

fluxed 14 hr.; additional cuprous cyanide (5 g., 0.0558 mole) was added and reflux was continued for 72 hr. The product was isolated by the method recommended by Friedman and Shechter.²⁴ The material isolated (4 g.) was sublimed at 110° (1 mm.) and then chromatographed on acid-washed alumina. Elution with carbon tetrachloride gave starting dichloride **33** (2.1 g.). Elution with acetone yielded **35** (1.2 g., 26%, m.p. 107–109°). The C≡N absorption was at 2280 cm.⁻¹.

Anal. Calcd. for C₉H₁₂ClN: C, 63.70; H, 7.13; Cl, 20.88. Found: C, 63.75; H, 7.25; Cl, 20.70.

1-Chloro-4-carboxybicyclo[2.2.2]octane (36).—Compound **35** (2.5 g., 0.0148 mole) was hydrolyzed with concentrated hydrochloric acid (140 ml.) at reflux for 18 hr. After cooling, the mixture was poured into cold water and the product taken up in ether. The ether solution was extracted with cold 3 *N* potassium hydroxide (50 ml.). The basic solution was acidified and the white precipitate collected, washed with water and sublimed at 120° (1 mm.). The sublimate was recrystallized from methanol-water to yield **46** (1.9 g., 68%, m.p. 268–269°).

Anal. Calcd. for C₉H₁₀ClO₂: Cl, 18.78. Found: Cl, 18.77.

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO, CHICAGO 37, ILLINOIS]

Dissociation Constants for 4-Substituted Bicyclo[2.2.2]octane-1-carboxylic Acids. Empirical and Theoretical Analysis¹

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Thermodynamic dissociation constants for ten 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids in 50% (weight) ethanol-water at 25° have been measured. The σ_1 -parameters yield a very precise correlation of the available results for 14 acids in the series. The σ_m and F, F' -constants offer a reasonable but less precise correlation. A theoretical treatment of the data based on Tanford's modification of the Kirkwood-Westheimer model yields calculated values of $\log(K_X/K_H)$ in only fair agreement with experiment. This model does, however, predict ΔpK_A for most substituents, hydrogen and alkyl excluded, with good accuracy. A theoretical dissection of $\log(K_X/K_H)$ into cavity and solvent terms reveals the major importance of the cavity transmission of the embedded end of the dipole as suggested by Dewar and Grisdale. Finally, the variations in D_E which are necessary for the identification of linear free energy relationships with electrostatic theory are shown to be the natural consequence of the structures of the acids.

Introduction

The energy change associated with the influence of dipolar and charged groups on the dissociation constants of acids may, in principle, be calculated from electrostatic theory. The early contributions of Bjerrum, Eucken, Smallwood, and Ingold are well known,^{3,4} as is the approach of Kirkwood and Westheimer.³⁻⁶ While highly useful for the interpretation of many experimental facts, the Kirkwood-Westheimer theory has proved less reliable for the computation of $\log(K_X/K_H)$ for dissociation of substituted carboxylic acids. Roberts and Moreland, for example, found a serious discrepancy between the calculated and experimental $\log(K_X/K_H)$ values for 4-bromo- and 4-cyanobicyclo[2.2.2]octane-1-carboxylic acids.⁷ Errors of this nature led Tanford to re-examine the approach.⁸ He pointed out that the most critical factor was the depth of the dipolar substituent within the cavity and showed that the adoption of a new definition of the cavity size greatly improved the agreement between theory and experiment. The discrepancy, however, remains significant.

More recently, Dewar and Grisdale proposed a somewhat different model.⁹ They suggested that substituent effects could be adequately treated by consideration of the charge associated with the end of

the dipole embedded within the molecular cavity. Using this idea, they devised a set of substituent parameters capable of the generation of the σ -constants for linear free energy relationships for any structural class. In the past decade, the application of such relationships to aliphatic molecules has been under study. Taft and his associates have shown the many applications of the polar substituent constants, σ_1 .¹⁰⁻¹² These constants are related to σ^* , the original polar parameters, by the equation: $\sigma_1 = \sigma' = 0.45\sigma^*$.¹³ The σ' -constants were assessed from data for the bicyclic acids by the equation of ρ for the ionization of the benzoic acids with that of the aliphatic acids.⁷ This approximation is difficult to substantiate empirically or theoretically.¹⁴

Neither the theoretical nor the empirical foundations of substituent dipole effects are completely secure. Uncertainties remain largely because the information on desirable model compounds is insufficient. Among the aliphatics only three series of carboxylic acids incorporating the substituent in a rigid structure free from resonance or steric interactions—1,4-bicyclo[2.2.2]octane,⁷ 1,4-*trans*-cyclohexane,¹⁵ and 1,3-adamantane¹⁶—have been examined. While these studies provide a basis for a discussion of the problem and for the initiation of new work, we thought it desirable to supplement the known results^{7,17,18} for the bicyclo[2.2.2]octane series before undertaking the investiga-

(1) Chemistry of the bicyclo[2.2.2]octanes. Part 111. This research was supported by Grants G14211 and G25190 from the National Science Foundation.

(2) Esso Educational Foundation Fellow, 1961–1962; Union Carbide Corporation Fellow, 1962–1963.

(3) L. P. Hammett, "Physical-Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 199.

(4) G. W. Wheland, "Advanced Organic Chemistry," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1960, Chapter 11.

(5) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938).

(6) F. H. Westheimer and J. G. Kirkwood, *ibid.*, **6**, 513 (1938).

(7) J. D. Roberts and W. T. Moreland, *J. Am. Chem. Soc.*, **75**, 2167 (1953).

(8) C. Tanford, *ibid.*, **79**, 5348 (1957).

(9) M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3539, 3548 (1962).

(10) R. W. Taft, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13.

(11) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, pp. 217–235.

(12) R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *J. Am. Chem. Soc.*, **85**, 709, 3146 (1963).

(13) R. W. Taft, *ibid.*, **79**, 1045 (1957).

(14) K. Bowden, *Can. J. Chem.*, **41**, 2781 (1963).

