

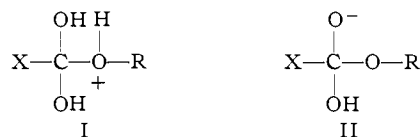# A Correlation of Chemical Shifts with Inductive Effect Parameters

BY ROBERT O. KAN

An attempt has been made to correlate the chemical shifts of the acetic acid and succinic acid protons of acetates and succinates with the polar substituent constant σ^* of the alcohol group of the esters. Factors responsible for deviations from linearity are discussed. σ^*-Values are proposed for the allyl and *n*-amyl groups.

Intrbduction

Considerable effort has been made in recent years to relate proton and F^{19} chemical shifts with the electronic properties of substituents.[1–7] Taft[8] has been particularly successful in correlating contributions through resonance and induction of substituents in the *para* and *meta* positions of fluorobenzenes with F^{19} chemical shift values.

The inductive effect of a substituent X can be expressed in terms of a polar substituent constant σ^*,[9] the value of which is obtained from the acidic and alkaline hydrolysis rates of esters of the type X–COOR, relative to the standard acetates. Underlying this method is the assumption that steric and resonance effects are the same in the acidic and alkaline hydrolyses, and thus do not enter into an expression featuring the ratio of the rate constants.

The transition states for such hydrolyses (I and II) clearly indicate not only a dependence on the electron-donating properties of X but also of R, a fact borne

(1) B. P. Dailey and J. N. Shoolery, *J. Am. Chem. Soc.*, **77**, 3977 (1955).
(2) H. S. Gutowsky, D. W. McCall, B. R. McGarvey, and L. H. Meyer, *ibid.*, **74**, 4809 (1952).
(3) R. W. Taft, Jr., *ibid.*, **79**, 1045 (1957).
(4) R. W. Taft, Jr., S. Ehrenson, I. C. Lewis, and R. E. Glick, *ibid.*, **81**, 5352 (1959).
(5) P. L. Corio and B. P. Dailey, *ibid.*, **78**, 3043 (1956).
(6) R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).
(7) G. E. Maciel, *J. Am. Chem. Soc.*, **86**, 1269 (1964).
(8) R. W. Taft, Jr., E. Price, I. R. Fox, I. C. Lewis, K. K. Andersen, and G. T. Davis, *ibid.*, **85**, 709 (1963); **85**, 3146 (1963).
(9) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 587.

out in those cases studied were R has been varied.[10] It is reasonable to conclude that the acyl and alkyl components are mutually dependent, and that the electronic properties of one will influence the electron density at the other. Such mutual dependence can be extended to the neutral ester molecule III, especially when one considers the existence of resonance structures such as IV, and a relation should exist between the

inductive effect parameter of the alkyl component and a physical property measuring the electron density at the acyl portion, such as the chemical shift of protons attached to it, which is a reliable measure *provided no other factors are operating.* For this reason we have examined the change in the proton chemical shifts of the acetic acid and succinic acid protons of various acetates and succinates, relative to methyl acetate and dimethyl succinate, respectively, against a change in

(10) C. M. Groocock, C. K. Ingold, and A. Jackson, *J. Chem. Soc.*, 1039 (1930); R. N. Rylander and D. S. Tarbell, *J. Am. Chem. Soc.*, **72**, 3021 (1950); J. R. Schaefgen, *ibid.*, **70**, 1308 (1948).

the nature of the alkyl group. The results of these studies are reported below.

Experimental

Acetates, when not commercially available, were obtained from the corresponding alcohols by treatment with an excess of acetyl chloride. Succinates were prepared from the alcohols and succinic acid or succinic anhydride, or using succinoyl chloride.[11] Di-*t*-butyl succinate was prepared following the procedure of Raha.[12] Table I lists the succinates and their physical constants that have thus far not been reported.

TABLE I
DIALKYL SUCCINATES

(CH₂COOR)₂, R =	B.p. °C.	Mm.	Calcd. C	Calcd. H	Found C	Found H
C₆H₅(CH₂)₃	191	0.15	74.56	7.39	74.72	7.44
Cyclo-C₆H₁₁CH₂	156	0.15	69.64	9.74	69.50	9.70
	M.p. 45–46					
t-C₄H₉CH₂	85	0.15	65.08	10.14	64.85	10.05
(*t*-C₄H₉)(CH₃)CH	120	0.12	67.09	10.56	67.27	10.66
CF₃CH₂	95–96	33	34.05	2.80	34.04	2.95

