ISOTOPE EFFECTS ON CHEMICAL EQUILIBRIA

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A Thesis

by

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PREFACE

The initial introduction to the thesis outlines the basic philosophy which prompted the present investigation. Prior to carrying out measurements which could prove definitive in the consideration of substituent effects on equilibrium isotope ratios, studies of the protium acids and their corresponding deuterium substituted analogues were conducted with a view to examining their suitability for measurement. This investigation led to a closer examination of the chemical and physical properties of phenylsulfinylacetic acid and some related compounds. This additional investigation was not anticipated in the original scope of the work, and to accommodate the resulting lapse in continuity between the two areas of study, the thesis is conveniently divided into Part I and Part II, each presenting separate Introduction, Experimental, Results and Discussion chapters.

P.D.G.

ABSTRACT

PART I

The thermodynamic equilibrium constants, $K_t(H)$, of five monosubstituted acetic acids, RCH_2COOH, where R = Cl, Ph, PhO, PhS, and $PhSO_2$, have been measured conductimetrically. The syntheses of five isotopically substituted acetic acids, RCD_2COOH, where R = Cl, PhO, PhS, PhSO, and $PhSO_2$, are described and the thermodynamic equilibrium constants, $K_t(D)$, of three of these, R = Cl, PhO, and PhS, are reported. The calculation of secondary isotope effects of the second kind for the three isotopic acid pairs, RCH_2COOH/RCD_2COOH, where R = Cl, PhO, and PhS, has been accomplished by the appropriate comparison of thermodynamic equilibrium constants, $K_t(H)/K_t(D)$, and by the comparison of isotopic slopes, $m_t(D)/m_t(H)$. These slopes, $m_t(D)$ and $m_t(H)$, are derived from linear least squares treatments of the Classical and Shedlovsky conductance equations, and their comparison is demonstrated as a superior method in the calculation of isotope effects.

A linear least squares interpolation to minimum deviation of Shedlovsky K_t values with variation of limiting equivalent conductance (Λ_0) is tested as a suitable method for the calculation of Λ_0. The effect of substituent variation on the isotope effects reported here disqualifies the simple inductive model as a legitimate description of secondary isotope effects of the second kind.

The correlation of diminishing isotope effect per deuterium atom with increasing acidity is also invalidated by the present results.

PART II

The syntheses of 9-thia-9,10-dihydrophenanthrene-9-oxide and thioxanthene-10-oxide are described. These compounds have been partially deuterated at their respective methylene positions by dissolution in alkaline deuterium oxide. Spectral evidence indicates stereoselectivity of the methylene protons in the exchange reactions of both compounds. Unlike phenylsulfinylacetic acid, interchange of the methylene proton chemical shifts does not occur for either compound when the solvent medium is varied from dimethyl sulfoxide-d_6 to trifluoroacetic acid. The proposed conformational change of thioxanthene-10-oxide from the pseudoequatorial array in chloroform-d to the pseudoaxial array in trifluoroacetic acid is considered.

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PART I

CHAPTER 1

INTRODUCTION

1-1. ON THE ORIGIN AND INTERPRETATION OF ISOTOPE EFFECTS

The correlation of structural change with corresponding reactivity change has remained a topic of interest in the field of contemporary physical-organic chemistry. Structural variations embracing a wide reactivity range have been statistically treated [c.f. (1)], and the philosophy of their interpretation has been carefully considered [c.f. (2)]. By definition, however, the most subtle variation in structure must be isotopic substitution, with the corresponding reactivity changes denoted as "isotope effects".

In the interests of clarity and continuity, this presentation will be restricted to the consideration of only one isotopic pair, namely hydrogen (H) and deuterium (D). In the case of chemical equilibria, an isotope effect is defined by the ratio of K(H) to K(D), K(H) being the equilibrium constant pertaining to the proton substituted structure and K(D) the equilibrium constant appropriate to the deuterium analogue. When rate measurements are of interest, the isotope effect is designated as the ratio of the corresponding rate constants k(H) to k(D). When the isotope effect is greater than unity, i.e. $K(H)/K(D)>1$ or $k(H)/k(D)\geq 1$, it is said to be a "normal" effect, and when less than unity, i.e. $K(H)/K(D)<1$ or $k(H)/k(D)<1$, it is described as an "inverse" or "reverse" isotope effect.

A further classification of isotope effects depends upon a consideration of the effect of the chemical process on the bond linking the isotopic atoms to the molecular residues. If this particular bond is ruptured or partially ruptured, a "primary" isotope effect results; but if the bond remains intact in the reactants, transition states, and products, the isotope effect is "secondary". Equations [1]* and [2] serve to illustrate a primary and a secondary isotope effect respectively.

$$Ph - CH_2 - COOH + H_2O \xrightleftharpoons{K(H)} Ph - CH_2 - COO^{(-)} + H_3O^{(+)}$$

[1]

$$Ph - CH_2 - COOD + D_2O \xrightleftharpoons{K(D)} Ph - CH_2 - COO^{(-)} + D_3O^{(+)}$$

$$Ph - CH_2 - COOH + H_2O \xrightleftharpoons{K(H)} Ph - CH_2 - COO^{(-)} + H_3O^{(+)}$$

[2]

$$Ph - CD_2 - COOH + H_2O \xrightleftharpoons{K(D)} Ph - CD_2 - COO^{(-)} + H_3O^{(+)}$$

Secondary isotope effects in which the bonds from the isotopic substituents to the molecular residues undergo spatial reorientation have been described by Streitweiser (3) as secondary isotope effects of the "first kind". Secondary isotope

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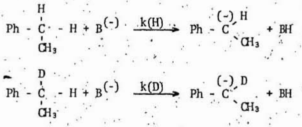
*Since hydroxyl protium and deuterium atoms exchange very rapidly in aqueous media, K(D) must be determined in D_2O. Consequently, K(H)/K(D) of equation [1] includes not only a primary isotope effect but also a "solvent isotope effect".

effects of the "second kind" are those in which no spatial reorientation of the bond occurs in the equilibrium or rate process under consideration. Examples of secondary isotope effects of the first and second kind are respectively given by Equations [3] and [4]. These examples form part of a series of reactions investigated by Streitweiser and co-workers (4).

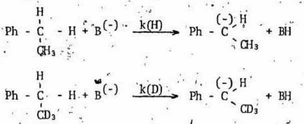
[3]



$$\mathrm{Ph-\overset{H}{\underset{CH_3}{C}}-H + B^{(-)} \xrightarrow{k(H)} Ph-\overset{(-)}{C}(H)(CH_3) + BH}$$

$$\mathrm{Ph-\overset{D}{\underset{CH_3}{C}}-H + B^{(-)} \xrightarrow{k(D)} Ph-\overset{(-)}{C}(D)(CH_3) + BH}$$

[4]



$$\mathrm{Ph-\overset{H}{\underset{CH_3}{C}}-H + B^{(-)} \xrightarrow{k(H)} Ph-\overset{(-)}{C}(H)(CH_3) + BH}$$

$$\mathrm{Ph-\overset{H}{\underset{CD_3}{C}}-H + B^{(-)} \xrightarrow{k(D)} Ph-\overset{(-)}{C}(H)(CD_3) + BH}$$

Mayer (5a), Bigeleisen (5), Melander (6), and others (5c, 7) have put forward rigorous theories based on statistical mechanics and the Redlich-Teller product rule [see (8)] which allow the accurate calculation of isotope effects in chemical reactions. Although these theories may differ slightly in emphasis, the differences are of little consequence in the present discussion. The calculation of isotope effects in rate processes requires a knowledge of the molecular vibrational frequencies of the isotopically substituted species in both the ground and transition states, and in the case of equilibria, these frequencies must be available for both the reactants and products. Hence, the theoretical approach proposed by Bigeleisen and Melander is of limited value in its final form, for the situation seldom occurs in which all the vibrational frequencies or the related force constants can be empirically determined [c.f. Bigeleisen and Wolfsberg (5c)]*. A notable exception is the investigation of the formic acid system by Bell and Crooks (12). The pK_a difference between HCOOH and DCOOH observed by these workers was in good agreement with the theoretically computed value using only empirical vibrational frequencies. However, the measurement and assignment of vibrational frequencies of more complex isotopically substituted molecules in a condensed phase, in which rates and equilibria are usually examined, is an exceedingly difficult task. Thus, an accurate calculation of isotope effects for equilibria and rates is generally impossible.

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*This is not possible for rate processes since the vibrational frequencies or related force constants of the transition states are not observables. However, several serious attempts have been made to calculate kinetic isotope effects by employing multicenter transition state models [c.f. Westheimer (9), Bell (10), and More O'Ferrall and Kouba (11)].

If hν in a pair of H and D substituted analogues is large relative to KT for all frequencies, the complex theoretical expressions can be simplified to a dependence on zero-point energy terms and the isotope effect is given by

$$[5] \quad \frac{K(H)}{K(D)} = \exp.\ \frac{-h}{2kT}\ (\Sigma\Delta\nu_H - \Sigma\Delta\nu_D).$$

where "h" is Planck's constant, "k" is Boltzmann's constant, "T" is the absolute temperature, and "ΣΔν" represents the difference in the frequency sums of the respective products and reactants. Equation [5] implies that isotope effects are quantum effects and that they depend largely on a double difference between the vibrational frequency sums of the products and reactants of the isotopic analogues.

By applying further approximations Equation [5] may be simplified to give

$$[6] \quad \frac{K(H)}{K(D)} = \exp.\ \frac{-h}{2kT}\ \left(1 - \frac{1}{c}\right)\ (\Sigma\nu_H - \Sigma\nu'_H)$$

In this equation only the sums of those frequencies primarily associated with the motion of the hydrogen atom at the position of interest in the non-deuterated product and reactant are required, and these sums are represented by $\Sigma\nu_H$ and $\Sigma\nu'_H$, respectively. These approximations were employed by Streitweiser for the calculation of isotope effects in rate processes. However, since k(H)/k(D) can be related to K(H)/K(D) (13)*, then isotope effects arising from equilibrium considerations may be calculated using Equation [6]. The constant "c" in Equation [6] has a theoretical value of $\sqrt{2}$ **, but Streitweiser (14) has determined the value of "c" to be about 1.35 from a consideration of suitable spectroscopic data. By employing Equation [6] to approximate an isotope effect, the sums of all the vibrational frequencies in both pairs of isotopically substituted reactants and products are no longer necessary. In extreme cases the summations may be reduced to a consideration of two or three vibrations or even a single vibration. [However, for more detailed calculations using the complete theory, see Wolfsberg and Stern (15) and Willi (16)].

It is generally accepted that protium-deuterium secondary isotope effects are primarily dependent upon zero-point energy differences incurred in going from reactants to products.

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*k(H)/k(D) is actually related to $[K(H)/K(D)]^{\ddagger}$ in which K(H) and K(D) are the quasi-equilibrium constants between the respective reactants and their transition states.

**The theoretical value of $\sqrt{2}$ results from the application of the "infinite mass-diatomic oscillator" approximation, in which the hydrogen atom is assumed to be only vibrating in conjunction with the much larger mass of the molecular residue.

These differences are in turn dependent upon force constant changes which can be attributed to steric interactions (14, 17, 18, 19, 20, 21, 22, 23) and such electronic effects as hyperconjugation (14, 17, 24, 25, 26, 27, 28), hybridization (14, 18, 19, 20, 29, 30), and induction (29, 31).

Streitweiser (32) has ascribed secondary isotope effects of the first kind to hybridization changes, but describes effects of the second kind as those which "behave like inductive effects". These criteria have been criticized by Halevi (29) who states, "a classification scheme based on the presence or absence of significant structural changes in the region of isotopic substitution is likely to survive longer than one based on theoretical concepts, no matter how well established these seem to be at the time". This criticism may well be considered trivial since structural changes are themselves usually based on theoretical concepts (e.g. postulated mechanisms). Indeed, in his review (29), Halevi attempts elaboration and interpretation of secondary isotope effects in terms of qualitative theoretical concepts related to changes which are electronic in nature. He states, "deuterium bonded to carbon is effectively more electropositive, but less polarizable, than protium. The principal factor responsible (for this electronic difference) seems to be the anharmonicity of the vibrations involving the motions of the hydrogen atoms, which leads to different average bond lengths and angles in deuterated and normal molecules", and hence, a different charge distribution. This hypothesis that secondary isotope effects of the second kind behave like inductive effects is supported by the effect of deuteration (at positions α and β to the carboxyl group) on the equilibria of the carboxylic acids listed in Table I. In the case of a few ammonium ion acids (33, 34, 35, 36), which show behaviour similar to that of the carboxylic acids in Table I, the effect is more marked; but this has been rationalized on the basis of opposing inductive and hyperconjugative effects in the carboxylic acids (29).

If secondary isotope effects behave like inductive effects, the magnitude of such effects might be expected to vary with structure and with position of deuteration, and consequently be amenable to a linear free energy treatment in much the same manner as Taft's (37) treatment of "large scale" inductive effects. Indeed, Streitweiser (32) has successfully applied the Taft equation to estimate the magnitude of isotope effects in certain aromatic ring compounds from the isotope effects of an aliphatic series.