(15) S. Siegel and J. M. Komarmy, *J. Am. Chem. Soc.*, **82**, 2547 (1960).

(16) H. Stetter and J. Mayer, *Chem. Ber.*, **95**, 667 (1962).

(17) C. D. Ritchie and E. S. Lewis, *J. Am. Chem. Soc.*, **84**, 591 (1962).

(18) C. F. Wilcox and J. S. McIntyre, unpublished results.

tion of other models. The data for 14 acids in this series are examined in this report.

Results

Measurements of the dissociation constants of the bicyclic acids were undertaken with the objective of the assignment of thermodynamic data with an accuracy of ± 0.01 pK_A unit. Grunwald and his associates developed a differential potentiometric method capable of such precision and their method was adopted.¹⁹

The mixed solvent selected was 50% weight ethanol-water to ensure easy duplication during the course of the investigations.

The cell: glass electrode | H^+ , Cl^- , solutes, 50% ethanol-water | $Ag-AgCl$ was used. Several silver-silver chloride electrodes were examined for reproducibility and reversibility. The electrode of choice was silver mirror-silver chloride on platinum, similar to that described by Purlee and Grunwald for use in 95% methanol-water.²⁰ A constant value for E° for the cell was determined by the investigation of solutions of hydrogen chloride and potassium chloride over a more extensive concentration range than actually employed in the pK_A determinations.

The bicyclo[2.2.2]octane acids²¹ were purified by recrystallization and sublimation prior to measurement. With a view to the achievement of absolute accuracy, observations were made on each acid with independently prepared solutions in different batches of the solvent and with different silver-silver chloride and glass electrodes. The reliability of the method was tested in each set of measurements involving different electrodes by a determination of the dissociation constant of benzoic acid before other observations were attempted, again in the course of the series of measurements and at the completion of the set. The data obtained indicated $10^7 K_A$ for benzoic acid was 18.3 ± 0.2 . The result of Grunwald and Berkowitz is 17.4 ± 0.9 in the same solvent.²² The results are summarized in Table I.

TABLE I

THERMODYNAMIC DISSOCIATION CONSTANTS FOR 4-SUBSTITUTED BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACIDS IN 50% WEIGHT ETHANOL-WATER AT 25°

4-Substituent	$10^7 K_A$	pK_A
Hydrogen	1.34 ± 0.09	6.87 ± 0.03
Methyl	$1.30 \pm .04$	$6.89 \pm .01$
Ethyl	$1.28 \pm .01$	$6.89 \pm .01$
Hydroxymethyl	$1.59 \pm .04$	$6.80 \pm .01$
Hydroxy	$3.24 \pm .24$	$6.50 \pm .03$
Methoxy	$3.97 \pm .12$	$6.40 \pm .02$
Carbethoxy	$3.98 \pm .18$	$6.40 \pm .02$
Chloro	$7.34 \pm .44$	$6.13 \pm .03$
Bromo	$7.30 \pm .22$	$6.14 \pm .01$
Nitro	$15.3 \pm .5$	$5.82 \pm .01$

The objective of 0.01 pK_A unit accuracy was not attained in each case. However, the pK_A value of benzoic acid was measured within the desired limits of error repeatedly. The single clue to the difficulty is the slightly larger random errors detected for the weak parent acid.

(19) For a summary and additional references: A. L. Bacarealla, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955).

(20) E. L. Purlee and E. Grunwald, *J. Phys. Chem.*, **59**, 1112 (1955).

(21) H. D. Holtz and L. M. Stock, *J. Am. Chem. Soc.*, **86**, 5183 (1964).

(22) E. Grunwald and B. J. Berkowitz, *ibid.*, **73**, 4939 (1951).

Discussion

Experimental Observations.—The results of several investigations are summarized in Table II.

TABLE II
EXPERIMENTAL VALUES FOR $\log(K/K_H)$ FOR 4-SUBSTITUTED BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACIDS IN AQUEOUS ETHANOL AT 25°

Substituent	$\log(K/K_H)$			
	This study ^{a,b}	Ref. 7 ^{c,d}	Ref. 18 ^{c,d}	Ref. 17 ^d
H	0.000	0.00	0.00	0.00
CH ₃	$-.013 \pm 0.032$			
C ₂ H ₅	$-.020 \pm .030$			
CH ₂ OH	$.074 \pm .031$			
OH	$.370 \pm .044$	0.42(0.46)		0.24
OCH ₃	$.472 \pm .032$			
CO ₂ Et	$.473 \pm .035$	0.44(0.48)	0.41(0.45)	0.48
CO ₂ H			.42(.46)	0.13
CO ₂ ⁻			$-.18(-0.20)^e$	
Cl	0.739 ± 0.039			
Br	0.736 ± 0.032	0.67(0.73)		0.57
CN		0.85(0.93)		0.54
NO ₂	1.058 ± 0.032			
N(CH ₃) ₃ ⁺			1.36(1.50)	0.84

^a Probable error is indicated. ^b 50% weight ethanol-water.

^c Second (value) is that expected for 50% weight ethanol-water.

^d 50% volume ethanol-water. ^e Statistically corrected.

The ratio (1.1) of the ρ -values for 50% weight (1.65, Fig. 1) and 50% volume (1.52²³) was used to compare the data for the two solvents. The results are presented parenthetically in Table II.

Data for the 50% volume solvent from the several laboratories are not in good agreement. However, Lewis and Ritchie note that their results are suspect because the *p*-nitrophenolate-carboxylic acid equilibrium used for the measurements is insufficiently sensitive in highly aqueous media.¹⁷ The agreement between our data and the extrapolated values of Roberts and Moreland⁷ is good. The large discrepancy, for hydroxy, is not within the limits of experimental uncertainty. Possibly this deviation is the consequence of the change in solvent,¹⁷ but the fact that it is an apparent value renders this interpretation less certain. The single acid included in the investigation of Wilcox and McIntyre¹⁸ and the other studies is the carbethoxy compound. The pK_A for this substance is within experimental error of our measurements.

Empirical Correlation.—The use of σ_1 ¹² for the correlation of $\log(K/K_H)$ for the 4-substituted bicyclo[2.2.2]-octane-1-carboxylic acids is examined in Fig. 1.