The n.m.r. spectra of the esters were obtained at 24° in carbon tetrachloride[14] with the methyl esters as internal standards. The concentration of all samples was 100 mg. per ml. of solvent, except for dibenzyl and dibenzhydryl succinate where it was less owing to the slight solubility of these esters in carbon tetrachloride. The chemical shift differences were measured at 50-cycle chart width and are accurate to 0.1 c.p.s. The values, constant over three separate traces, are listed in Table II with the σ*-values of the alkyl groups.[15] In separate determina-

TABLE II
CHEMICAL SHIFT CHANGES AND POLAR SUBSTITUENT CONSTANTS

R	Shift of CH_3COOR from CH_3COOCH_3, c.p.s.	Shift of $(CH_2COOR)_2$ from $(CH_2COOCH_3)_2$, c.p.s.	σ*
CH₃	0	0	0.000
C₂H₅	−0.9	−1.6	−0.100
n-C₃H₇	−0.5	−0.3	−0.115
i-C₃H₇	−2.5	−3.9	−0.190
n-C₄H₉	−0.8	−1.2	−0.130
sec-C₄H₉	−1.7	−2.4	−0.210
i-C₄H₉	0	0	−0.125
t-C₄H₉	−5.5	−9.0	−0.300
n-C₅H₁₁	−0.8	−1.2	.....
Cyclo-C₅H₉	−2.9	−4.7	−0.20
Cyclo-C₆H₁₁	−1.8	−2.5	−0.15
Cyclo-C₆H₁₁CH₂	−0.6	−0.8	−0.06
t-C₄H₉CH₂	1.2	2.3	−0.165
(*t*-C₄H₉)(CH₃)CH	−0.8	−0.1	−0.28
(C₂H₅)₂CH	0	0	−0.225
Cl(CH₂)₂	3.9	5.5	0.385
CF₃CH₂	8.8	12.4	0.92
CH₂=CHCH₂	2.0	3.1	.....
C₆H₅	14.4	23.1	0.600
C₆H₅CH₂	3.2	5.5	0.215
C₆H₅(CH₂)₂	0	−1.7	0.080
C₆H₅(CH₂)₃	0	0	0.02
C₆H₅(CH₃)CH	1.7	...	0.11
(C₆H₅)₂CH	...	11.4	0.405
H	3.3	...	0.490
CH₃CO	12.3	...	1.65
CH₃COCH₂	5.0	...	0.60

(11) P. Ruggli and A. Maeder, *Helv. Chim. Acta*, **26**, 1476 (1943).

(12) C. Raha, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 263.

(13) Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(14) A Varian Associates A-60 spectrometer equipped with a variable temperature probe was used.
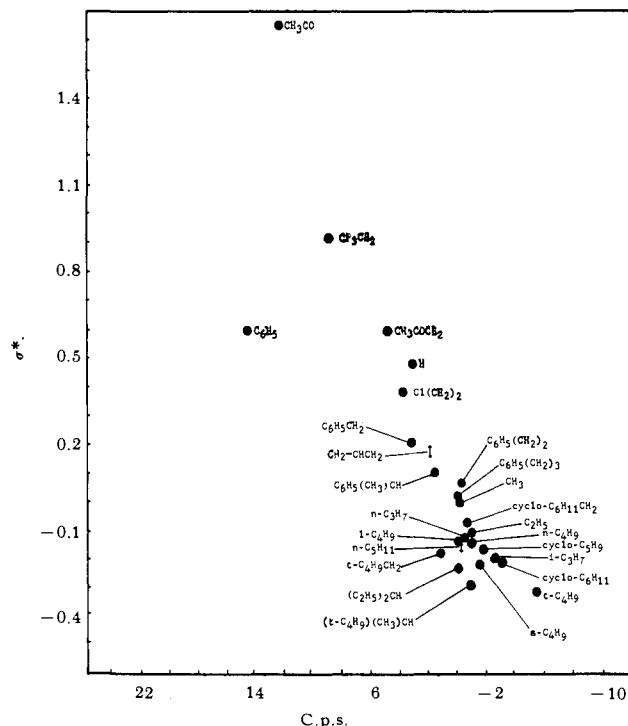
(15) R. W. Taft, Jr., ref. 9, p. 619.

Fig. 1.—Change in acetate proton chemical shifts from methyl acetate.

tions the chemical shift differences of di-*t*-butyl succinate and dineopentyl succinate were obtained at one tenth and at one hundredth of the concentration used in the remainder of the work, and found to be unchanged. The values obtained for di-isopropyl succinate and dineopentyl succinate in bromoform at 24° were found to be identical with those obtained at 60 and at 120°.