Using the premise that inductive effects are additive, Scott and Barnes (38) have modified the Taft equation (37) from

[7] $$\log_{10}K = (1.721 \pm 0.025)\sigma^* - 4.76$$

to

[8] $$pK_a = -(0.550 \pm 0.059)\ \Sigma\sigma^* + 5.200 \pm 0.014$$

TABLE I

SOME PREDICTED AND OBSERVED ISOTOPE EFFECTS [TAKEN FROM (38)]*

ISOTOPIC PAIR	K(H)/K(D)	
	OBSERVED (REFERENCE)	CALCULATED
CH_3COOH/CD_3COOH	1.035 (32)	--
$(CH_3)_3COOOH/(CD_3)_3COOOH$	1.04 (32)	--
$HCOOH/DCOOH$	1.08 (29)	1.03
$CH_3CH_2COOH/CD_3CH_2COOH$	1.01 (34)	1.014
$CH_3CH_2COOH/CH_3CD_2COOH$	1.08 (34)	1.021
$PhCH_2COOH/PhCD_2COOH$	1.12 (34)	1.021
$\overset{(+)}{CH_3NH_3}/\overset{(+)}{CD_3NH_3}$	1.13 (36)	1.083
$(CH_3)_2\overset{(+)}{NH_2}/(CD_3)_2\overset{(+)}{NH_2}$	1.32 (36)	1.18

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*The recent measurements of the K(H)/K(D) values reported in (38) for $R\text{-}PhCH_2COOH/R\text{-}PhCD_2COOH$, where R = H, 4-MeO, 4-$NO_2$, are given in Table III, p. 28.

where σ^* is the Taft inductive parameter for a substituent "X" attached to the carboxyl group of a carboxylic acid. When "X" can be considered as a substituted methyl group ($-CX_1X_2X_3$), then $\Sigma\sigma^*$ is defined as

[9] $\Sigma\sigma^* = \sigma^*(X_1) + \sigma^*(X_2) + \sigma^*(X_3)$

This modification is similar to Hall's (39) relationships, which are given by

[10] $pK_a = 13.23 - 3.14\ \Sigma\sigma^*$

for primary amines and

[11] $pK_a = 12.13 - 3.23\ \Sigma\sigma^*$

for secondary amines. In these equations the $\Sigma\sigma^*$ parameter refers to the sum of the Taft constants for the groups attached to the nitrogen atom. The $\Sigma\sigma^*$ values were calculated by Scott and Barnes (38) for twenty-three carboxylic acids listed in Table II, and used in the correlation of $\Sigma\sigma^*$ and pK_a shown in Figure I. The correlation of σ^* and $\Sigma\sigma^*$ (see Figure II) gives a straight line which does not pass through the origin and the slope of which is not unity. However, this plot indicates that the premise upon which the modification of the Taft equation is dependent, namely that inductive effects are additive, is by and large a good one. Although the correlation of $\Sigma\sigma^*$ and pK_a based on the modification

TABLE II

ACID STRENGTH DATA RELATED TO THE TAFT CORRELATION FOR SUBSTITUTED ACETIC ACIDS [TAKEN FROM (38)]

			$X = CX_1X_2X_3$			
ACID (X-COOH)	pK_a†	σ*	X_1	X_2	X_3	Σσ*‡
CF_3COOH	0.23	--	F	F	F	9.30
CCl_3COOH	0.65	2.65	Cl	Cl	Cl	8.70
CBr_3COOH	0.66	--	Br	Br	Br	8.40
CHF_2COOH	1.24	2.05	F	F	H	6.69
$CHCl_2COOH$	1.29	1.94	Cl	Cl	H	6.29
$(CH_3)_3\overset{(+)}{N}CH_2COOH$	1.83	1.90	$(CH_3)_3\overset{(+)}{N}$	H	H	--
$CNCH_2COOH$	2.43	1.30	CN	H	H	4.62
CH_2FCOOH	2.59	1.10	F	H	H	4.08
$CH_2(COOH)_2$	2.83	1.05	COOH	H	H	--
$CH_2ClCOOH$	2.87	1.00	Cl	H	H	3.88
$CH_2BrCOOH$	2.90	0.92	Br	H	H	3.78
CF_3CH_2COOH	3.07	0.85	CF_3	H	H	--
$C_6H_5OCH_2COOH$	3.12	0.85	PhO	H	H	--
CH_2ICOOH	3.18	0.52	I	H	H	3.38
CH_3OCH_2COOH	3.53	0.60	CH_3O	H	H	---
HCOOH	3.77	0.49	-	-	-	--
$NO_2CH_2CH_2COOH$	3.81	0.50	NO_2CH_2	H	H	1.48

....Cont'd

TABLE II (Cont'd)

ACID (X-COOH)	pK_a†	σ^*	$X = CX_1X_2X_3 -$ X_1	 X_2	 X_3	$\Sigma\sigma^*$‡
$(C_6H_5)_2CHCOOH$	3.94	0.45	C_6H_5	C_6H_5	H	2.45
$(C_6H_5)_3CCOOH$	3.96	--	C_6H_5	C_6H_5	C_6H_5	2.94
CH_2ClCH_2COOH	4.08	0.385	CH_2Cl	H	H	2.52
$C_6H_5CH_2COOH$	4.31	0.215	C_6H_5	H	H	1.58
$CF_3CH_2CH_2COOH$	4.49	0.320	CF_3CH_2	H	H	1.50
$C_6H_5CH_2CH_2COOH$	4.66	0.080	$C_6H_5CH_2$	H	H	1.195
CH_3COOH	4.76	0.00	H	H	H	1.47
$(CH_3)_2CHCOOH$	4.86	-0.19	CH_3	CH_3	H	0.49
CH_3CH_2COOH	4.88	-0.10	CH_3	H	~~H~~	0.98
$CH_3CH_2CH_2COOH$	4.82	-0.115	CH_3CH_2	H	H	0.88
$CH_3CH_2(CH_3)CHCOOH$	4.78	-0.21	CH_3CH_2	CH_3	H	0.39
$(CH_3)_3CCOOH$	5.05	-0.30	CH_3	CH_3	CH_3	0.00

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†All pK_a values were taken from (41) except those of the monohalogenoacetic acids, which were taken from (42).

‡The $\Sigma\sigma^*$ values are taken from the correlation given by Equation [8] (see Figure I) and are not derived from Equation [9].

FIGURE I

A CORRELATION BETWEEN $\Sigma\sigma^*$ AND pK_a FOR A SERIES OF SUBSTITUTED ACETIC ACIDS [TAKEN FROM (44)]

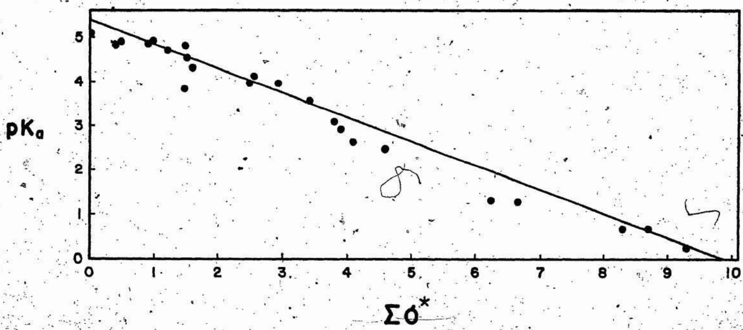
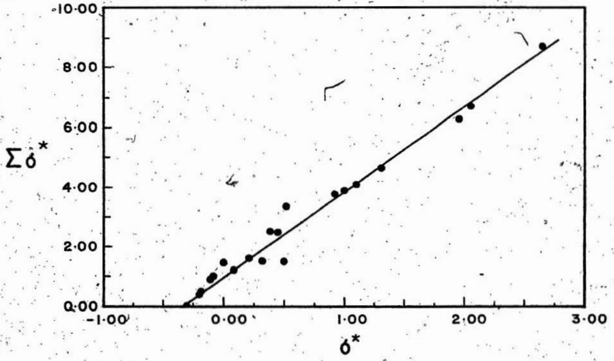


FIGURE II

A CORRELATION BETWEEN $\Sigma\sigma^*$ AND σ^* FOR A SERIES OF SUBSTITUTED ACETIC ACIDS [TAKEN FROM (44)]



(see Figure I) is inferior to that originally given by Taft, a more extensive range of structures is embraced by Equation [8] than was used to establish Equation [7]. Deviations from the strict additivity of inductive effects may be a consequence of steric effects, but these should be negligible in the case of H, D, CH_3 and CD_3 substituents [However, see Bartell's investigation of nonbonded interactions (18, 19, 20)].

The value of σ^* (D) was obtained from equilibrium constant measurements made by Bates et al. (40) on the CH_3COOH/CD_3COOH system, and similarly the value of σ^* (CD_3) was obtained from an investigation of the $(CH_3)_3COOH/(CD_3)_3COOH$ system by Streitweiser and Klein (32). Substitution of the pK_a's of CD_3COOH and $(CD_3)_3COOH$ into Equation [8] allowed Scott and Barnes (38) to calculate values of 0.482 and -0.011 for σ^* (D) and σ^* (CD_3), respectively. These values of σ^* (D) and σ^* (CD_3) were then used in conjunction with the values of σ^* (H), σ^* (CH_3) and σ^* (Ph) (see Table II) to calculate the $\Sigma\sigma^*$ values of the following isotopic acid systems: $HCOOH/DCOOH$, $CH_3CH_2COOH/CD_3CH_2COOH$, $CH_3CH_2COOH/CH_3CD_2COOH$, $PhCH_2COOH/PhCD_2COOH$, $CH_3\overset{(+)}{N}H_3/CD_3\overset{(+)}{N}H_3$, and $(CH_3)_2\overset{(+)}{N}H_2/(CD_3)_2\overset{(+)}{N}H_2$. From the calculated $\Sigma\sigma^*$ values Scott and Barnes (38) have recently predicted the isotope effects of the latter systems, and these are compared (see Table I) with experimentally observed values determined by Halevi (34) and Robertson (36, 43). Although the predictions of the isotope effects for these acid systems are qualitatively verified, the observed isotope effects generally exceeded the predicted effects by several percent.

To provide more data with which to test the Halevi-Streitweiser-Taft inductive treatment of isotope effects, Scott and Barnes (38, 44) carried out conductance measurements to determine the K(H)/K(D) ratios for the isotopic weak acid pairs $4\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}COOH/4\text{-}NO_2\text{-}C_6H_4\text{-}CD_2\text{-}COOH$ and $4\text{-}MeO\text{-}C_6H_4\text{-}CH_2\text{-}COOH/4\text{-}MeO\text{-}C_6H_4\text{-}CD_2\text{-}COOH$. They also redetermined the isotope effect of the $PhCH_2COOH/PhCD_2COOH$ pair. These acid systems were chosen to test the adequacy of the inductive treatment, since the inductive model requires to a first approximation that isotope effects be independent of the nature of any group substituted in the 4-position of the ring in the aromatic side chain.

Although the isotope effect ratios determined by Scott and Barnes (38, 44) are in qualitative agreement with the Halevi-Streitweiser-Taft inductive model, a comparison of $1/n \log_{10}K(H)/K(D)$ and $pK_a(H)$ has been deemed greater in significance and interest.* The inclusion of the data for the acetic acid system (40) with the results of the latter three arylacetic acid pairs suggests a trend in which the isotope effect per deuterium atom declines as the strength of the acid increases (see Figure III).

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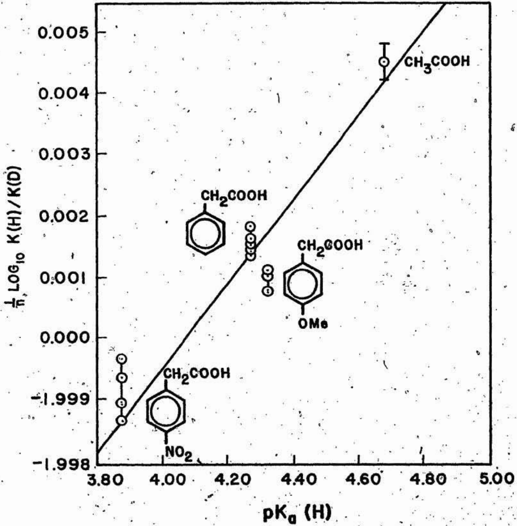
*V.J. Shiner (17) originally proposed the formula $1/n \log_{10}K(H)/K(D)$ in which n = 3 for CH_3COOH/CD_3COOH and n = 2 for the arylacetic acids.

FIGURE III

A PLOT OF $\frac{1}{n}$ LOG$_{10}$ K(H)/K(D) vs. pK$_a$(H) [TAKEN FROM (44)]



Two observations emerge from the correlation of $pK_a(H)$ with $1/n\ \log_{10}K(H)/K(D)$:

(1) The predicted value of 1.02 for the isotope effect of the $PhCH_2COOH/PhCD_2COOH$ acid pair based on $\sigma^*(D)$ is now much closer to the observed value of 1.01, i.e. the inductive treatment is partially verified.

(2) The isotope effect appears to be variable and depends on the structure of the acid (38,44). This is not consistent with the simple inductive model, which requires that the inductive effect per deuterium atom be independent of the molecular environment of the isotopic substituent.

The aim of the present work was to furnish further data which would test the correlation of diminishing isotope effect per deuterium atom with increasing acidity (see Figure III). The relatively strong isotopic acid pairs $ClCH_2COOH/ClCD_2COOH$, $PhOCH_2COOH/PhOCD_2COOH$, $PhSCH_2COOH/PhSCD_2COOH$, $PhSOCH_2COOH/PhSOCD_2COOH$, and $PhSO_2CH_2COOH/PhSO_2CD_2COOH$ were chosen for investigation because previous studies have shown the protium acids to be suitable for conductance measurements (42, 45, 46) and these pairs would furnish points in the low $pK_a(H)$ portion of the correlation (see Figure III). A linear least squares treatment of the data for the carboxylic acids examined by Scott and Barnes (38, 44) was employed to determine a tentative relationship between $1/n\ \log_{10}K(H)/K(D)$ and $pK_a(H)$. The resulting equation is

[12] $1/n \log_{10}K(H)/K(D) = (6.56 \times 10^{-3})\ pK_a(H) - (2.66 \times 10^{-2})$

This relationship was employed to predict the isotope effects anticipated for the isotopic acid pairs under consideration in the present investigation (see Table III and Figure IV).