An excellent correlation of the dissociation constants is found for a very broad range of substituents. The quality of the correlation confirms the reliability of these constants as a measure of polar influences.

The σ_1 -constants¹² for the methyl (-0.05) and ethyl (-0.03) groups are appreciably less than the parameters, methyl (-0.008) and ethyl (-0.012) deduced from eq. 1.

$$\log(K_X/K_H) = 1.65\sigma_1 \quad (1)$$

These observations suggest the polar effects of alkyl groups bonded to sp^3 carbon are small. There have been numerous reports in recent years concerning the electronic effects of alkyl groups.²⁴ The long-standing

(23) The ρ -value for the bicyclic acids was originally adopted as 1.45 in 50% volume ethanol-water.⁷ The parameter was later estimated to be 1.52; H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953); D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

(24) The views of many authors are presented in two publications: *Tetrahedron*, **5**, 105 (1959), and M. J. S. Dewar, "Hyperconjugation," Ronald Press, New York, N. Y., 1962.

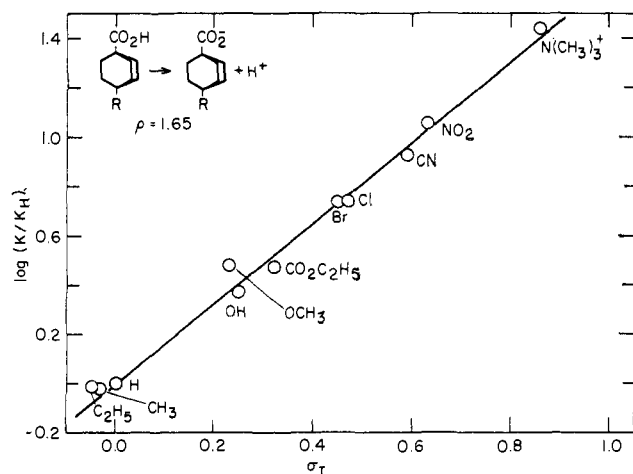


Fig. 1.—Correlation of acid dissociation constants of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids with σ_I . Carboxylate substituent, not shown, obeys this relationship.

view that alkyl groups are electron donors relative to hydrogen has received much support.²⁴⁻²⁶ Kwart and Miller, however, observed a reversal in the polar effect of the alkyl and hydrogen substituents in the addition of 2,4-dinitrobenzenesulfonyl chloride to substituted cyclohexenes and norbornenes.^{27a} It was suggested²⁷ that the alkyl substituents were electron-withdrawing groups. Ritchie, on the other hand, has argued on the basis of an empirical analysis that the hydrogen and alkyl groups exhibit no important differences in polar properties.²⁸ Our observations indicate the alkyl groups exert a negligible polar effect in agreement with Ritchie's suggestion. Caution in the assignment of large rate and equilibrium changes exclusively to the polar contributions of alkyl substituents appears necessary.

A comparison of substituent effects on the acidity of the bicyclic acids and *meta*-substituted benzoic acids tests the postulate that the ρ -values for the two reactions are identical.⁷ Data for the bicyclic acids in the 50% volume solvent (datum for nitro obtained by the interpolation noted previously) are correlated with the results²⁹ for the *meta* derivatives in the same solvent (Fig. 2).

The correlation line is based on the data for the parent acids and their trimethylammonium derivatives and indicates

$$\rho_I \sigma_I = 0.86 \rho \sigma_m \quad (2)$$

Most substituents (C_2H_5 , H, CN, NO_2 , $N(CH_3)_3^+$) obey the relationship with positive deviations found for groups with donor resonance (Br, OH) and small negative deviations for groups with acceptor resonance ($CO_2C_2H_5$, NO_2) as expected.³⁰ If the ρ -constants are equated,⁷ σ_I is $0.86\sigma_m$. The known σ_I -parameters are compatible with this prediction. Several arguments can be advanced to support the view that σ_I should be less than σ_m . One pertinent observation is

(25) E. A. Lucken, *Tetrahedron*, **19**, 123 (1963).

(26) E. Heilbronner, *ibid.*, **19**, 289 (1963).

(27) (a) H. Kwart and L. J. Miller, *J. Am. Chem. Soc.*, **83**, 4552 (1961);

(b) H. Kwart and T. Takeshita, *ibid.*, **86**, 1161 (1964).

(28) C. D. Ritchie, *J. Phys. Chem.*, **65**, 2091 (1961).

(29) J. D. Roberts, E. A. McElhill, and R. Armstrong, *J. Am. Chem. Soc.*,

71, 2923 (1949); J. D. Roberts and E. A. McElhill, *ibid.*, **72**, 628 (1950);

J. D. Roberts, R. A. Clement, and J. J. Drysdale, *ibid.*, **73**, 2181 (1951);

J. D. Roberts and C. M. Regan, *ibid.*, **75**, 4102 (1953).

(30) R. W. Taft and I. C. Lewis, *ibid.*, **80**, 2436 (1958); **81**, 5343 (1959).

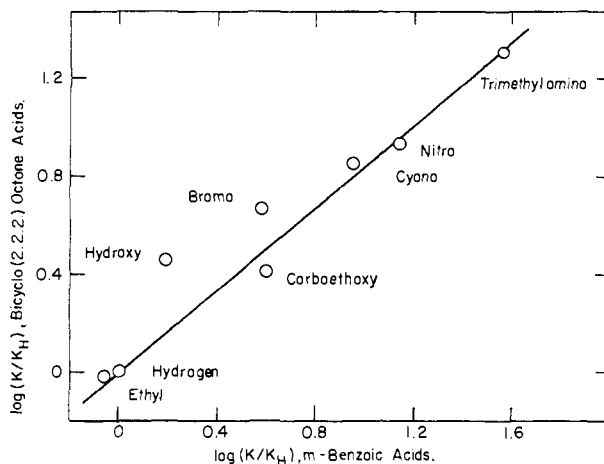


Fig. 2.—Relationship between dissociation constants of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and *m*-substituted benzoic acids in 50% volume water-ethanol at 25°.

the fact that the dipole moment of nitrodurene (3.62 D.) differs from that of nitrobenzene (4.01 D.) by an amount only 0.5 that of the difference between nitrobenzene and a nitroparaffin.^{31,32} The π -electron resonance contribution measured by the steric inhibition technique does not account for total charge.^{32,33} A small increase in the dipole contribution of aryl substituents would account for the larger value of σ_m . The alternative analysis of eq. 2, the identity of σ_I and σ_m , is considered in the following paragraph, but it is clear that the ρ -values can differ by no more than 15%.