Discussion

Figure 1 shows a plot of the change in chemical shift of the acetate protons from methyl acetate against the σ*-values of the alkyl groups, and Fig. 2 shows the change in succinate proton chemical shift from dimethyl succinate against the σ*-values.

It is apparent from Fig. 1 and 2 that there exists a general correspondence between the two quantities, but that the data defy any attempt at a linear correlation. A comparison between Fig. 1 and 2 shows moreover that deviations are consistent in the two series and are not likely to be accidental.

The departure from linearity of the aromatic esters is not unexpected, considering the magnetic anisotropy of the aromatic ring. It is interesting to note, however, that the effect decreases almost linearly as the aromatic ring recedes from the acyl portion of the molecule, as seen from Fig. 3, where the aromatic succinates are presented alone. In fact, a rough measure of the magnitude of the anisotropy effect can be obtained from Fig. 3. Exact calculations of these effects have been made by Johnson and Bovey.[16]

More disconcerting is the poor correlation obtained from aliphatic esters; most are shown to have a deshielding effect on the acyl protons. As stated above, the electronic interdependence of X and R in the neutral molecule depends here largely on the existence of resonance structures such as IV. Structure IV is apparently responsible for the greatly restricted rotation about the alkyl carbon–oxygen bond, as evidenced by the small dipole moments of the

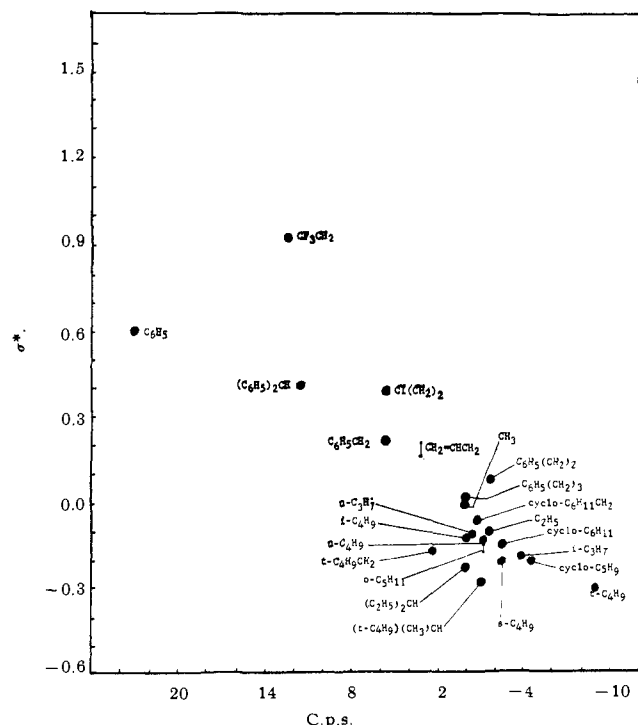(16) C. E. Johnson and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

Fig. 2.—Change in succinate proton chemical shifts from dimethyl succinate.

Fig. 3.—Chemical shift changes of aromatic succinates from dimethyl succinate.

esters and their temperature independence.[17a] Whereas in III electron donation by R must take place entirely by induction, such transfer is relatively facile in IV, with the effect of partly restoring the electron density at X, which in turn results in an upfield shift of the protons attached to X.

Should contributions from IV to the resonance be reduced, electron withdrawal from X will be enhanced and the chemical shift of the protons at X must be changed to lower fields. An inhibition of resonance can find its origin in a less favorable conformation of the molecule such that when the four atoms

$$-\overset{-}{C}=\overset{}{O}-C-$$ lie in a plane (a requirement for IV)
$$\underset{O^-}{|}$$

rotation about the alkyl carbon–oxygen bond becomes restricted as R increases in size. Such a restriction can be caused either by eclipsing of the protons of X with alkyl groups at R, or by interaction between the carbonyl oxygen and R. *It is seen to be most severe when the first carbon atom of R bears substituents that are larger than methyl*—i.e., $(CH_3CH_2)_2CH$, $(CH_3)_3$-CCH_2, $(CH_3)_3C(CH_3)CH$, and $(CH_3)_2CHCH_2$—and is simply an example of Newman's Rule of Six.[17b]

A second cause for deshielding might be found in the field effects operating through space. However, such effects usually vary with temperature,[18] and diminish at higher temperatures. Our studies have shown this to be unlikely: the chemical shifts of the acyl protons of dineopentyl and of diisopropyl succinate do not vary from 24° to 60° and to 120°.