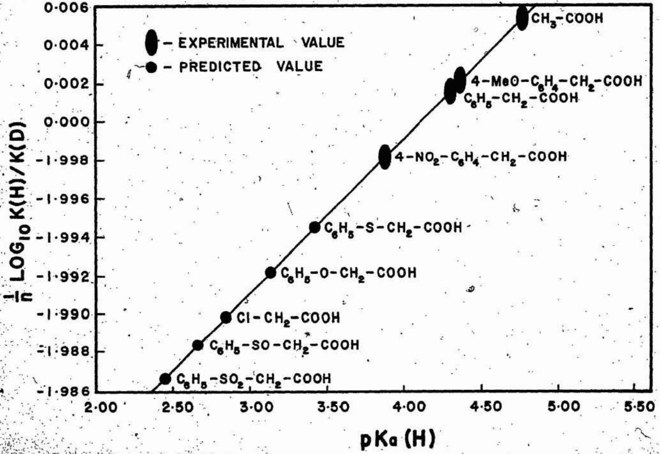
TABLE III

THE PREDICTED ISOTOPE EFFECTS OF SOME CARBOXYLIC ACIDS CALCULATED FROM A LINEAR LEAST SQUARES TREATMENT OF OBSERVED pK_a(H) AND ISOTOPE EFFECT VALUES

PROTIUM ACID	pK_a(H) [TAKEN FROM (41)]	K(H)/K(D) CALCULATED FROM EQUATION [12]	OBSERVED K(H)/K(D) [TAKEN FROM (44)]
CH_3COOH	4.76	1.032	1.035
4-$MeOC_6H_4CH_2COOH$	4.36	1.009	1.005
$C_6H_5CH_2COOH$	4.31	1.007	1.008
4-$NO_2C_6H_4CH_2COOH$	3.88	0.994	0.996
$C_6H_5SCH_2COOH$	3.43	0.981	----
$C_6H_5OCH_2COOH$	3.14	0.972	----
$ClCH_2COOH$	2.85	0.964	----
$C_6H_5SOCH_2COOH$	2.66	0.959	----
$C_6H_5SO_2CH_2COOH$	2.44	0.952	----

FIGURE IV

THE PREDICTED LINEAR LEAST SQUARES CORRELATION OF $\frac{1}{n}$ LOG$_{10}$ K(H)/K(D) vs. pK$_a$(H) FOR SOME SUBSTITUTED ACETIC ACIDS



1-2. THE CALCULATION OF EQUILIBRIUM CONSTANTS FROM CONDUCTANCE MEASUREMENTS

1-2a. AN INTRODUCTION TO THE CONDUCTANCE METHOD

As several excellent accounts of conductance measurements on electrolytic solutions are available (47, 48, 49, 50, 51, 52), this introduction attempts only a brief history of the calculation of equilibrium constants from concentration-equivalent conductance data.

Early conductance theory attempted a distinction between electrolytes, classifying them as either weak or strong. Both classifications evolved from a consideration of the relative conductances of their solutions at comparable concentrations, the strong electrolytes having larger conductances than the weak. Electrolytes which obeyed the Ostwald Dilution Law (53),

$$[13] \qquad \frac{1}{\Lambda} = \frac{1}{\Lambda_o} + \frac{\Lambda \cdot c}{K_c \cdot \Lambda_o^2}$$

were classified as weak electrolytes.* Strong electrolytes appeared to follow the Square Root Law, empirically formulated by

---

*The parameters of equivalent conductance (Λ), limiting equivalent conductance (Λ_o), concentration (c), and equilibrium constant (K_c) in Equations [13] and [14] are defined more formally below.

Kohlrausch (54). This relationship is expressed by

$$[14] \qquad \Lambda = \Lambda_0 - B(c)^{\frac{1}{2}}$$

in which B is the limiting slope. This distinction, however, was not sharply defined and in several instances the classifications tended to overlap.

Modern electrolyte theory classifies electrolytes as either ionogens or ionophores. The former are typified by covalent molecules which rapidly produce thermodynamically stable* ions by a dissociation process in aqueous media, and the latter are electrolytes which exist as ionic lattices in the pure form.

The specific conductance of a solution depends upon the number of ions per cubic centimeter of solution (n_i for the i^{th} kind of ion), their charges ($z_i e$) and their mobilities (u_i), i.e. their velocities per unit of field strength (55). Hence, the specific conductance, L, is described by

$$[15] \qquad L = \sum_i n_i |z_i e| u_i$$

---

*Certain organic reactions which produce thermodynamically unstable carbonium ions have also been described as "ionogenic reactions". The distinction between these and the above is obvious.

In practice the specific conductance is an empirical observable related to the resistance (R) of the solution by

[16] $$L = \kappa/R$$

where κ is the cell constant, the determination of which is described below (see 3-1. CELL CONSTANTS, pp. 83 - 85).

The equivalent conductance (Λ) of the solution is readily obtained from the specific conductance by employing the relationship

[17] $$\Lambda = \frac{L\cdot 10^3}{c}$$

in which the concentration (c) is expressed in moles per 1000 g of water.* For a single neutral solute having a degree of ionization α, the ionic concentration is αc and the total charge per molal unit is αcF, where F is a charge of one Faraday. In conjunction with Equations [15] and [17] this leads to

[18] $$\Lambda = \alpha F(u_+ + u_-)$$

---

*Concentration is sometimes expressed as equivalents per unit volume of solvent, but in the present case of 1:1 weak carboxylic acids dissolved in water, molal concentrations were used in the calculation of equilibrium constants.

where u_+ and u_- are the appropriate ionic mobilities of the species present at any finite concentration.

Hence, the variation of the equivalent conductances of ionophores completely dissociated in solvents of high dielectric constant is primarily a function of the variation of ionic mobilities with concentration. Although the mobility factor remains important for solutions of ionogens, it is superimposed upon the more dominant effect of the degree of ionization.

Kohlrausch's Law (56) implies that ionic mobility at infinite dilution is limited solely by localized interaction with solvent molecules, as no other ions are within a finite distance. Thus, the limiting equivalent conductance at infinite dilution (Λ_0) is the sum of the contributions of each ionic species, independent of the nature of the other species present, such that

[19] $$\Lambda_0 = F(u^o_+ + u^o_-)$$

and this can be also expressed by

[20] $$\Lambda_0 = \lambda^o_+ + \lambda^o_-$$

From Equations [18] and [19]

[21] $$\frac{\Lambda}{\Lambda_0} = \frac{\alpha(u_+ + u_-)}{(u^o_+ + u^o_-)}$$

may be obtained.

From theoretical considerations based on an "ion atmosphere" model, Debye and Hückel (57, 58) proposed an expression for the electrostatic potential at a finite distance from an ion. This expression allows the calculation of the electrostatic free energy* of an ion relative to a neutral particle of the same mass and size in a medium of known dielectric constant (D) and temperature (T). This model provides an expression relating the mean activity coefficient ($f_{\pm}$) to the ionic strength of solution (I), the ionic charges ($z_1 z_2$) and a constant (A) described as the Debye-Hückel limiting slope which is proportional to $(DT)^{2/3}$. The expression for the mean molal ionic activity coefficient ($f_{\pm}$) is given by

$$[22] \qquad -\log f_{\pm} = AI^{\frac{1}{2}}|z_1 z_2|$$

in which I is defined by the equation

$$[23] \qquad I = \tfrac{1}{2} \sum_i z_i^2 c_i$$

where z_i is the charge on the i^{th} ion at concentration c_i. Equation [22] applies to extremely dilute solutions only but it has been empirically modified to accommodate higher concentrations by altering the denominator and adding a term containing c_i.

---

*Both the Born charging (61) and ion atmosphere terms are given by this treatment, but these are easily separated. The latter term only is considered in the present discussion.

[see (59) and (60)].

From a consideration of Equations [13],[21] and [22] an expression for the thermodynamic equilibrium constant of a weak monocarboxylic acid is given by

$$[24] \qquad K_t = \frac{\alpha^2 \cdot c \cdot f_{\pm}^2}{(1-\alpha)f_u}$$

in which f_u is the activity coefficient of the undissociated acid at concentration c. Equations [13], [22] and [24] can be combined to yield

$$[25] \qquad \log K_t = \log K_c - 2Ac_i^{\frac{1}{2}}$$

for a 1:1 electrolyte if $f_u \rightarrow 1$. Hence a relationship between the "classical" equilibrium constant (K_c) described in Equation [13] and the "thermodynamic" equilibrium constant (K_t) in Equation [24] is obtained.

Using the Debye-Hückel model, Onsager (62, 63) has rationalized the Square Root Law and successfully predicted the magnitude of the limiting slope (B) in Equation [14]. His treatment postulates two factors which influence interionic motion in electrolytic solutions subjected to an electric field. The first factor is derived from the opposing motion of an ion and its oppositely charged ion atmosphere, and is known as the electrophoretic effect. The second factor, the relaxation effect, results from the perturbation of the ion atmosphere by an external field. The ion atmosphere is continually "decaying" and "reforming" as the ion moves through the solution. Although the mathematical treatment of these effects is outside the scope of this thesis, the resulting equation which accommodates these effects is relevant and is given by

$$[26] \qquad \Lambda = \Lambda_o - (\beta + \gamma\Lambda_o)(\alpha c)^{\frac{1}{2}}$$

in which β is the electrophoretic constant and γ is the relaxation constant. The numerical values of β and γ used in the present thesis are based on values of the dielectric constant and viscosity of water (64) recommended by Fuoss and Accascina (65). Equation [26] is a limiting formula in which linearity with $(\alpha c)^{\frac{1}{2}}$ is anticipated up to concentrations of ca. 0.001 N, beyond which curvature appears in the plots corresponding to a progressive decrease in the slope with increasing concentration.

More elaborate theoretical equations for conductance have been proposed by Pitts (66) and Fuoss and Onsager (67). The Pitts equation has been satisfactorily applied to the conductance of hydrochloric acid. The equation proposed by Fuoss and Onsager treats the ions as spheres rather than point charges and takes the form of

$$[27] \qquad \Lambda = \Lambda_o - S(c)^{\frac{1}{2}} + E(c \log c) + J(c)$$

in which S is the Onsager coefficient $(\beta + \gamma\Lambda_o)$ of the limiting law {see Equation [26]}, E is a constant defined in the same variables as S, and J is a function defined by ion size.

The Pitts and the Fuoss-Onsager equations will not be discussed further as both are outside the scope of the present work. Indeed, the validity of their application to acid solutions has been questioned in as much as these treatments consider ionic migration as "submarine-like" motion, whereas "proton jumps" might be anticipated for the migration of hydronium ions.

1-2b. INDIRECT METHODS: THE SIMULTANEOUS GENERATION OF K_t and Λ_0

The Classical Plot. - Equation [24] provides an expression for the calculation of thermodynamic equilibrium constants and is stated as

$$[24] \qquad K_t = \frac{\alpha^2 \cdot c \cdot f_\pm^{\,2}}{(1 - \alpha) f_u}$$

The classical approximations proposed by Arrhenius (68) assumed no mobility differential with varying concentration and neglected interionic forces. If constant mobility is assumed then

$$[28] \qquad \alpha = \frac{\Lambda}{\Lambda_o}$$

and if interionic forces are negligible, Equation [24] then becomes

$$[29] \qquad K_c = \frac{\alpha^2 c}{(1 - \alpha)}$$

which is the classical expression proposed by the Arrhenius Dissociation Hypothesis. The Ostwald Dilution Law is obtained by combining Equations [28] and [29]. With rearrangement these yield the expression stated previously as Equation [13], namely

$$[13] \qquad \frac{1}{\Lambda} = \frac{1}{\Lambda_o} + \frac{\Lambda \cdot c}{K_c \cdot \Lambda_o^{\,2}}$$

A plot of $1/\Lambda$ against $\Lambda \cdot c$ generates solutions for Λ_o from the $1/\Lambda$ intercept and K_c from the slope value of $1/K_c \cdot \Lambda_o^{\,2}$.

The Fuoss and Kraus Method. - Fuoss and Kraus (69) have proposed a treatment of conductance data which accommodates both long-range interionic forces and ion mobilities. Employing an abbreviated form of the Fuoss-Onsager Equation {see Equation [27]} for 1:1 ionogen solutions, the proposed relationship can be described by

$$[30] \qquad \alpha = \frac{\Lambda}{\Lambda_o[1 - S(\alpha c)^{1/2}/\Lambda_o]}$$

which is a cubic equation in α, the degree of ionization associated with the ion concentration αc. A corrected value of α can then be obtained from Equation [30] by successive substitution of α into the correction factor represented by the bracketed term in the denominator of the right hand side of Equation [30]. This iterative process rapidly converges to yield a corrected value of α.

The correction factor $1 - S(\alpha c)^{1/2}/\Lambda_o$ in the denominator of the right hand side of Equation [30] may be expressed as

$$[31] \qquad F(z) = 1 - z\{1 - z[1 - z(\text{etc.})^{-1/2}]^{-1/2}\}^{-1/2}$$

where z is $S(\Lambda \cdot c)^{1/2}/\Lambda_o^{3/2}$. Alternatively, the continued fraction can be described in terms of the following cosine relationship

$$[32] \qquad F(z) = {}^4/_3 \cos^2[{}^1/_3 \cos^{-1}(-3^{3/2}z/2)]$$

The degree of ionization, α, then can be expressed in the abbreviated form of

$$[33] \qquad \alpha = \frac{\Lambda}{\Lambda_o F(z)}$$

Combining Equations [24] and [33], and rearranging these to a form analogous to Equation [13] yields

$$[34] \qquad \frac{F(z)}{\Lambda} = \frac{1}{\Lambda_o} + \frac{\Lambda \cdot c \cdot f_{\pm}^2}{K_t \cdot \Lambda_o^2 \cdot F(z)}$$

If f_u is assumed to be unity.