Dewar and Grisdale proposed two new constants, F and M , for the definition of polar field and mesomeric interactions of substituents in a general way.⁹ These parameters were shown to predict σ -constants for groups in the several positions of naphthalene and biphenyl with reasonable accuracy and the extension of the approach to aliphatics was proposed. The F -constants are equal to $1.73\sigma_m$. The factor is the distance separating the 1,3-positions in benzene in units of the C-C bond in benzene, and σ_m is taken as a measure of the field effect of the substituent. The σ_{14} -constants applicable for the bicyclic acids are $1.73\sigma_m/1.82$. With reference to eq. 2, this analysis suggests $\rho_I = 0.86\rho_m$ since σ_{14} differs negligibly from σ_m . The σ_{14} -constants predicted by the F -parameters³⁴ correlate the data satisfactorily, but some serious deviations are apparent (Fig. 3). Each deviation may be identified with the expected resonance contributions of the substituent contained in σ_m and hence in σ_{14} . While the estimate of the polar field effect by σ_m greatly simplifies the problem, it masks the significance of resonance effects contributing to σ_m .³⁰ Nevertheless, the approach should prove very useful for the evaluation of approximate σ -constants for many systems, particularly the aromatics.

Electrostatic Theory.—At the outset it must be acknowledged that the model devised by Kirkwood and Westheimer^{5,6} is artificial in many respects.⁸ However, the data for the bicyclo[2.2.2]octane acids of fixed

(31) H. Kofod, L. E. Sutton, W. A. deJong, P. E. Verkade, and B. M. Wepster, *Rec. trav. chim.*, **71**, 521 (1952).

(32) H. Kofod, L. E. Sutton, P. E. Verkade, and B. M. Wepster, *ibid.*, **78**, 790 (1959).

(33) K. B. Everard and L. E. Sutton, *J. Chem. Soc.*, 2818 (1951).

(34) F -constants, ref. 9, yield sensibly the same results.

geometry³⁵ are, as will be shown, quite well accommodated by the theory.

In brief, the Kirkwood-Westheimer⁴⁻⁶ theory compares the acidity of a molecule with a bond or group moment, μ , the midpoint of which is positioned at a distance R from the removable proton with connecting lines oriented at an angle θ , with a hypothetical acid of the same size and shape but without a dipolar substituent. The dissociation constant of the real acid with a substituent (K_X) and the hypothetical molecule without a dipolar group (K_i) is given by

$$\log (K_X/K_i) = \frac{e\mu \cos \theta}{2.3 kTR^2D_E} \quad (3)$$

where the other symbols have their usual significance and D_E is defined as the effective dielectric constant determined by the geometry of the molecule and an estimate of the molar volume.

In most applications the equation has been used in the form

$$\log (K_X/K_H) = \frac{e\mu \cos \theta}{2.3 kTR^2D_E} \quad (4)$$

with the values of R , $\cos \theta$, and D_E defined by the structure of the substituted acid and μ assessed from the difference in dipole moment of two appropriate model molecules, RX and RH . Another approach is the definition of $\log (K_X/K_H)$ from the difference between $\log (K_X/K_i)$ and $\log (K_H/K_i)$.

$$\log (K_X/K_H) = \left(\frac{e}{2.3kT} \right) \left[\left(\frac{\mu \cos \theta}{R^2D_E} \right)_X - \left(\frac{\mu \cos \theta}{R^2D_E} \right)_H \right] \quad (5)$$

To apply this equation, the values of the bond moments μ_{C-X} and μ_{C-H} are needed; R , D_E , and $\cos \theta$ are independently fixed by the structures of the substituted and parent acids. Method 4 requires the approximation that R , D_E , and $\cos \theta$ are the same for the substituted and unsubstituted compounds. The alternative 5 incorporates the actual values of these parameters but requires K_i to remain invariant as the size of the cavity changes. For the bicyclo[2.2.2]octanes, eq. 4 yields larger values of $\log (K_X/K_H)$ in better agreement with experiment. The alternative procedure, however, would appear to be physically more correct because the variation in the location of the dipole within the cavity has a far more important bearing on the calculation that does its size.⁵ In our computations eq. 5 is used.

The application of 5 requires an assignment of the moments for the substituents. The magnitude and direction of the C-H bond moment then influences the results. Although there is general agreement concerning the magnitude of this moment, the direction remains uncertain. For completeness, bond moments based on both assignments were examined.³⁶ Although

(35) It has been suggested that the structure is twisted to relieve non-bonded hydrogen repulsions; J. B. Hendrickson, private communication. However, structural studies indicate the molecules of this series possess D_{2h} symmetry. The evidence has been discussed by P. von R. Schleyer and R. D. Nicholas, *J. Am. Chem. Soc.*, **83**, 2700 (1961). This conclusion was confirmed in this laboratory by X-ray study of 1,4-dichlorobicyclo[2.2.2]octane; E. B. Fleischer, unpublished results.