An additional factor of influence was thought to be the bulk magnetic susceptibility of the substituents.

While such possible effects were minimized by using the corresponding methyl esters as internal standards, they were further discounted by the virtual concentration independence of some representative chemical shifts.

It might seem logical to attempt to correlate the chemical shifts with a quantity embodying both the polar substituent constant σ^* and the steric substituent constant E_s, but further reflection will show that, whereas the steric substituent constants are a measure of steric effects at reaction centers in the immediate vicinity of groups, the present case is concerned with effects experienced at some distance away from the point of attachment and no correlation can be expected, a fact easily verified.

Thus E_s for the t-butyl group is considerable (-1.54),[19] whereas methyl groups attached to the first carbon atom of the alkyl group are not expected to interfere with the acyl protons at all. The isobutyl group has a smaller negative value for E_s (-0.93),[19] but here the much larger isopropyl group is attached to the first carbon atom and will result in some steric inhibition of resonance.

Such effects must also be called upon to account for the poor correlation in the series methyl, ethyl, n-propyl, n-butyl; i.e., the ethyl and n-propyl substituents in the latter two esters will be a cause for deshielding. More significant is the fact that, although the σ^*-values for the series methyl, ethyl, n-propyl, n-butyl, which have been determined with greatest accuracy, decrease in that order, the base strength of the corresponding primary amines decreases in the order ethyl > methyl > n-propyl > n-butyl![20] It is attractive to speculate that such reversal of order, both in the base strength of the amines and in the chemical shift changes, finds its origin in an electron withdrawal of certain methyl groups relative to hydrogen, a

(17) (a) G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, p. 235; (b) M. S. Newman, *J. Am. Chem. Soc.*, **72**, 4783 (1950).

(18) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 383.
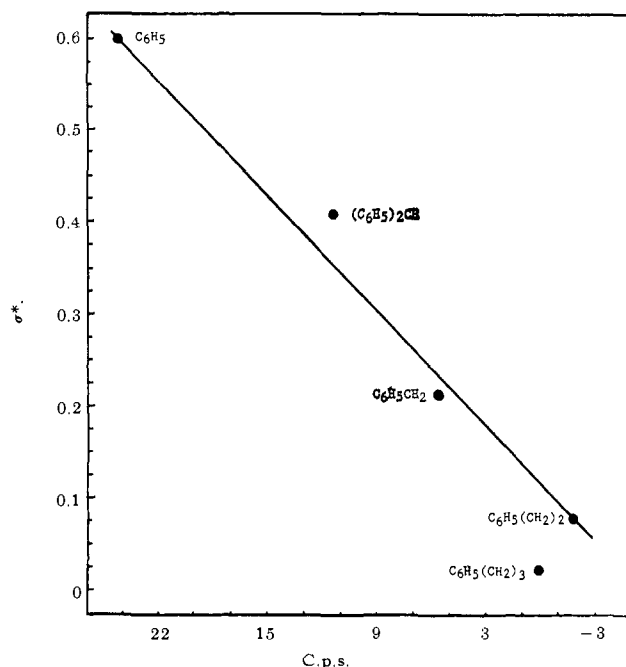
(19) R. W. Taft, Jr., ref. 9, p. 598.

(20) T. S. Moore and T. F. Winmill, *J. Chem. Soc.*, **101**, 1635 (1912); C. W. Hoerr, M. R. McCorkle, and A. W. Ralston, *J. Am. Chem. Soc.*, **65**, 328 (1943).

phenomenon being currently taken to account for other anomalous n.m.r. data,[21] as well as in some loss of entropy attributed to restricted freedom of rotation.[22]

Interestingly, when the σ^* values in Fig. 1 are replaced by the K_A values of the corresponding primary amines, the resulting plot is quite similar to Fig. 1, indicating again that the base strength of primary amines is not greatly dependent on steric effects.

It may be noted that the alicyclic esters examined show little deviation; here substituents are held back rigidly enough to cause no interference.

The chemical shift changes of two esters for which no σ^*-values exist at present have also been determined. The size of the *allyl* group should lead to no serious

(21) R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).
(22) H. C. Brown, M. D. Taylor, and S. Sujishi, *J. Am. Chem. Soc.*, **73**, 2464 (1951).

steric effects, so that the value of $+0.17$–0.19 found for σ^* is probably very realistic, especially when compared to that of $+0.13$ for the methallyl group. Assuming similar steric factors to be operating for the *n*-butyl and *n*-amyl groups, the σ^*-value for the latter is placed at -0.14 to -0.16.