A linear least squares treatment of the $F(z)/\Lambda$ and $\Lambda \cdot c \cdot f_{\pm}^2/F(z)$ variables, which have been calculated from an approximate value of Λ_o, leads to a new value of Λ_o, the least squares intercept. This generated value of Λ_o is used to replace the approximate Λ_o used initially and the correlation is repeated. The iterative process is continued until two successive values of Λ_o are the same within predetermined precision limits. The final value of Λ_o is used to calculate K_t from $1/K_t \cdot \Lambda_o^2$, the final least squares slope.

<u>The Shedlovsky I Method</u>. -- By replacing α with Λ/Λ_o in the abbreviated Fuoss-Onsager Equation {see Equation [30]} and rearranging the terms Shedlovsky (70, 109) proposed the following quadratic expression in $\alpha^{\frac{1}{2}}$,

$$\alpha - \frac{S(c)^{1/2}}{\Lambda_0^{2}}\,\alpha^{1/2} - \frac{\Lambda}{\Lambda_0} = 0 \qquad [35]$$

which can be solved in terms of the z variable {see Equation [31]}. This yields

$$\alpha = \frac{\Lambda}{\Lambda_0}\,\{z/2 + (1 + z^2/4)^{1/2}]^2 = \frac{\Lambda}{\Lambda_0}\cdot S(z) \qquad [36]$$

This S(z) function is sometimes expressed as a power series, such that

$$S(z) = 1 + z + z^2/2 + z^3/8 - z^5/128 + \ldots \qquad [37]$$

and numerical values of S(z) have been tabulated by Daggett (71).

If f_u is assumed to be unity and Equations [24] and [36] are combined and rearranged, the expression becomes

$$\frac{1}{\Lambda\cdot S(z)} = \frac{1}{\Lambda_0} + \frac{\Lambda\cdot c\cdot f_{\pm}^{2}\cdot S(z)}{K_t\cdot\Lambda_0^{2}} \qquad [38]$$

Solution of this equation for K_t is achieved in a manner similar to that of the previous method but the variables in this instance are generated via the S(z) function rather than the F(z) function.

The Ives Method. - Ives (72) has developed a method for the calculation of equilibrium constants from a consideration of a modified form of the Ostwald Dilution Law. The acidity constant is expressed as

$$K_t = \frac{\Lambda^2\cdot c\cdot f_{\pm}^{2}}{\Lambda_x(\Lambda_x - \Lambda)f_u} \qquad [39]$$

in which f_u is assumed to be unity and

[40] $$\alpha = \frac{\Lambda}{\Lambda_x}$$

where Λ_x is the sum of the equivalent conductances of the ions at ionic concentration αc. Λ_x is obtained by applying the abbreviated Fuoss-Onsager Equation {see Equation [30]} to the ionized part of the solute, such that

[41] $$\Lambda_x = \Lambda_o - S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}$$

in which S is the Onsager slope. Then Equation [39] may be rewritten as

[42] $$\Lambda + S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}} = \Lambda_o - \frac{\Lambda^2 \cdot c \cdot f_\pm{}^2}{K_t[\Lambda_o - S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}]}$$

The substitution of $10^{-2A(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}}$ for $f_\pm{}^2$ leads to

[43] $$\Lambda + S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}} = \Lambda_o - \frac{\Lambda^2 \cdot c \cdot 10^{-2A(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}}}{K_t[\Lambda_o - S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}]}$$

where A is the Debye-Hückel coefficient.

By employing an approximate value of Λ_o, a linear least squares plot of the $\Lambda + S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}$ and $\Lambda^2 \cdot c \cdot 10^{-2A(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}} / \Lambda_o - S(\Lambda \cdot c/\Lambda_x)^{\frac{1}{2}}$ variables leads to the generation of a new value of Λ_o obtained from the intercept by extrapolation. This new value is incorporated into the iterative process and the calculation is repeated. The appropriate value of K_t is accepted when the value of Λ_σ shows no improvement within predetermined precision limits.

1-2c. DIRECT METHODS: THE DETERMINATION OF K_t BY DIRECT SUBSTITUTION OF PREDETERMINED Λ_0 VALUES

The Robinson-Stokes Method. - From activity coefficient and mobility considerations both Sherrill and Noyes (73) and MacInnes (74) defined the degree of ionization (α) in dilute solutions of weak electrolytes as

$$[44] \qquad \alpha = \frac{\Lambda}{\Lambda_i}$$

where Λ_i is the equivalent conductance of the hypothetical, fully-ionized electrolyte at ionic concentration c_i.

By employing an estimated value of Λ_i obtained from Λ_0 and a theoretical equation for Λ versus c which assumes the electrolyte is strong (see Salt Method below), MacInnes and Shedlovsky (75) were able to successively approximate the value of α to convergence from empirical equations. This improved value of α was subsequently used to calculate K_t from Equation [24] with f_u taken as unity.

In a more extensive treatment, Robinson and Stokes (76) divided the square root term of the Onsager Limiting Law (see Equation [26]) by the factor $(1 + \kappa a)$* to allow for the finite

---

*κ is the ion atmosphere constant of the Debye-Hückel Theory which can be put into the form $\kappa^2 = B^2\alpha c$ where αc is the ionic strength of the solution and B is a constant at given temperature for a particular medium.

size of the ions (aÅ), which has an estimated mean value of 4Å (77). The resulting equation is

$$[45] \qquad \Lambda_i = \Lambda_o - \frac{(\beta + \gamma\Lambda_o)(\alpha c)^{\frac{1}{2}}}{1 + Ba(\alpha c)^{\frac{1}{2}}}$$

The activity coefficient $f_{\pm}$ at the ionic concentration αc is now given by

$$[46] \qquad f_{\pm} = 10^{-A(\alpha c)^{\frac{1}{2}}/1 + Ba(\alpha c)^{\frac{1}{2}}}$$

The value of Λ_i will not be very sensitive to the value ascribed to mean ion size if the ionization of the weak electrolyte is not extensive (77).

The initial substitution of Λ_o for Λ_i in Equation [44] leads to an approximate value of α. Subsequent introduction of this value into Equation [45] yields an improved value of Λ_i. Iteration of this process leads to rapid convergence of α which is then introduced into Equations [46] and [24] to yield a value of K_t for each concentration-equivalent conductance data point. The resulting K_t values over the entire concentration range are averaged and the associated standard deviation is calculated.

The Shedlovsky II Method. - This direct method was designed by Barnes (44) and Scott et al. (38, 78) as a simple modification of the Shedlovsky I Method described previously. A predetermined value of Λ_o is introduced into the Shedlovsky Equation (see

Equation [38]} and, as no iteration is necessary, a value of K_t is generated for each concentration-equivalent conductance data point. As in the Robinson-Stokes Method these values of K_t are averaged, with the resulting standard deviation being ascribed to the error associated with their measurement and calculation.

1-2d. THE DETERMINATION OF LIMITING EQUIVALENT CONDUCTANCES (Λ_0) FOR WEAK CARBOXYLIC ACIDS (HB)

The Salt Method. - Dissociation is considered complete and association negligible in solutions of sodium and potassium salts of weak carboxylic acids. A value of Λ_0 for a weak carboxylic acid can be obtained by an extrapolation procedure based on a modification of Equation [20], namely

$$\Lambda_0(\mathrm{HB}) = \Lambda_0(\mathrm{H}^+) + \Lambda_0(\mathrm{B}^-) \qquad [47]$$

The calculation of Λ_0(HB) can be achieved if the appropriate limiting transport numbers are available in existing tables [c.f. (47) and (48)].

Alternatively, Λ_0(NaB) can be obtained by extrapolation of empirical conductance values at various concentrations of the sodium salt of the weak acid. This value can then be combined with tabular values of the limiting equivalent conductances of the Na^+ and H^+ ions, such that

$$\Lambda_0(\mathrm{HB}) = \Lambda_0(\mathrm{H}^+) - \Lambda_0(\mathrm{Na}^+) + \Lambda_0(\mathrm{NaB}) \qquad [48]$$

This method has universal application for the determination of Λ_0(HB), with the exception noted by Ives (42) that the anion, B^-, have sufficient thermodynamic stability to maintain its molecular integrity over the period of measurement.

Iterative Methods. - The Indirect Methods discussed above may be used to determine values of Λ_o(HB) by employing the appropriate repetitive processes. Table IV compares values of Λ_o(HB) for various weak carboxylic acids determined by the Indirect Methods with those determined by the previously described Salt Method.

The Shedlovsky IV Method. - A statistical modification of the foregoing Shedlovsky I iterative technique was devised by Barnes (44) and Scott et al. (79) to determine the "best" value of Λ_o(HB) based solely on a least squares treatment of the concentration-equivalent conductance data. The thermodynamic equilibrium constant, K_t, and the standard deviation associated with this parameter, δ, are calculated for a series of arbitrarily chosen Λ_o(HB) values whose range falls on either side of the "true" Λ_o(HB) value. This calculation not only develops a functional relationship between the averaged K_t values and Λ_o(HB), but more significantly, the standard deviation (δ) of the averaged K_t values may for any given value of Λ_o(HB) be expressed as a function of Λ_o(HB). The value of Λ_o(HB) which occurs at the minimum of the curve resulting from a plot of δ versus Λ_o(HB) is accepted as the "best" value of Λ_o(HB) on a least squares basis.

Sample plots of the δ and K_t (average) parameters versus Λ_o(HB) are shown respectively by Figures V and VI using data derived from Table V. Values of Λ_o(HB) calculated by this method are compared with those calculated via the Salt Method and the Indirect Methods in Table IV.

TABLE IV

A COMPARISON OF SOME WEAK CARBOXYLIC ACID LIMITING EQUIVALENT CONDUCTANCE VALUES (Λ_0)* CALCULATED BY VARIOUS METHODS

METHOD OF CALCULATION	Λ_0 OF $R\text{-}CH_2COOH$ (REFERENCE)**			
	R = H	R = C_6H_5	R = 4-MeO-C_6H_4	R = 4-NO_2-C_6H_4
SALT METHOD	389.6 (75)	379.6 (80)	377.3 (81)	376.6 (80)
	390.7 (82)	383.7 (83)	383.7 (83)	383.0 (83)
CLASSICAL METHOD	359.9	367.0	370.0	376.5
SHEDLOVSKY I METHOD	389.6	380.5	380.2	378.9
IVES METHOD	--	381.7	379.5	378.9
SHEDLOVSKY IV METHOD	391.4	381.7	379.8	378.5

---

*Λ_0 values are on the molality scale and have units of g $cm^{-1}\Omega^{-1}$ $equiv^{-1}$.

**All unreferenced values are taken from (44).

TABLE V

SHEDLOVSKY IV RESULTS FOR THE CONCENTRATION-EQUIVALENT CONDUCTANCE DATA OF IODOACETIC ACID AT 25°C [TAKEN FROM (44)]*

Λ_0	AVERAGED $K_t \times 10^4$	AVERAGED DEVIATION (δ) $\times 10^6$
375.0	7.866	5.42
376.0	7.777	4.96
377.0	7.690	4.51
378.0	7.606	4.09
379.0	7.522	3.68
380.0	7.441	3.29
381.0	7.361	2.91
382.0	7.282	2.55
383.0	7.206	2.20
385.0	7.056	1.54
386.0	6.985	1.24
387.0	6.912	0.94
388.0	6.842	0.65
389.0	6.773	0.38
390.0	6.705	0.12
391.0	6.640	0.13
392.0	6.574	0.37
393.0	6.510	0.61
394.0	6.447	0.84
395.0	6.385	1.05
400.0	6.090	2.02

---

*The concentration-equivalent conductance data were taken from (42). K_t and δ values are not quoted for Λ_0 = 384.0 in the Table as these were omitted in the original [see (44)].

FIGURE V

A PLOT OF THE DEVIATIONS (δ) OF AVERAGED K_T VALUES vs. Λ_0 FROM A SHEDLOVSKY IV TREATMENT OF IODOACETIC ACID DATA [TAKEN FROM (44)]

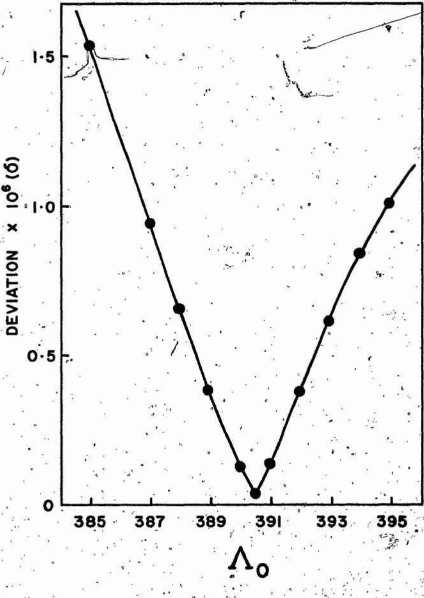
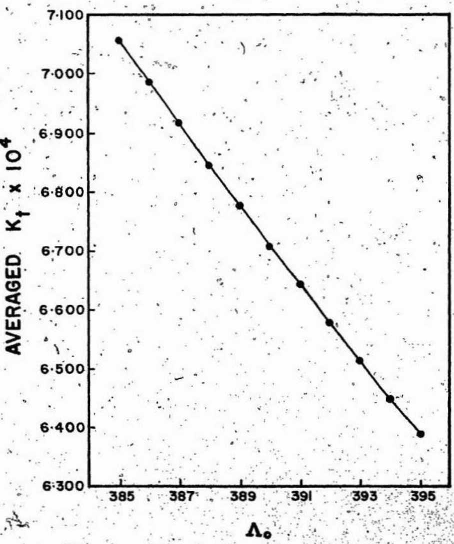


FIGURE VI

A PLOT OF AVERAGED K_t VALUES vs. Λ_0 FROM A SHEDLOVSKY IV TREATMENT OF IODOACETIC ACID DATA [TAKEN FROM (44)]



1-3. THE CALCULATION OF ISOTOPE EFFECTS

Previous Calculations. - Isotope effects can be directly determined through the use of Equation [48] [c.f. (12)],

$$[48] \qquad \text{isotope effect} = \frac{K_t^{\circ}(H)}{K_t^{\circ}(D)}$$

in which the thermodynamic equilibrium constants of the isotopically substituted acids are obtained from the aforementioned Direct and Indirect Methods of calculation [c.f. (36, 43)], but less rigorous methods of comparison have been employed (32).