(36) Bond moments based on the assignment of carbon as the negative terminus were taken from the information presented by C. P. Smyth, "Dielectric Behavior and Structure," McGraw-Hill Book Co., Inc., New

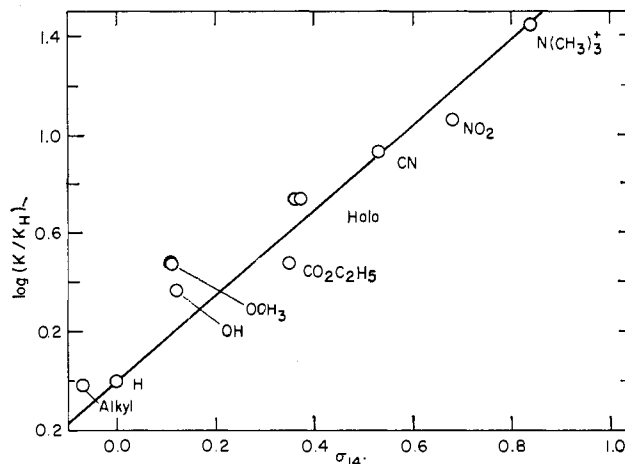


Fig. 3.—Correlation of acid dissociation constants of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids with σ_{14} derived from the F parameters.

$\log (K_X/K_i)$ differs appreciably, $\log (K_X/K_H)$ depends significantly on the choice of the direction of the C-H moment only for the alkyl groups. The results, for hydrogen as the negative terminus only, are presented in Table III.³⁷

TABLE III
CALCULATED VALUES FOR $\log (K/K_H)$ AND PARAMETERS FOR
4-SUBSTITUTED BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACIDS
AT 25°

Group	Parameters ^a		—Ellipsoid ^b — Traube volume		—Sphere ^b — $d = 1.5 \text{ \AA}$.		log (K/K_H), obsd.
	$R, \text{ \AA}$.	$\mu, \text{ D}$.	D_E	log (K/K_H)	D_E	log (K/K_H)	
H	6.92	0.4	6.4	0.00	4.4	0.00	0.00
CH ₃	7.30	.4	9.4	-.04	5.2	-.05	-.01
C ₂ H ₅	7.44	.4	9.5	-.05	5.2	-.05	-.02
CH ₂ OH	7.42	1.6	10.6	.06	5.2	.17	.07
OH	6.45	1.1	6.9	.11	4.5	.19	.37
OCH ₃	6.66	1.2	6.7	.12	4.5	.23	.47
CO ₂ C ₂ H ₅	7.65	1.8	10.7	.06	5.4	.17	.47
Cl	6.44	2.5	6.6	.37	4.6	.53	.74
Br	6.53	2.4	6.8	.34	4.8	.48	.74
CN	7.65	4.4	12.7	.22	5.4	.58	.93
NO ₂	6.58	4.1	6.9	.61	4.8	.88	1.06

^a The bond moments are given as projections on the 1,4-axis.

^b The $\log (K_X/K_H)$ results are based on the calculated difference $\log (K_X/K_i) - \log (K_H/K_i)$. The values of $\log (K_H/K_i)$ are 0.084 and 0.12.

The original model of Kirkwood and Westheimer⁶ underestimates ΔpK_A for the acids with similar values of D_E by a factor of 2. For other substituents with large values of R , e.g., cyano, carboxy, the agreement between theory and experiment is still less satisfactory. Tanford's model⁵ is considerably better. This model is less rigorous in the sense that the volume of the cavity is arbitrarily adjusted to place the dipole more deeply within it. However, it is unwise to rely on the Traube rule.³⁸ This empirical assignment of the volume makes no allowance for the specific 1,4-location of the substituents nor for solvent interactions. The net effect of the redefined volume is a more uniform and smaller D_E . Still, the calculated pK_A changes are smaller than observed experimentally, but the errors are much less.

York, N. Y., 1955, pp. 244, 253. Bond moments based on the assignment of hydrogen as the negative terminus were taken from the information presented by G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, p. 209.

(37) Further details are summarized in the Experimental part.

(38) For comparison the volumes of the 4-bromobicyclo[2.2.2]octane cavity are: Traube, 275 \AA^3 ; Tanford sphere, 600 \AA^3 .

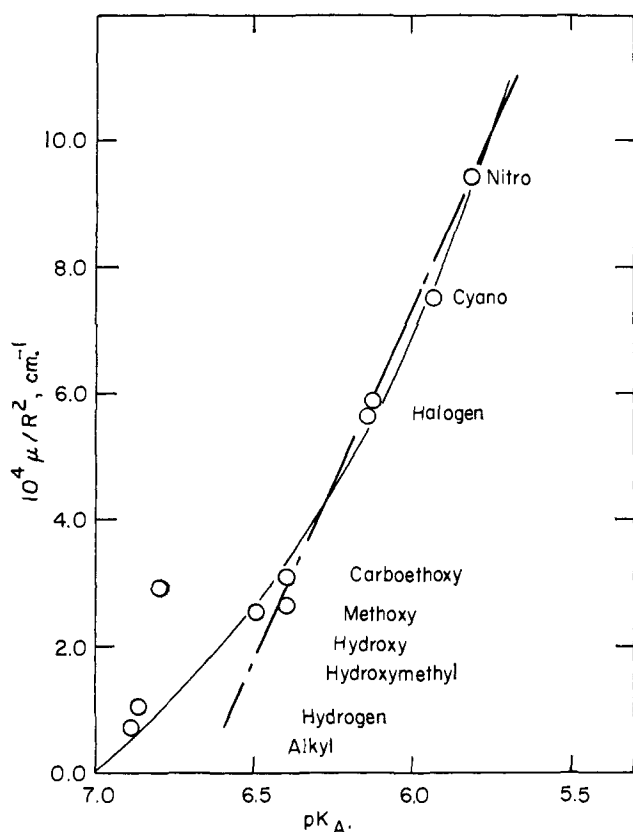


Fig. 4.—Relationship between μ/R^2 and pK_A of the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids. The slope of the dashed line indicates D_E is 5.6.