Conclusions

While there exists a general correspondence between the electron-donating properties of alkyl groups of esters and the chemical shifts of protons attached to the acyl group, no linear correlation is obtained, a fact which may be explained in part by the magnetic anisotropy of aromatic substituents present and in part by steric factors related to the size and type of the aliphatic groups, especially by means of Newman's Rule of Six.

The Preparation of 1-Carboxy-4-substituted Bicyclo[2.2.2]octanes[1]
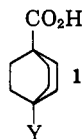
By Hans D. Holtz[2] and Leon M. Stock

Syntheses of 1-carboxy-4-substituted bicyclo[2.2.2]octanes are described.

Introduction

The 1,4-disubstituted bicyclo[2.2.2]octane acids (1) are excellent models for the study of the influence of nonconjugative polar effects and the mode of transmission of these polar effects to reaction sites.


Roberts and Moreland[3] first recognized the utility of this structure and several members of the series were prepared.[4] More recently, Ritchie and Lewis examined the dependence of the polar effects on the nature of the solvent.[5]

The major advantages of the bicyclo[2.2.2]octane system dictated its choice as one of the models for our studies. Methods for the preparation of these acids are summarized in this report.

Results and Discussion

The synthesis of 1-carboxybicyclo[2.2.2]octane (5) is outlined in Chart I.

CHART I
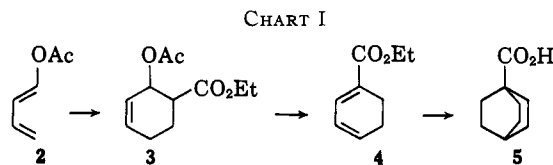
(1) Chemistry of the bicyclo[2.2.2]octanes. Part II. This research was supported by Grants G 14211 and G 25190 from the National Science Foundation.
(2) Esso Educational Foundation Fellow, 1961–1962; Union Carbide Corporation Fellow, 1962–1963.
(3) J. D. Roberts and W. T. Moreland, *J. Am. Chem. Soc.*, **75**, 2167 (1953).
(4) J. D. Roberts, W. T. Moreland, and W. Frazer, *ibid.*, **75**, 637 (1953).
(5) C. D. Ritchie and E. S. Lewis, *ibid.*, **84**, 591 (1962).

The sequence is a composite of two other known routes to the parent acid 5.[6,7] The Diels–Alder condensation of 1-acetoxybuta-1,3-diene (2) with ethyl acrylate yielded 1-carbethoxy-2-acetoxycyclohex-3-ene (3). The stereochemistry of this compound has not been established. The adoption of ethyl acrylate rather than methyl acrylate[6] allowed the preparation of a solid ester (3) rather than the liquid methyl ester employed by Sayigh.[6] The diene 4 was obtained by the pyrolysis of the ethyl ester 3 under basic conditions. The subsequent transformations in this sequence follow the synthesis described by Grob and his associates.[7]

Other methods were employed for the preparation of the disubstituted acids. One approach is summarized in Chart II.

CHART II
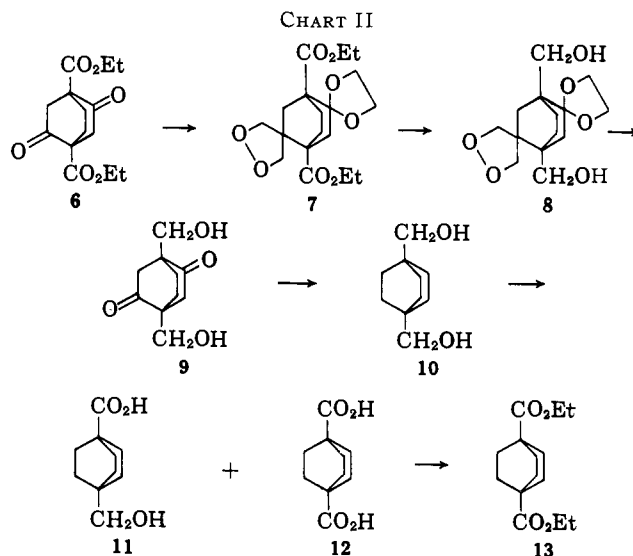
(6) A. A. Sayigh, Thesis, Columbia University Libraries, 1952.
(7) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta*, **41**, 1191 (1958).