The Shedlovsky III Method. - The Shedlovsky Equation {see Equation [38]} has been modified in a novel way by Barnes (44) and Scott et al. (78) to directly calculate isotope effects. In this method the intermediate steps of equilibrium constant calculation are unnecessary. In Equation [38],

$$[38] \qquad \frac{1}{\Lambda \cdot S(z)} = \frac{1}{\Lambda_o} + \frac{\Lambda \cdot c \cdot f_{\pm}^2 \cdot S(z)}{K_t \cdot \Lambda_o^2}$$

the correction terms $1/S(z)$ and $f_{\pm}^2 \cdot S(z)$ for the variables $1/\Lambda$ and $\Lambda \cdot c$ require a knowledge of Λ_o for their calculation. If a value of $\Lambda_o(H)$* is available and assuming that $\Lambda_o(H) = \Lambda_o(D)$**,

---

*The bracketed or subscripted H and D notations refer to the respective protium and deuterium substituted acids.

**The validity and implications of this assumption are discussed in some detail below.

both correction terms for the hydrogen and deuterium substituted acids may be calculated. The Shedlovsky variables $1/\Lambda\cdot S(z)$ and $\Lambda\cdot c\cdot f_{\pm}^{2}\cdot S(z)$ can then be determined for both isotopic acids to give

$$[49] \qquad \frac{1}{\Lambda(H)\cdot S(z)_H} = \frac{1}{\Lambda_o(H)} + \frac{\Lambda(H)\cdot c(H)\cdot S(z)_H\cdot f_{\pm}^{2}(H)}{K_t(H)\cdot\Lambda_o^{2}(H)}$$

and

$$[50] \qquad \frac{1}{\Lambda(D)\cdot S(z)_D} = \frac{1}{\Lambda_o(D)} + \frac{\Lambda(D)\cdot c(D)\cdot S(z)_D\cdot f_{\pm}^{2}(D)}{K_t(D)\cdot\Lambda_o^{2}(D)}$$

The slopes of the correlations, $m_t(H)$ and $m_t(D)$, are given by

$$[51] \qquad m_t(H) = 1/K_t(H)\Lambda_o^{2}(H)$$

and

$$[52] \qquad m_t(D) = 1/K_t(D)\Lambda_o^{2}(D)$$

Hence, the isotope effect is given by

$$[53] \qquad \frac{K_t(H)}{K_t(D)} = \frac{m_t(D)}{m_t(H)}$$

If a value of Λ_o is unavailable, the utility of this method remains undiminished, since the technique of variation of Λ_o over a range of values falling on either side of the true value of Λ_o (described in the foregoing discussion of the Shedlovsky

IV Method) can be incorporated into this treatment.

A further refinement of this method results from a consideration of the isotope effect calculation on a "cell by cell" basis. If the value of Λ is replaced by $\kappa \cdot 10^3/R$ in Equations [49] and [50], then the resulting slope values for a single cell (cell constant κ_1) can be algebraically reduced to

$$[54] \qquad m_t^{\,1}(H) = (\kappa_1 \times 10^3)^2/K_t(H) \cdot \Lambda_o^2(H)$$

and

$$[55] \qquad m_t^{\,1}(D) = (\kappa_1 \times 10^3)^2/K_t(D) \cdot \Lambda_o^2(D)$$

Hence, the isotope effect value for a single cell will be

$$[56] \qquad \frac{K_t(H)}{K_t(D)} = \frac{m_t^{\,1}(D)}{m_t^{\,1}(H)}$$

This implies that although values of κ_1 and Λ_o are required to calculate the $1/S(z)$ and $f_\pm^2 \cdot S(z)$ terms (which are small), the influence of cell constant values and their associated errors may be largely excluded from isotope effects calculated on a single cell basis.

Barnes (44) and Scott <u>et al</u>. (78) have shown that the precision of the Shedlovsky III Method is higher than the precision associated with methods which compare thermodynamic equilibrium constants to determine isotope effects. They attribute the increase in precision to the insensitivity of the Shedlovsky slopes to Λ_0 in the immediate range of the true value of Λ_0 and the elimination of cell constant values as major contributors in the isotope effect calculation.

Tables VI and VII illustrate the slopes of an isotopically substituted acid pair [$m_t(H)$ and $m_t(D)$, respectively] as functions of Λ_0, while Table VIII shows the resultant isotope effects and demonstrates the reliability of this method. A comparison of the results of this method is made with those of other methods of computing isotope effects in Table IX.

TABLE VI

SLOPE $[m_t(H)]$ vs. Λ_o FROM A SHEDLOVSKY III TREATMENT OF PHENYLACETIC ACID DATA [TAKEN FROM (44)]

Λ_o	SLOPE $[m_t(H)]$ x 10				
	CELL I	CELL II	CELL III	CELL IV	CELL V
374	1.4185 ± 0.0015	1.4153 ± 0.0013	1.4174 ± 0.0015	1.4173 ± 0.0015	1.4133 ± 0.0016
376	1.4184 ± 0.0014	1.4153 ± 0.0013	1.4173 ± 0.0015	1.4173 ± 0.0015	1.4132 ± 0.0016
378	1.4183 ± 0.0014	1.4152 ± 0.0013	1.4173 ± 0.0015	1.4172 ± 0.0015	1.4131 ± 0.0016
380	1.4182 ± 0.0014	1.4151 ± 0.0013	1.4172 ± 0.0015	1.4171 ± 0.0015	1.4130 ± 0.0016
382	1.4181 ± 0.0014	1.4150 ± 0.0013	1.4171 ± 0.0015	1.4170 ± 0.0015	1.4130 ± 0.0016
384	1.4180 ± 0.0014	1.4149 ± 0.0013	1.4170 ± 0.0015	1.4169 ± 0.0015	1.4129 ± 0.0016
386	1.4179 ± 0.0014	1.4148 ± 0.0013	1.4169 ± 0.0015	1.4168 ± 0.0015	1.4128 ± 0.0016
388	1.4179 ± 0.0014	1.4147 ± 0.0013	1.4168 ± 0.0015	1.4167 ± 0.0015	1.4127 ± 0.0016
390	1.4178 ± 0.0014	1.4147 ± 0.0013	1.4167 ± 0.0015	1.4167 ± 0.0015	1.4126 ± 0.0016

TABLE VII

SLOPE $[m_t(D)]$ vs. Λ_o FROM A SHEDLOVSKY III TREATMENT OF PHENYLACETIC-2,2-d_2 ACID DATA [TAKEN FROM (44)]

Λ_o	SLOPE $[m_t(D)]$ x 10				
	CELL I	CELL II	CELL III	CELL IV	CELL V
374	1.4277 ± 0.0014	1.4263 ± 0.0014	1.4271 ± 0.0019	1.4275 ± 0.0015	1.4255 ± 0.0014
376	1.4276 ± 0.0014	1.4264 ± 0.0014	1.4270 ± 0.0019	1.4274 ± 0.0015	1.4254 ± 0.0014
378	1.4275 ± 0.0014	1.4261 ± 0.0014	1.4269 ± 0.0019	1.4274 ± 0.0015	1.4253 ± 0.0014
380	1.4275 ± 0.0014	1.4260 ± 0.0014	1.4268 ± 0.0019	1.4273 ± 0.0015	1.4252 ± 0.0014
382	1.4274 ± 0.0014	1.4259 ± 0.0014	1.4267 ± 0.0019	1.4272 ± 0.0015	1.4251 ± 0.0014
384	1.4273 ± 0.0014	1.4259 ± 0.0014	1.4266 ± 0.0019	1.4271 ± 0.0015	1.4251 ± 0.0014
386	1.4272 ± 0.0014	1.4258 ± 0.0014	1.4265 ± 0.0019	1.4270 ± 0.0015	1.4250 ± 0.0014
388	1.4271 ± 0.0014	1.4257 ± 0.0014	1.4265 ± 0.0019	1.4269 ± 0.0015	1.4249 ± 0.0014
390	1.4270 ± 0.0014	1.4256 ± 0.0014	1.4264 ± 0.0019	1.4268 ± 0.0015	1.4248 ± 0.0014

TABLE VIII

ISOTOPE EFFECTS CALCULATED VIA THE SHEDLOVSKY III TREATMENT OF PHENYLACETIC ACID AND PHENYLACETIC-2,2-d_2 ACID DATA [TAKEN FROM (44)]

Λ_0	ISOTOPE EFFECTS $[m_t(D)/m_t(H)]$				
	CELL I	CELL II	CELL III	CELL IV	CELL V
374	1.0065 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
376	1.0065 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
378	1.0065 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
380	1.0066 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
382	1.0066 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
384	1.0066 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
386	1.0066 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014
388	1.0065 ± 0.0014	1.0078 ± 0.0013	1.0067 ± 0.0017	1.0071 ± 0.0015	1.0084 ± 0.0014
390	1.0065 ± 0.0014	1.0078 ± 0.0013	1.0066 ± 0.0017	1.0071 ± 0.0015	1.0083 ± 0.0014

TABLE IX

ISOTOPE EFFECTS CALCULATED FROM VARIOUS TREATMENTS OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA [TAKEN FROM (44)]

ACID, $R-C_6H_4-CH_2COOH$	ISOTOPE EFFECTS CLASSICAL	ROBINSON & STOKES	SHEDLOVSKY II	SHEDLOVSKY III	IVES
R = H	1.0072 ±0.0004	1.0035 ±0.005	1.0034 ±0.005	1.0082 ±0.0015	1.018 ±0.005
R = 4-NO_2	0.9973 ±0.002	1.0005 ±0.005	1.004 ±0.005	0.9975 ±0.0017	0.9936 ±0.005
R = 4-MeO	1.0045 ±0.0007	1.0077 ±0.002	1.0076 ±0.0023	1.0041 ±0.0019	0.9975 ±0.005

CHAPTER 2

EXPERIMENTAL

2

2-1. GENERAL INSTRUMENTATION

Nuclear magnetic resonance (n.m.r.) spectra were recorded on Varian A-60 and HA-100 instruments at 60 MHz and 100 MHz respectively, with probe temperatures ca. 40°C unless otherwise specified. Chemical shifts are reported on the τ scale, i.e., relative to the internal standard signal of tetramethylsilane. Infrared (i.r.) spectra were recorded on Perkin-Elmer 237B or 225 spectrometers. Each i.r. spectrum was calibrated against a portion of a polystyrene spectrum. Melting points (m.p.) were determined on a Fisher-Johns melting point apparatus. Melting points and boiling points (b.p.) are uncorrected. Chemical microanalyses were carried out by the Alfred Bernhardt Mikroanalytisches Laboratorium, West Germany.

2-2. CONDUCTANCE INSTRUMENTATION

Conductivity Bridges. - The resistances of the potassium chloride and acid solutions were measured by a General Radio Impedance Comparator (G.R.I.C.) bridge. In the case of solutions of phenoxyacetic and phenoxyacetic-2,2-d_2 acids, resistance measurements from the G.R.I.C. bridge were compared with those obtained at various frequencies from a Jones-Josephs type bridge (84) manufactured by Tinsley Company. A description of the Tinsley and G.R.I.C. bridges is presented in Appendix I. The Tinsley bridge auxiliary equipment and the constant temperature baths were constructed prior to this study (44) by the Technical Services Department, Memorial University of Newfoundland, and their assembly is also described in Appendix I.

Thermometry. - A Tinsley Platinum Resistance Thermometer (type 5187 H) calibrated by the National Physical Laboratory (Teddington, England), in conjunction with a Mueller Temperature Bridge (type 4772), was employed to adjust the constant temperature bath to 25.000 ± 0.002°C. The balance point of the Mueller Temperature Bridge was determined by a Leeds and Northrup DC Null Detector (9834).

A Honeywell recorder was used to monitor the bath temperature over long periods. The recorder served as a detector in a Wheatstone Bridge circuit, with a Fenwal Thermistor serving as one arm of the bridge. Five resistors (62.5Ω to 10kΩ) were used to control the sensitivity of the recorder. The 625Ω resistor gave a sensitivity of 0.02°C for 10 small divisions on the recorder chart paper.

During the initial study of one of the acids, namely phenylacetic acid, the value of the equilibrium constant determined led to the conclusion that the bath temperature was adjusted slightly above 25.000°C. A new Tinsley Platinum Resistance Thermometer indicated that the bath temperature was 25.051 ± 0.002°, and the temperature was readjusted to 25.000 ± 0.002°C.

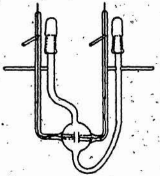
The former Platinum Resistance Thermometer was recalibrated at the National Research Council of Canada Laboratories (Ottawa). The temperature of the bath was measured with the recalibrated thermometer and found to be 25.000 ± 0.002°C; hence the two Platinum Resistance Thermometers were in excellent agreement.

After monitoring the bath for three months with the Honeywell recorder, one of three Beckman thermometers, calibrated against the Platinum Resistance Thermometers, was used as a continual check on the bath temperature instead of the recorder. The Beckman thermometer calibration was periodically checked against the Platinum Resistance Thermometers throughout the remainder of the study.