The source of the residual discrepancy is of interest. Initially, Roberts and Moreland suggested the disagreement was possibly the result of nonthermodynamic measurements but more probably the consequence of an additional inductive contribution.⁷ Westheimer³⁹ commented that he believed the deviation resulted from the inherent limitations of the theory, *e.g.*, the definition of the volume, the defined position of the proton, and the untreated problems of electrosaturation and electrostriction.³⁹

Other factors require consideration. The underestimation might be interpreted as a reflection of some specific feature of the bonding arrangement of the novel, very compact structure. The fact that the rear lobes of bonding orbitals are directed to the interior of the carbon skeleton could create a distinctly different dielectric environment from that associated with other aliphatic molecules. Indeed, if the overlap of the back lobes were sufficient, the dipole effect might be augmented.⁴⁰ Nuclear magnetic resonance coupling constants for nonbonded, distant hydrogens offer a sensitive test of the probable importance of interactions of this character. According to theory, the 1,4-hydrogens are ideally suited for long-range coupling.⁴¹ However, Garbisch has found that such couplings are undetectably small in bicyclo[2.2.2]octanes in contrast to other examples where long-range couplings are observed for hydrogen nuclei separated by even greater distances.⁴² While the dielectric character of the in-

terior of the bicyclic nucleus may be unique, direct interaction between the 1- and 4-atoms is not large.

The possibility that the discrepancy originates in an inductive contribution of the substituent which complements the dipolar field effect cannot be discounted. However, theoretical and empirical analyses conclude inductive contributions operating over three saturated bonds should be negligibly small.^{9,14,43,44}

Closer examination of the results presented in Table III reveals that ΔpK_A is predicted quite satisfactorily by the Tanford model for all the groups other than hydrogen and alkyl (Table IV).

TABLE IV
CALCULATED AND MEASURED VALUES FOR $\log(K/K_{NO_2})$
FOR 4-SUBSTITUTED BICYCLO[2.2.2]OCTANE-1-CARBOXYLIC ACIDS

Substituent	$-\log(K/K_{NO_2})$		
	Kirkwood-Westheimer ellipsoid	Tanford sphere	Experimental
NO ₂	0.00	0.00	0.00
CN	-.39	-.30	-.13
Br	-.27	-.40	-.32
Cl	-.24	-.35	-.32
CO ₂ Et	-.55	-.61	-.59
OCH ₃	-.49	-.65	-.59
OH	-.50	-.69	-.69
H	-.61	-.88	-1.06

A diagram of pK_A vs. μ/R^2 confirms the accurate prediction of the theory for the acid-strengthening groups and the more unique behavior of the hydrogen and alkyl groups (Fig. 4).⁴⁵

The results are best described by a smooth curve indicating that no single value of D_E is entirely satisfactory^{7,16,46} for all the acids. However, a secondary linear relationship for the substituents other than hydrogen is apparent. The slope of this secondary line determines D_E as 5.6 in remarkable agreement with the predictions of the Tanford model. This independent assessment of D_E suggests the model may be more reliable than has been the general view.

Several rather speculative interpretations for the results in Fig. 4 are possible. The smooth curve could be understood as an electrosaturation effect induced by the local fields of the larger dipole moments.^{38,47} Another viewpoint adopts the secondary linear behavior as normal and the results for the hydrogen and alkyl derivatives as exceptional. This behavior could be regarded as the consequence of solvent interactions with the substituent related to the lyophobic properties of the hydrogen and alkyl groups and the other lyophilic groups. In terms of the Kirkwood-Westheimer model, this view implies that the solvent continuum begins closer to the lyophobic groups than to substituents capable of large solvent interactions with solvent incorporated within the cavity.³⁸

In terms of the Dewar-Grisdale model,⁹ the result reflects the greater solvent interactions with the electro-negative substituents decreasing the importance of the exposed negative end of the dipole while having a lesser influence on the hydrogen or alkyl groups. Un-

(39) F. H. Westheimer, footnote 24 in ref. 7, and ref. 4.

(40) K. W. Bowers, G. J. Nolfi, and F. D. Greene, *J. Am. Chem. Soc.*, **85**, 3707 (1963).

(41) K. B. Wiberg, B. R. Lowry, and B. J. Nist, *ibid.*, **84**, 1594 (1962).

(42) E. W. Garbisch, unpublished results.

(43) J. C. McGowan, *J. Appl. Chem. (London)*, **10**, 312 (1960).

(44) An experimental model is under examination.

(45) The diagram and the interpretation are not altered by a reversal in the sign of the carbon-hydrogen bond moment.

(46) S. Winstein, E. Grunwald, and L. I. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

(47) C. K. Ingold, *J. Chem. Soc.*, 2179 (1931).

fortunately, the available experimental results do not allow a differentiation between these ideas and other interpretations.

Two concepts, the dominant contribution of the point charge of the end of the dipole embedded in the cavity and the error associated with the point dipole approximation, prompted the prediction of a $1/r$ dependence.⁹ These suggestions may be examined quantitatively by a less general form of the Kirkwood–Westheimer equation applicable for two-point charges⁴⁸ from which the considerably simplified eq. 3 may be derived. Adoption of the same dimensions for the cavity as used for the Tanford spherical model, Table III, leads to the results for the 4-bromobicyclo[2.2.2]-octane-1-carboxylic acid presented in Table V.

TABLE V

TWO-POINT CHARGE MODEL, SOLVENT, AND CAVITY CONTRIBUTIONS TO THE FIELD EFFECT^a

Substituent ^b	Positive charge		Negative charge		log (K/K_i)
	Solvent	Cavity	Solvent	Cavity	
H	0.05	0.18	-0.04	-0.06	0.13
Br	0.16	0.71	-0.11	-0.10	0.66

^a In units of log (K/K_i). ^b 4-Substituted bicyclo[2.2.2]-octane-1-carboxylic acid.

The point dipole estimate of log (K_{Br}/K_H), 0.48, is about 10% less than the computed value, 0.53, of the two-point charge formulation. This calculation shows the point dipole approximation is somewhat in error even at the rather large molecular distances (5–7 Å.) of the bicyclo[2.2.2]octanes. The error already approaching significance in this case should not be neglected in discussions of dipole influences at shorter distances. The two-point charge model also partitions the contribution of each point charge between solvent and cavity. The dominant term is clearly that associated with the effect of the positive charge transmitted through the cavity as proposed by Dewar and Grisdale.⁹ Both their suggestions are substantiated by the use of the more definitive form of the Kirkwood–Westheimer equation. However, their approach does not allow a theoretical treatment of the large solvent effects on ΔpK_A . Ritchie and Lewis report log (K_{Br}/K_H) to be 0.6 in methanol, 0.7 in ethanol, and 0.9 in acetone.¹⁷ Since the contribution of the positive charge transmitted through the cavity is independent of the solvent, these variations must be accommodated empirically. The Kirkwood–Westheimer theory, on the other hand, permits at least a semiquantitative understanding of the ΔpK_A changes allowing for the greater effect of substituents in media of lower dielectric constant. The additional solvent term for the positive point charge and the additional terms associated with the negative point charge are important in this sense.