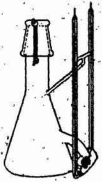
Conductivity cells. - The conductivity cells were constructed with shiny platinum electrodes in three different designs (see Figure VII). The cells were designed to give cell constants

FIGURE VII

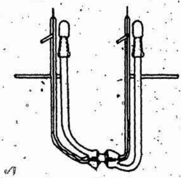
DIAGRAMS OF THREE TYPES OF CELLS



(a) Shedlovsky (85) cell design



(b) Kraus (86) cell design



(c) Robertson (87) cell design

ranging from 0.08 to 0.37 cm^{-1}. The bulk of the measurements were accomplished using cells of the Shedlovsky type (85), like those employed by Scott and Barnes (38, 44) [see Figure VII(a)]. Measurements in other types of cells [see Figures VII(b) and VII(c)] were made in conjunction with these for purposes of comparison.

Cleaning procedure. - The cells were washed initially with warm ethanol (95%) and rinsed with "conductivity water" (see preparative description below, p. 76). They were filled with aqueous hydrofluoric acid (*ca.* 3%) for 5 min and rinsed with conductivity water. They were subsequently treated for 3 days with concentrated nitric acid *ca.* 100°C. The nitric acid treatment was repeated four times, and the cells were then filled with hot (*ca.* 100°C) conductivity water. The cells were rinsed and refilled daily with fresh conductivity water for 10 days while the temperature was kept near the boiling point.

Subsequent to this treatment the resistance of the conductivity water in the cells remained constant to 0.01% over a period of 12 h, indicating that the removal of surface ions was essentially complete. The cells were then conditioned with three solutions of potassium chloride (*ca.* 1 x 10^{-3}M) for 72 h (total), and subsequently treated twice with a solution of purified phenylacetic acid (*ca.* 5 x 10^{-3}M) for 48 h (total). Following the second treatment with the latter, the resistance of a freshly prepared solution of purified phenylacetic acid (*ca.* 5 x 10^{-3}M) remained constant for a 24 h period.

The cleaning procedure, except the hydrofluoric acid treatment, was applied to all glassware used in the preparation of solutions for conductivity measurements.

2-3. MATERIALS

Potassium chloride. - (i) A sample (Fisher Scientific; A.R. Grade) of potassium chloride (100 g; 1.34 mole) was precipitated from a saturated conductivity water solution by the addition of purified ethanol (95%) and collected. This procedure was repeated four times. The salt was then filtered, washed several times with purified ethanol (95%) and dried in vacuo at 110°C for two days. The salt was then powdered in a clean agate mortar and dried an additional three days in vacuo at 110°C. The purified potassium chloride was stored over silica gel in a vacuum desiccator.

(ii) A second sample of potassium chloride (25 g; 0.335 mole) was precipitated from a saturated conductivity water solution by the addition of concentrated hydrochloric acid. This procedure was repeated twice, and the salt was then treated in the manner described in (i) above.

(iii) A third sample (Aldrich; optically-pure) of potassium chloride (25 g; 0.335 mole) was treated by the procedure outlined in (i) above.

Phenylacetic acid. - A sample (British-Drug Houses; Reagent Grade) of phenylacetic acid (50 g; 0.367 mole) was dissolved in an aqueous solution of sodium hydroxide (2M) prepared from conductivity water and solid sodium hydroxide. The solution was doubly filtered and the acid was precipitated from the cold solution by the dropwise addition of a slight excess of hydrochloric acid (2M). The acid was collected and air-dried, and the procedure was repeated with double filtration after dissolution. The acid was collected and recrystallized from purified (88) benzene-petroleum ether (b.p. 30-60°C). After subsequent collection and air-drying, the sample was sublimed (ca. 60°C; <1 mm Hg). After the recrystallization and sublimation procedures had been repeated four times, the acid was subjected to three successive sublimations. The material was crushed and dried in vacuo over silica gel for 48 h.

(ii) A sample of the latter (5 g; 0.0367 mole) was zone-refined (21 passes over 7 days), sublimed and dried in a manner similar to the above, m.p. 76.2 - 76.6°C [lit. m.p. 76.7°C (89)].

Phenoxyacetic acid. - A sample (Eastman Organic Chemicals; 99+%) of phenoxyacetic acid (100 g; 0.657 mole) dissolved in aqueous sodium hydroxide (500 ml; 2M) was washed with three portions (200 ml total) of diethyl ether. The aqueous layer was acidified with a slight excess of hydrochloric acid (520 ml; 2M), and the volume of the solution was reduced (ca. 200 ml). The solution was cooled to ca. 0°C and the resulting precipitate was collected. Seven alternate recrystallizations (conductivity water) and sublimations (96°C; <1 mm Hg) were then carried out on the material, and subsequent to an additional sublimation, the material was crushed and dried in vacuo over silica gel for 72 h, m.p. 99.0 - 99.5°C [lit. m.p. 99 - 100°C (90)].

Phenoxyacetic-2,2-d_2 acid. - Phenoxyacetic acid (200 g; 1.31 mole), dissolved in deuterium oxide (99.75%; 50 ml) and triethylamine (150 g; 1.48 mole), was sealed in a glass tube and heated to 125°C for 24 h. The water and excess triethylamine were removed by distillation under reduced pressure and new quantities of deuterium oxide (50 ml) and triethylamine (10 g; 0.099 mole) were added to the residue. The mixture was again heated to 125°C for 24 h. This procedure for isotopic exchange was repeated four times, and the final residue was purified in a manner similar to that for phenoxyacetic acid, m.p. 99.1 - 99.5°C. Several n.m.r. spectra ($CDCl_3$) indicated that deuteration at the methylene position was not less than 98.2%. The percent deuteration was computed by comparison of the reduced methylene signal with that of the methyl group of acetonitrile (1%), introduced as a standard.

Chloroacetic acid. - Purified (91) red phosphorus (6 g; 0.048 mole) and glacial acetic acid (150 g; 2.50 mole) were mixed in a round-bottomed flask, weighed and heated to 100°C. Chlorine gas was bubbled through the reaction mixture for a period of 3 h and the temperature was maintained at 105 - 110°C. Upon cooling, the flask and contents were weighed, and the procedure repeated until the weight of the reaction mixture had increased by 80 g (92). The reaction mixture was distilled, and the fraction collected over the b.p. range of 150 - 200°C was redistilled twice, the final distillate being colourless chloroacetic acid (107 g; 42% yield), b.p. 188 - 190°C and m.p. 56.1 - 58.5°C [lit. b.p. and m.p. are 189.4°C and 63.0°, respectively (93)].

N.m.r. spectra (CD_3COCD_3) were recorded as a measure of the purity of the chloroacetic acid. A comparison of the absorptions at 4.0 τ (CH of dichloroacetic acid) and 5.9 τ (CH_2 of chloroacetic acid) indicated the distillate was 93.5% pure.

The crude sample of chloroacetic acid was recrystallized three times ($CHCl_3$), m.p. 59.2 - 59.6°C, and found to be 96% pure by n.m.r. analysis. The acid (50 g; 0.529 mole) was melted under reduced pressure (ca. 0.1 mm Hg) in a sublimation apparatus and the temperature was slowly raised to 62.5°C. Temperature and pressure were maintained for 48 h, after which the sublimed material was recrystallized ($CHCl_3$), m.p. 60.0 - 60.5°C. This process was repeated but n.m.r. measurements indicated that it did not increase the purity of the chloroacetic acid beyond 98.2%.

Sublimed chloroacetic acid (40 g; 0.423 mole), recrystallized from chloroform, was heated to 60.5°C; nitrogen was continuously bubbled into the molten material and the temperature was raised 0.5°C at hourly intervals. After 5 h the acid was cooled and recrystallized ($CHCl_3$), m.p. 60.9 - 62.3°C. N.m.r. measurements indicated that this process failed to raise the purity of the acid beyond 99.6%. This process was repeated until crystals began to form at 62.5°C. The temperature was then raised to 63.5°C and the liquid was allowed to cool slowly. When two-thirds of the material solidified, the remaining liquid portion was immediately decanted from the newly formed crystals.

This fractional crystallization procedure was repeated twice and the remaining needles (4 g; 0.042 mole) were washed with cold chloroform and dried in vacuo, m.p. 63.0 - 63.2°C. N.m.r. measurements could not detect the presence of dichloroacetic acid in a sample of the required acid. This material was then zone-refined (21 passes over 7 days), recrystallized from spectroscopically-pure chloroform and sublimed (60°C; <1 mm Hg). The acid was crushed and dried in vacuo over silica gel for 72 h.

Chloroacetic-2,2-d_2 acid. - Chloroacetic-2,2-d_2 acid was prepared and purified by following the procedure outlined above for chloroacetic acid, except that glacial acetic-2,2,2-d_3 acid was substituted for the protium acid. An n.m.r. spectrum (CD_3-$COCD_3$) of this material (m.p. 62.9 - 63.3°C) indicated not less than 98.7% deuterium at the methylene position.

Phenylthioglycollic acid. - A sample (Aldrich; 99+%) of phenylthioglycollic acid (100 g; 0.595 mole) dissolved in aqueous sodium hydroxide (500 ml; 2M) was washed with diethyl ether (200 ml total), and the solution was acidified with a slight excess of hydrochloric acid (520 ml; 2M). A white precipitate of the acid was collected subsequent to reduction of the solution volume (ca. 200 ml) and cooling to 0°C. The air-dried material was recrystallized (conductivity water) and sublimed (61°C; <1 mm Hg). The material was subjected to five alternate recrystallizations (conductivity water) and sublimations followed by two additional sublimations. The acid was crushed and dried in vacuo over silica gel for 72 h, m.p. 62.8 - 63.5°C [lit. m.p. 62.5 - 63.5°C (46)].

Phenylthioglycollic-2,2-d_2 acid. - Phenylthioglycollic acid (150 g; 0.892 mole) was added to deuterium oxide (99.75%; 50 ml) and triethylamine (125 g; 1.235 mole), and the resulting solution was heated in a sealed glass tube at 125°C for 24 h. The water and excess triethylamine were removed by distillation under reduced pressure, and a second exchange was carried out in a manner similar to the first using fresh deuterium oxide (50 ml) and triethylamine (20 g; 0.198 mole) with the partially exchanged acid. Three further exchanges followed by recovery of the acid yielded a material which, on purification by recrystallization and sublimation (see procedure for protium-acid), had a m.p. 62.5 - 63.5°C. An n.m.r. spectrum (CD_3COCD_3) of the acid indicated not less than 97.8% deuteration at the methylene position.

Phenylsulfinylacetic acid. - Purified phenylthioglycollic acid (33.8 g; 0.206 mole) was dissolved in absolute ethanol at 0 - 5°C and 30% hydrogen peroxide (24 g; ca. 0.22 mole) was added dropwise to the solution. After standing for 2 h, the excess hydrogen peroxide, ethanol and water were removed by distillation under reduced pressure. The oily residue was taken up in hot benzene-ethyl acetate (3:1 by volume) and on cooling yielded white prisms of phenylsulfinylacetic acid (29.8 g; 81% yield), m.p. 118.5 - 119.2°C [lit. m.p. 118 - 119.5°C (94)] [Found: C, 52.24; H, 4.37; O, 26.01; S, 17.52. $C_8H_8O_3S$ requires C, 52.16; H, 4.39; O, 26.06; S, 17.40%].

The acid had three absorptions in its n.m.r. spectrum (CD_3COCD_3), a singlet at 6.1 τ (CH_2), a broad singlet extending from 3.5 τ to 3.4 τ (OH) and a multiplet from 3.0 τ to 2.5 τ (protons attached to the aromatic ring). The intensities of the signals at 6.1 τ and 2.5 - 2.1 τ were in the ratio of 2 to 5. An i.r. spectrum ($CHCl_3$) of the acid showed strong absorptions for the SO stretching vibration at 1028 cm^{-1}, and the carbonyl stretching vibration at 1730 cm^{-1}. The acid was recrystallized six times from purified (95) ethyl acetate and dried in vacuo over silica gel for 72 h.

Phenylsulfinylacetic-2,2-d_2 acid. - Purified phenylsulfinylacetic acid (36.8 g; 0.200 mole) was dissolved in deuterium oxide

(99.75%; 100 ml) and stirred for 10 h at 50°C. The deuterium oxide was removed by lyophilization and a fresh portion (100 ml) was added. The exchange process was repeated six times and the residue was taken up in boiling anhydrous benzene-ethyl acetate (3:1). Phenylsulfinylacetic-2,2-d_2 acid (27.6 g; 75% yield) crystallized from the cold solution as white prisms, m.p. 114.5 - 115.0°C. This material was recrystallized six times from purified (95) ethyl acetate and dried in vacuo over silica gel for 72 h.

Phenylsulfinylacetic-2,2-d_2 acid had two absorptions in its n.m.r. spectrum (CD_3COCD_3), a broad singlet at 3.5 - 3.4 τ (OH) and a multiplet from 3.0 τ to 2.5 τ (protons attached to the aromatic ring). This assignment was partially confirmed by a marked increase in the intensity of the former absorption after a small addition of trifluoroacetic acid. Although the amplitude of the spectrum was increased, the presence of protons in the methylene position could not be detected. An i.r. spectrum ($CHCl_3$) of the acid was similar to that of phenylsulfinylacetic acid with the exception of a broad shoulder in the region of 2350 - 2200 cm^{-1}.

Phenylsulfonylacetic acid. - Purified phenylthioglycollic acid (33.8 g; 0.206 mole) was suspended in water (150 ml), and sodium carbonate (10.6 g; 0.110 mole) was slowly added to the suspension with stirring. After the evolution of carbon dioxide, potassium permanganate (31.8 g; ca. 0.202 mole) dissolved in water

(800 ml) at 0°C was added dropwise, and the solution was stirred for 18 h. The manganese dioxide precipitate was removed by filtration through "Celite", and the clear aqueous filtrate was acidified with hydrochloric acid (6M). The solution was then extracted four times with diethyl ether (400 ml total) and the combined ethereal extracts were dried over anhydrous magnesium sulfate. The solvent was removed by distillation under reduced pressure, and the syrupy residue was taken up in a minimum of hot benzene. On cooling, white prisms of phenylsulfonylacetic acid (27.5 g; 68% yield) crystallized from the mother liquor. This material was alternately recrystallized from purified (88), anhydrous benzene and sublimed (102°C; <1 mm Hg) six times, followed by an additional sublimation, m.p. 113.8 - 114.2°C [lit. m.p. 113.5 - 114°C (46)] [Found: C, 48.16; H, 4.04; O, 31.86; S, 15.85. $C_8H_8O_4S$ requires C, 47.99; H, 4.04; O, 31.96; S, 16.01%]. The acid was crushed and dried *in vacuo* over silica gel for 72 h.

An i.r. spectrum (Nujol mull) of phenylsulfonylacetic acid showed strong absorptions at 1305 cm^{-1} and 1170 cm^{-1} due to the respective asymmetric and symmetric stretching vibrations of the SO_2 group, and at 1715 cm^{-1}, the carbonyl stretching frequency. The acid had three absorptions in its n.m.r. spectrum (CD_3COCD_3), a singlet at 5.7 τ (CH_2), a broad singlet extending from 5.0 τ to 4.6 τ (OH) and a multiplet at 2.4 - 1.9 τ (protons attached to the aromatic ring). The intensities of the absorptions at 5.7 τ

and 2.4 - 1.9 τ were in the ratio of 2 to 5.

Phenylsulfonylacetic-2,2-d_2 acid. - Purified phenylsulfonylacetic acid (40.0 g; 0.200 mole) was treated in a manner similar to the exchange process outlined above for phenylsulfinylacetic-2,2-d_2 acid. The resulting phenylsulfonylacetic-2,2-d_2 acid was alternately recrystallized and sublimed in the manner described for its corresponding protium acid. The white prisms (31.5 g; 78% yield) were crushed and dried in vacuo over silica gel for 72 h, m.p. 113.6 - 114.0°C.

An i.r. spectrum (Nujol mull) of the acid was similar to that of the protium acid except for the presence of a broad shoulder in the 2375 - 2200 cm^{-1} region. The compound showed two absorptions in its n.m.r. spectrum (CD_3COCD_3), a broad singlet from 5.0 τ to 4.6 τ (OH) and a multiplet from 2.4 τ to 1.9 τ (protons attached to the aromatic ring). The presence of protons at the methylene position (5.7 τ) was detected, but the signal intensity was inseparable from base line noise.

Conductivity water. - Tap water was fed through a Fulflo commercial water filter and then distilled by a Corning AG-1b still (maximum distillation rate, 1 ℓ/h). The distillate was collected in a glass reservoir (capacity of 12 gallons) and fed via a glass siphon into a Barnstead still (distillation rate, 0.5 gallon/h). This still, with a borosilicate glass condensing system, was designed to produce a water distillate of not more than 0.001 parts per million (ppm) total solid content, with electrical resistances ranging from 1.5 - 5 million ohms per cm^3. Two three-necked, round-bottomed flasks (total capacity of 20 l), fitted with Teflon joints were used as conductivity water reservoirs. These flasks were previously cleaned according to the procedure described above, p. 65.

A purified nitrogen atmosphere (see following subsection, this page) was introduced into the Barnstead still prior to and during distillation. A continuous flow of nitrogen was maintained over the water distillate in the reservoirs at all times. The water was siphoned without further treatment through glass and Nalgon tubing to the apparatus used for transferring the conductivity water to the solution flasks (see Figure VIII).

When in continual use, the Barnstead still was drained and refilled daily with freshly distilled water, as were the two conductivity water reservoirs. The specific conductivity of the water ranged from (1.7 to 3.5) x $10^{-7}\Omega^{-1}cm^{-1}$ and water having a higher specific conductivity was discarded.

Nitrogen purification. - Nitrogen (L-grade, Liquid Air of Canada) was successively led through cleaning towers with sintered glass bubblers containing concentrated sulfuric acid, aqueous sodium hydroxide (50%), aqueous barium chloride (saturated solution) and conductivity water. Empty towers were located between the various towers containing solutions to eliminate possible

FIGURE VIII (a)

A DIAGRAM OF THE CELL FILLING APPARATUS

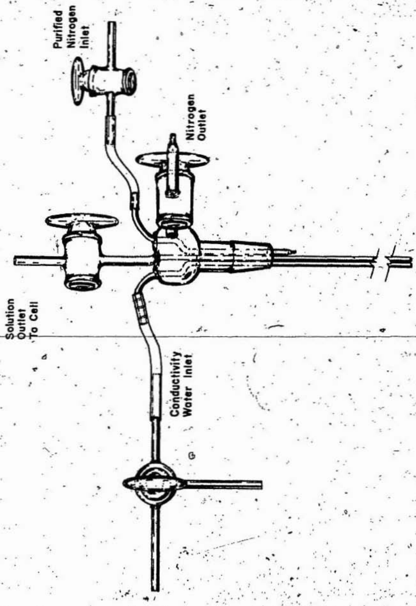
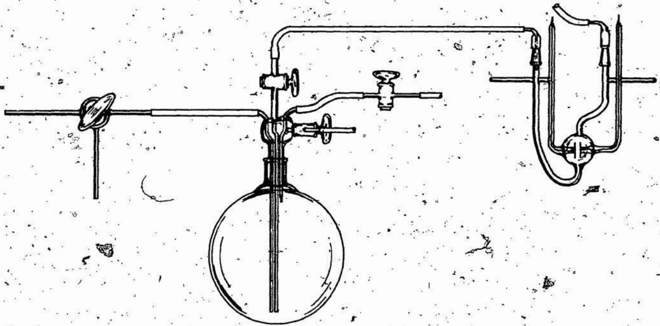


FIGURE VIII (b)

A DIAGRAM OF THE CELL FILLING APPARATUS SHOWING A 3-LITER SOLUTION FLASK AND A CONDUCTIVITY CELL ATTACHED TO THE APPARATUS



reactions between the scrubbing reagents. Separate outlets from the nitrogen train to the atmosphere were installed in the Nalgon tubing used to join the towers. Dust particles were trapped by a flask packed with glass wool located at the end of the system. The purified nitrogen was led through Nalgon tubing to the Barnstead still, the conductivity water reservoirs, and the apparatus used for transferring the conductivity water to the solution flasks.

Preparation of potassium chloride solutions. - Potassium chloride solutions for conductivity measurements were prepared by weight (concentrations expressed in mole/1000 g of water) in the following manner. A clean, oven-dried (110°C) flask (3 l) was weighed on a Stanton (H.D.I. model) two-pan balance against calibrated [National Bureau of Standards, Washington (N.B.S.)], stainless steel weights (serial number 4022). The flask was then connected to the filling apparatus shown in Figure VIII and thoroughly flushed with purified nitrogen. With continuous nitrogen flushing, conductivity water was led into the flask by gravity flow from the reservoirs through a glass delivery system. The flask was washed twice with conductivity water to remove any surface ions on the glass. Pressure exerted by the nitrogen flow into the closed system was employed to drive the water from the flask through a Nalgon delivery tube to a conductivity cell. A third washing was only undertaken if the specific conductivity of the water from the second washing was above $3.5 \times 10^{-7}\Omega^{-1}\text{cm}^{-1}$. The flask was then filled with water of known specific conductivity, capped and reweighed.

A clean, oven-dried vial containing a weighed sample of potassium chloride was dropped into the solution flask. The potassium chloride sample was weighed by difference on a Stanton (M.C.I.A. model) two-pan analytical balance against calibrated (N.B.S.) stainless steel weights (SS 5482). The vial was manipulated with clean, dry forceps throughout the entire procedure.

After homogeneous dissolution of the potassium chloride was achieved by vigorous shaking, the flask was reconnected to the filling apparatus and flushed with nitrogen. Pressure exerted by the nitrogen flow into the closed system was again used to force the potassium chloride solution into a cell attached to the filling apparatus. Prior to being filled, the cell was flushed with nitrogen and washed with ca. 400 ml of the solution. The cell was subsequently filled, capped and placed in the constant temperature bath. This procedure was repeated for each of the cells used in the conductivity measurements of the potassium chloride solution.

All glassware and cells were thoroughly washed with conductivity water following the measurements. The glassware was oven-dried and the cells were filled with conductivity water.

Preparation of acid solutions. - Solutions of the acids were prepared following the procedure outlined above for potassium chloride solutions. An exception to the latter was the weighing procedure used for chloroacetic and chloroacetic-2,2-d_2 acids. Due to the hygroscopic nature of these acids, the entire weighing procedure was carried out in a dry box flushed with dry nitrogen. This precaution proved satisfactory as the weight of the samples did not appear to increase during the weighing procedure.

Resistance measurements. - Resistances of solutions were recorded *thirty-five minutes after the cell entered the constant* temperature bath. In some cases resistance measurements were repeated after the cells had remained in the bath for a further period of time. For both potassium chloride and acid solutions, resistances were found to change less than 0.1% over a period of 12 h.

CHAPTER 3

RESULTS

3-1. CELL CONSTANTS

Cell constants. - Cell constants were determined using independently-purified samples of potassium chloride (described above, p. 67). The weights of the potassium chloride and the solvent in air were corrected for bouyancy effects using the expression

$$[57] \qquad M = W + W\left(\frac{1}{\rho} - \frac{1}{D}\right)\sigma$$

in which M is the true mass of a body in vacuo, W is the weight of the body in air, D is the density of the standard weights, ρ is the density of the body, and σ is the density of air at room temperature [c.f. (96)].

Since the solutions were prepared on the molality scale (m) and the equation relating the equivalent conductance of potassium chloride to concentration is given using the molarity scale (M), conversion between the scales was required (97). This was achieved using the expression

$$[58] \qquad V = N_0 V_0^{0} + N_1 \phi_1$$

in which V is the volume of the solution, N_0 is the number of moles of water, N_1 is the number of moles of potassium chloride and V_0^{0} is the volume of one mole of water at 25°C. The density of water was taken as 0.997075 g ml^{-1} at this temperature. The molal volume $\emptyset_1$, was obtained from

[59] $$\emptyset_1 = 26.52 + 2.327 (c)^{\frac{1}{2}}$$

in which c is the approximate concentration of the solution.

The specific conductance of an electrolyte in solution, $L_{(s)}$, is defined in Equation [17], which rearranged is

[60] $$L_{(s)} = \Lambda \cdot c \cdot 10^{-3}$$

in which Λ is the equivalent conductance and c is the molar concentration. The true specific conductance, L, is obtained from

[61] $$L = L_{(s)} - L_{(w)}$$

where $L_{(w)}$ is the specific conductance of the water.

The equivalent conductance of each concentration of potassium chloride was computed from the following equation proposed by Fuoss (98),

[62] $$\Lambda = 149.93 - 94.65 c^{\frac{1}{2}} + 58.74 c \log c + 198.4 c$$

By substituting the computed values of Λ and c into Equation [60], corresponding values of L were derived from Equation [61]. Cell constant values were then obtained from Equation [16] rearranged to

$$\kappa = LR \qquad [63]$$

where κ is the cell constant and R is the resistance in ohms.

The cell constants were determined subsequent to the cell cleaning and conditioning previously described. The constants were periodically redetermined throughout the study and are recorded in Table XI. All equivalent conductances determined for the acid solutions were calculated using the appropriate cell constants listed in Table XII.

Density measurements. - The weights of all solid samples and water were corrected to true mass *in vacuo* by the calculation described above in the cell constant subsection. The correction requires density values for the various compounds and these densities are listed in Table XIII. The densities of the deuterated acids were assumed equal to those of their protium analogues in all cases. The values listed without reference in Table XIII were determined in the following manner.

Cylindrical blocks of fused material were weighed in air, and either the dimensions of the fused blocks were measured with microcalipers or the blocks were weighed in a solvent of known density (water or cyclohexane). The latter were completed rapidly so that dissolution of the acids in the solvent was negligible. The material was fused by melting with slow cooling or by compression with a hydraulic press (*ca.* 3 x 10^4 lb/in^2). Relevant comparisons indicated that the methods of fusion and volume measurement did not appreciably affect the results.

TABLE XI

CELL CONSTANT DETERMINATIONS

RUN NUMBER	CONCENTRATION OF KCl SOLUTIONS (MOLAR x 10^3)	CELL CONSTANTS, cm^{-1}				
		CELL I	CELL II	CELL III	CELL IV	CELL V
1	1.0003	0.29294	0.30632	0.30857	0.35791	0.36284
2	0.98801	0.29292	0.30632	0.30853	0.35790	0.36284
3	1.0139	0.29296	0.30635	0.30860	0.35794	0.36287
4	1.0026	0.29296	0.30632	0.30854	0.35789	0.36283
5	0.98853	0.29298	0.30633	0.30853	0.35789	0.36286
6	1.0062	0.29292	0.30638	0.30863	0.35791	0.36291
7	1.0007	0.29292	0.30638	0.30863	0.35792	0.36292
8	1.0126	0.29293	0.30637	0.30864	0.35794	0.36291
9	1.0083	0.29295	0.30638	0.30863	0.35801	0.36297
10	1.0102	0.29295	0.30638	0.30862	0.35800	0.36297

....Cont'd.

TABLE XI (Cont'd)

CELL CONSTANT DETERMINATIONS

RUN NUMBER	CONCENTRATION OF KCl SOLUTIONS (MOLAR x 10^3)	CELL CONSTANTS, cm^{-1}				
		CELL VI	CELL VII	CELL VIII	CELL IX	CELL X
11	0.88539	0.08375	0.19876	0.24599	0.26096	0.26557
12	1.0041	0.08376	0.19876	0.25002	0.26096	0.26559
13	0.98364	0.08379	0.19875	0.24599	0.26094	0.26558
14	0.98733	0.08376	0.19871	0.24594	0.26098	0.26553
15	1.0038	0.08377	0.19877	0.24598	0.26099	0.26553
		CELL XI*	CELL XII*	CELL XIII**		
16	0.96564	0.28477	0.28829	0.36581		
17	0.99309	0.28483	0.28840	0.36587		
18	0.99103	0.28487	0.28837	0.36577		
19	1.00701	0.28480	0.28826	0.36579		
20	1.00815	0.28483	0.28840	0.36584		

---

*Kraus cells, see Figure VII(b).