For the ionization of *m*- and *p*-benzoic acids and for the bicyclo[2.2.2]octanes ρ was shown in a previous section to be equal. This parameter is 1.4 for 3-substituted adamantane-1- and *trans*-4-substituted cyclohexane-1-carboxylic acids. The quantity, $(\mu \cos \theta)/R^2$ of eq. 3, may be determined by reference to a particular substituent. For the bromo acids, the quantity differs by more than a factor of 2, yet ρ shows no important change. The result is very puzzling and has been taken as support for the operation of

inductive effects. The equation of linear free energy relationships for carboxylic acids A and B with the Kirkwood–Westheimer equations for these same acids yields eq. 6.

$$\frac{(\rho\sigma)_A}{(\rho\sigma)_B} = \frac{(\mu \cos \theta / R^2 D_E)_A}{(\mu \cos \theta / R^2 D_E)_B} \quad (6)$$

Reference to the bromo acids allows the definition of all the quantities except the effective dielectric constant. Solution of the equation for the ratio, D_E^A/D_E^B , where D_E^B is the value for 4-bromobicyclo[2.2.2]octane-1-carboxylic acid, gives the values summarized in Table VI.

TABLE VI

FACTORS CONTRIBUTION TO ρ

Bromocarboxylic acid	$10^4 \mu \cos \theta / R^2$, e.s.u. cm. ⁻¹	ρ	$-D_E/D_E^B$	
			Eq. 6	Calcd.
1,4-Bicyclo[2.2.2]octane	5.65	1.5	1.0	1.0
1,4-Benzoic	4.57	1.5	0.9	1.0
1,3-Adamantane	2.23	1.4	0.4	0.4
1,3-Benzoic	2.95	1.5	0.6	0.6
1,4- <i>trans</i> -Cyclohexane	5.20	1.4	1.0	1.1

Large variations in D_E/D_E^B are necessary for the equality expressed as eq. 6 to be valid. Recourse to the two-point charge form of the Kirkwood–Westheimer equation allows the assessment of this ratio by theory. Inasmuch as D_E may not be extracted from the equation, we adopted the approximate procedure of the calculation of log (K/K_i) for the bromo acid from the two-point charge formulation and using the result solved eq. 3 for D_E . The calculated results presented in Table VI are in excellent agreement with the ratios of D_E/D_E^B demanded by eq. 6. Although the exact agreement may be fortuitous, the Kirkwood–Westheimer field effect approach is clearly able to justify the constancy of ρ for these acids of rigid but divergent structure.^{49a}

Experimental

Materials.—The solvent, 50% weight ethanol–water, was prepared from weighed quantities of water (redistilled from basic permanganate) and 95% ethanol (distilled from sodium ethoxide). In all operations the solvent was protected from atmospheric carbon dioxide. The final composition of the solvent was established as $50.00 \pm 0.02\%$ by density determination. Standard solutions of hydrochloric acid and sodium hydroxide were also prepared in the same solvent. National Bureau of Standards acidimetric reagents, benzoic acid and potassium acid phthalate, were used as reference standards. The 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids²¹ were recrystallized several times and sublimed prior to study. Benzoic acid, NBS, was used as obtained.

pK_A Determination.—The method described by Grunwald and his associates was used.¹⁹ A Beckman Model GS meter capable of 0.2 mv. precision was used in conjunction with a glass electrode (Beckman No. 40485) meeting the specifications of Gutbezahl and Grunwald^{49b} and a silver–silver chloride electrode. The latter electrode was similar to that described by Purlee and Grunwald.²⁰ A strip of platinum foil (0.004 in. thick) of about 5 cm.² area was spotwelded to a length of silver wire (C.P., 1 mm. diam.). The silver wire was passed through a glass capillary (20 cm. long) and soldered to a copper lead wire for connection to the meter. The end of the capillary was sealed with paraffin wax. The platinum foil was cleaned with concentrated nitric acid and ammonia–water. It was then soaked in distilled water and doubly distilled water. Finally, five coats of silver (20 min. each) were deposited by the Rochelle salts method.²⁰ The electrode was again rinsed with water and was anodized at 1 ma. for 3.5 min. in

(48) Equations 12–18 of ref. 5; see Experimental part.

(49) (a) See, however, J. D. S. Ritter and S. I. Miller, *J. Am. Chem. Soc.*, **86**, 1507 (1964); (b) B. Gutbezahl and E. Grunwald, *ibid.*, **75**, 559 (1953)!

a stirred 0.05 *M* hydrochloric acid solution. The cathode was a platinum wire. The finished electrode was stored in 50% aqueous ethanol saturated with potassium chloride and silver chloride.

The cell consisted of a jacketed beaker of 100-ml. capacity with a Bakelite top. Three holes accommodated two glass and the silver-silver chloride electrodes. An inlet part for nitrogen (saturated with the solvent) and two smaller holes for the burets were also available. Water from a constant temperature bath was circulated through the jacket. The solution was stirred magnetically. Grunwald's procedure¹⁹ was used without important modification. The results are summarized in Table I.

Kirkwood-Westheimer Calculations. Table III.—The distance from the removable proton to the midpoint of the dipole was assessed for the case with the dipole oriented along the 1,4-axis from conventional values for bond distances. Where several atoms were involved in the group moment aligned along that axis, *e.g.*, nitro, the midpoint of the dipole was taken as the midpoint of the projected bond distances along the same axis. For other substituents, *e.g.*, hydroxy, with the group dipole not coincident with the 1,4-axis, the distance was taken to the midpoint of the projected dipole on the molecular axis. Effective dielectric constants were derived from the published tables of Westheimer, Jones, and Lad.⁵⁰ The volume of the cavity was determined by

(50) F. H. Westheimer, W. A. Jones, and R. A. Lad, *J. Chem. Phys.*, **10**, 478 (1942).

Traube's rule for the Kirkwood-Westheimer ellipsoidal model and by the assignment of *d* (the distance from the midpoint of the dipole to the edge of the cavity) as 1.5 Å. for the Tanford modification.⁸ The results for the Tanford elliptical model, not presented in Table III, are in poorer agreement with experiment as previously found.⁸

Table V.—A two-point charge model was employed. The cavity was assigned the same dimensions as the Tanford sphere to allow a direct comparison between the two approaches. The charges were positioned at the carbon and bromine nuclei and assigned as μ/l where *l* is the bond length.

Table VI.—Unfortunately D_E for dipole substituents has not been ascertained for substituents not oriented on the principal axis of the molecule and the two-point charge form of the Kirkwood-Westheimer equation cannot be factored to provide D_E . To estimate the parameter, $\log(K/K_i)$ was calculated for each acid from the two-point charge formulation. In each case the center of the parent hydrocarbon was taken as the center of the cavity and the radius of the cavity assigned as the sum of the distances from the origin to the ionizable proton and an additional 1.5 Å. With this definition of the radius and the knowledge of the other angles and distances as defined by the structure, the value of $\log(K/K_i)$ was calculated. Using the result for $\log(K/K_i)$ eq. 3 was solved for D_E . D_E and $\log(K/K_i)$ for 4-bromobicyclo[2.2.2]octane-1-carboxylic acid are 4.2 and 0.65, respectively.

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Reactions of the Cyclooctatetraenyl Dianion with *gem*-Dihalides. The Preparation of Derivatives of Bicyclo[6.1.0]nonatriene. Synthesis of the Cyclononatetraenyl Anion

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The reactions of dipotassium or dilithium cyclooctatetraenide in tetrahydrofuran (THF) with methylene chloride, chloroform, carbon tetrachloride, and dichloromethyl methyl ether yield bicyclo[6.1.0]nonatriene and its *anti*-9-chloro, 9,9-dichloro, and *anti*-9-methoxy derivatives. *anti*-9-Chlorobicyclo[6.1.0]nonatriene is thermally rearranged at 70° to 1-chloro-8,9-dihydroindene. The former reacts with lithium in THF to yield lithium cyclononatetraenide. Similarly, *anti*-9-methoxybicyclo[6.1.0]nonatriene with potassium in THF gives potassium cyclononatetraenide. Some physical properties and chemical reactions of the cyclononatetraenyl anion are presented.

Introduction

Although the familiar cyclically conjugated hydrocarbon molecules and ions¹ are those with six unsaturation electrons, derivatives of the two-electron cyclopropenium ion,¹ of the ten-electron cyclooctatetraenyl dianion² and cyclononatetraenyl anion,^{3,4} and of macrocyclic hydrocarbons with 12, 14, 16, 18, 20, 24, and 30 unsaturation electrons⁵ have recently been synthesized. The ten-electron compounds are a challenge since medium-sized rings are expected to oppose in a number of ways the formation of an aromatic system. If the rings were of the planar all-*cis* conformation, bond angles would be severely strained; if some of the bonds were *trans*, nonbonded atoms would clash in the center.⁶

In either case the skeletal strain could be relieved by a distortion from planarity,⁷ which would, however,

interfere with the cyclic conjugation of the unsaturation electrons, or by a valence tautomerization,⁸ which would interrupt conjugation completely.

Despite these obstacles, the cyclooctatetraenyl dianion² and cyclononatetraenyl anion^{3,4} are aromatic. Cyclodecapentaene, however, is reported to be unstable with respect to its valence tautomer, *cis*-9,10-dihydronaphthalene,⁹ but a related dihydronaphthalene¹⁰ is reported to valence tautomerize spontaneously to the corresponding cyclodecapentaene derivative.

The cyclononatetraenyl anion was synthesized by Katz and Garratt by the procedure outlined in eq. 1.³ The details of this synthesis are reported below. A similar synthesis of the anion was achieved independently by LaLancette and Benson.⁴

Results

The Synthesis of Derivatives of Bicyclo[6.1.0]nonatriene.—A few derivatives of bicyclo[6.1.0]nonatriene are known. The first reported was 9-carboethoxybicyclo[6.1.0]nonatriene (IIa), prepared by the

(1) (a) "Non-Benzenoid Aromatic Compounds," D. Ginsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959; (b) M. E. Vol'pin *Russ. Chem. Rev.*, **29**, 129 (1960).

(2) (a) T. J. Katz, *J. Am. Chem. Soc.*, **82**, 3784 (1960); (b) H. P. Fritz and H. Keller, *Chem. Ber.*, **95**, 158 (1962).

(3) T. J. Katz and P. J. Garratt, *J. Am. Chem. Soc.*, **85**, 2852 (1963).

(4) E. A. LaLancette and R. E. Benson, *ibid.*, **85**, 2853 (1963).

(5) F. Sondheimer, "Congress Lectures Presented at the XIXth International Congress of Pure and Applied Chemistry," Butterworths, London, 1963; see also, V. Boekelheide and J. B. Phillips, *J. Am. Chem. Soc.*, **85**, 1545 (1963).

(6) K. Mislow, *J. Chem. Phys.*, **20**, 1489 (1952).

(7) Cyclooctatetraene is nonplanar (*cf.* R. A. Raphael, Chapter VIII in *ref. 1a*).

(8) E. Vogel, *Angew. Chem. Intern. Ed. Engl.*, **2**, 1 (1963).

(9) E. E. van Tamelen and B. Pappas, *J. Am. Chem. Soc.*, **85**, 3296 (1963). See also J. J. Bloomfield and W. T. Quinlin, *ibid.*, **86**, 2738 (1964).

(10) E. Vogel and H. D. Roth, *Angew. Chem.*, **76**, 145 (1964). See also W. S. Johnson, J. D. Bass, and K. L. Williamson, *Tetrahedron*, **19**, 861 (1963).