**Fringe effect cell, see Figure VII(c).

TABLE XII

AVERAGED VALUES OF CELL CONSTANTS EMPLOYED IN THE CALCULATION OF ACID EQUILIBRIUM CONSTANTS

ACID	CELL I	CELL II	CELL III	CELL IV	CELL V
$C_6H_5OCH_2COOH$	0.29292	0.30638	0.30863	0.35791	0.36291
	±0.00002	±0.00002	±0.00002	±0.00002	±0.00002
$C_6H_5OCD_2COOH$	0.29292	0.30638	0.30863	0.35791	0.36291
	±0.00002	±0.00002	±0.00002	±0.00002	±0.00002
$ClCH_2COOH$	0.29295	0.30638	0.30863	0.35801	0.36297
	±0.00002	±0.00002	±0.00002	±0.00003	±0.00003
$ClCD_2COOH$	0.29292	0.30638	0.30863	0.35791	0.36291
	±0.00002	±0.00002	±0.00002	±0.00002	±0.00002
$C_6H_5SCH_2COOH$	0.29295	0.30638	0.30863	0.35801	0.36297
	±0.00002	±0.00002	±0.00002	±0.00003	±0.00003
$C_6H_5SCD_2COOH$	0.29295	0.30638	0.30863	0.35801	0.36297
	±0.00002	±0.00002	±0.00002	±0.00003	±0.00003

....Cont'd.

TABLE XII (Cont'd)

AVERAGED VALUES OF CELL CONSTANTS EMPLOYED IN THE CALCULATION OF ACID EQUILIBRIUM CONSTANTS

ACID	CELL I	CELL II	CELL III	CELL IV	CELL V
$C_6H_5SO_2CH_2COOH$	0.29295 ±0.00002	0.30638 ±0.00002	0.30863 ±0.00002	0.35801 ±0.00003	0.36297 ±0.00003
	CELL VI	CELL VII	CELL VIII	CELL IX	CELL X
$C_6H_5CH_2COOH$	0.08376 ±0.00002	0.19876 ±0.00001	0.24599 ±0.00004	0.26096 ±0.00005	0.26557 ±0.00003
	CELL XI*	CELL XII*	CELL XIII*		
$C_6H_5OCH_2COOH$	0.28482 ±0.00004	0.28834 ±0.00002	0.36582 ±0.00003		

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*These cells were used in conjunction with cells I to V for purposes of comparison.

TABLE XIII

DENSITY VALUES EMPLOYED IN BUOYANCY CORRECTIONS

COMPOUND	DENSITY, g/ml	REFERENCE
Water	0.997075	(99)
Potassium chloride	1.98	(100)
Phenylacetic acid	1.23	(89)
Phenoxyacetic acid	1.31	
Chloroacetic acid	1.58	(101)
Phenylthioglycollic acid	1.37	
Phenylsulfinylacetic acid	1.42	
Phenylsulfonylacetic acid	1.48	

3-2. CONCENTRATION-EQUIVALENT CONDUCTANCE DATA AND THERMODYNAMIC EQUILIBRIUM CONSTANTS

The concentration-equivalent conductance data for phenylacetic, phenoxyacetic, phenoxyacetic-2,2-d_2, chloroacetic, chloroacetic-2,2-d_2, phenylthioglycollic, phenylthioglycollic-2,2-d_2, and phenylsulfonylacetic acids in conductivity water at 25.000 ± 0.002°C (with the exception of phenylacetic acid solutions, noted above as 25.051 ± 0.002°C) are recorded in Tables XIV to XXI (inclusive).

Equivalent conductances recorded in these Tables are computed from the relationship

$$[64] \qquad \Lambda = \frac{\kappa \cdot 10^3}{R \cdot c}$$

which is derived by combining and rearranging Equations [60] and [63].

The abbreviated results of the statistical treatments (detailed above, pp. 38 - 40) employed to calculate thermodynamic equilibrium constants from the concentration-equivalent conductance data of the acids are presented in Tables XXII to XXIX (inclusive). The latter also tabulate some equilibrium constants of these acids previously determined by other workers. The computations associated with these results were accomplished with the aid of an I.B.M. 360/90 high speed digital computer and the Fortran IV programs appropriate to the various methods of calculation are detailed in Appendix II.

TABLE XIV

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENYLACETIC ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL VI	CELL VII	CELL VIII	CELL IX	CELL X
61.0877	33.15	33.17	33.15	33.16	33.15
47.3282	37.42	37.43	37.43	37.43	37.43
37.7965	41.59	41.60	41.58	41.60	41.60
21.9981	53.49	53.49	53.48	53.48	53.50
10.7172	73.96	73.98	73.99	73.98	73.99
9.6954	77.31	77.33	77.35	77.35	77.35
8.2337	83.03	83.05	83.06	83.06	83.06
6.7758	90.32	90.34	90.36	90.35	90.36
6.2448	93.49	93.51	93.53	93.52	93.53
5.3392	99.92	99.94	99.96	99.93	99.96
3.9793	112.80	112.85	112.88	112.82	112.85
2.9584	127.00	127.03	127.06	127.06	127.06
1.9878	148.00	148.04	148.09	148.05	148.06
0.9947	188.15	188.22	188.32	188.29	188.25

TABLE XV

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENOXYACETIC ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL I	CELL II	CELL III	CELL IV	CELL V
60.4898	113.62	113.62	113.63	113.61	113.63
50.1886	122.56	122.58	122.57	122.57	122.56
40.2898	133.62	133.64	133.64	133.64	133.64
30.0870	149.37	149.36	149.34	149.35	139.35
20.0980	172.70	172.70	172.70	172.69	172.68
9.8170	217.46	217.45	217.45	217.44	217.45
9.0590	222.69	222.72	222.70	222.72	222.68
7.9804	230.62	230.62	230.62	230.64	230.62
7.0822	238.24	238.21	238.22	238.23	238.20
5.9228	249.50	249.47	249.48	249.51	249.46
5.0050	259.86	259.86	259.87	259.90	259.87
3.9889	273.19	273.22	273.23	273.25	273.20
3.0042	289.05	289.04	289.05	289.07	289.03
2.0058	308.71	308.69	308.71	308.73	308.69
1.0179	333.71	333.66	333.65	333.72	333.67

....Cont'd.

TABLE XV (Cont'd)

CONCENTRATION x 10^4 (MOLAL)	CELL XI	CELL XII	CELL XIII
60.4898	113.61	113.63	113.64
50.1886	122.57	122.58	122.58
40.2898	133.63	133.64	133.65
30.0870	149.36	149.35	149.34
20.0980	172.71	172.70	172.70
9.8170	217.44	217.45	217.45
9.0590	222.70	222.69	222.70
7.9804	230.63	230.62	230.62
7.0822	238.21	238.22	238.21
5.9228	249.47	249.48	249.47
5.0050	259.88	259.88	259.86
3.9889	273.22	273.21	273.24
3.0042	289.04	289.05	289.04
2.0058	308.70	308.71	308.71
1.0179	333.67	333.69	333.66

TABLE XVI

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENOXYACETIC-2,2-d_2 ACID

CONCENTRATION $\times 10^4$ (MOLAL)	EQUIVALENT CONDUCTANCE CELL I	CELL II	CELL III	CELL IV	CELL V
60.0890	113.45	113.46	113.46	113.43	113.42
50.5520	121.66	121.68	121.66	121.65	121.64
40.0041	123.42	133.43	133.43	133.42	133.41
30.1594	148.60	148.58	148.59	148.58	148.59
20.0584	172.05	172.07	172.09	172.05	172.07
10.0233	215.36	215.37	215.37	215.37	215.35
9.0449	222.00	222.02	222.00	222.06	222.04
7.9858	229.71	229.69	229.74	229.74	229.70
6.9940	238.25	238.25	238.26	238.26	238.25
5.8409	249.52	249.50	249.50	249.52	249.53
5.0591	258.38	258.38	258.40	258.42	258.41
3.9671	272.61	272.61	272.60	272.61	272.60
3.0403	287.42	287.43	287.44	287.46	287.45
1.9357	309.60	309.63	309.61	309.63	309.64

TABLE XVII

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR CHLOROACETIC ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL I	CELL II	CELL III	CELL IV	CELL V
50.1012	161.95	161.95	161.94	161.95	161.94
44.7823	168.58	168.59	168.58	168.58	168.58
39.9727	175.48	175.47	175.48	175.46	175.47
35.0181	183.76	183.77	183.77	183.76	183.75
29.8696	193.77	193.79	193.78	193.76	193.78
24.6989	205.97	205.95	205.96	205.95	205.96
20.0424	219.44	219.45	219.45	219.46	219.45
15.1206	237.93	237.96	237.95	237.94	237.94
10.1041	263.79	263.81	263.80	263.81	263.81
8.8361	271.92	271.91	271.94	271.92	271.92
8.0417	277.65	277.65	277.66	277.66	277.66
6.9425	285.95	285.95	285.98	285.98	285.98
6.2139	292.26	292.25	292.27	292.27	292.26
5.0722	303.58	303.58	303.58	303.60	303.58

TABLE XVIII

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR CHLOROACETIC-2,2-d_2 ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL I	CELL II	CELL III	CELL IV	CELL V
49.6202	161.95	161.97	161.97	161.94	161.95
44.1062	168.90	168.89	168.90	168.88	168.89
40.1143	174.61	174.61	174.62	174.60	174.58
34.5537	183.77	183.77	183.75	183.75	183.74
29.5648	193.55	193.56	193.53	193.54	193.55
24.7359	204.95	204.96	204.94	204.92	204.94
20.0241	218.66	218.67	218.68	218.64	218.65
14.7642	238.58	238.58	238.58	238.53	238.55
9.8575	264.56	264.56	264.57	264.54	264.56
9.2727	268.39	268.39	268.39	268.38	268.38
7.6456	280.22	280.23	280.23	280.25	280.24
6.6833	288.19	288.21	288.20	288.20	288.20
6.0399	294.01	294.03	293.99	294.00	294.00
4.4945	310.04	310.04	310.04	310.06	310.04

TABLE XIX

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENYLTHIOGLYCOLLIC ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL I	CELL II	CELL III	CELL IV	CELL V
50.0798	81.74	81.74	81.74	81.74	81.74
45.3731	85.33	85.34	85.33	85.32	85.33
40.2440	89.86	89.86	89.86	89.86	89.86
34.9642	95.42	95.41	95.42	95.42	95.42
30.1880	101.51	101.51	101.51	101.52	101.51
25.0388	109.70	109.70	109.70	109.71	109.70
19.8472	120.55	120.55	120.55	120.56	120.55
15.1224	134.20	134.20	134.21	134.21	134.20
9.9417	157.22	157.22	157.23	157.23	157.23
9.0333	162.79	162.80	162.80	162.81	162.80
8.0962	169.27	169.27	169.27	169.27	169.27
6.8950	178.91	178.89	178.91	178.90	178.91
6.0080	187.39	187.39	187.40	187.37	187.37
5.0275	198.50	198.47	198.50	198.47	198.48

TABLE XX

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENYLTHIOGLYCOLLIC-2,2-d_2 ACID

CONCENTRATION $\times 10^4$ (MOLAL)	EQUIVALENT CONDUCTANCE CELL I	CELL II	CELL III	CELL IV	CELL V
50.0812	81.01	81.01	81.01	80.99	81.00
45.2952	84.65	84.65	84.65	84.64	84.64
40.1200	89.20	89.20	89.21	89.19	89.19
35.0359	94.53	94.54	94.54	94.52	94.52
30.1813	100.67	100.67	100.68	100.66	100.66
25.0760	108.74	108.75	108.75	108.74	108.73
20.0153	119.23	119.23	119.23	119.22	119.22
15.0394	133.53	133.52	133.53	133.53	133.52
10.0253	155.70	155.70	155.70	155.71	155.70
9.0059	161.84	161.84	161.85	161.85	161.84
8.0781	168.27	168.27	168.27	168.27	168.27
7.0211	176.69	176.69	176.69	176.70	176.69
5.9933	186.35	186.34	186.34	186.34	186.34
5.0232	197.24	197.23	197.23	197.22	197.23

TABLE XXI

A SUMMARY OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA FOR PHENYLSULFONYLACETIC ACID

CONCENTRATION	EQUIVALENT CONDUCTANCE				
x 10^4 (MOLAL)	CELL I	CELL II	CELL III	CELL IV	CELL V
50.1061	217.59	217.60	217.57	217.57	217.60
45.3305	223.93	223.95	223.96	223.92	223.91
40.1804	231.60	231.62	231.64	231.61	231.63
35.0687	240.25	240.28	240.26	240.26	240.26
30.2359	249.58	249.58	249.57	249.55	249.55
25.0841	260.86	260.87	260.84	260.86	260.86
20.0247	274.11	274.14	274.14	274.15	274.13
15.0929	290.13	290.12	290.13	290.11	290.13
10.0297	310.21	310.20	310.21	310.20	310.21
8.9795	314.84	314.85	314.86	314.85	314.84
8.0937	319.32	319.31	319.32	319.32	319.31
6.9700	325.11	325.10	325.11	325.11	325.11
5.9956	330.81	330.81	330.82	330.82	330.82
5.0571	336.40	336.39	336.40	336.39	336.40

TABLE XXII

EQUILIBRIUM CONSTANTS OF PHENYLACETIC ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (61.09 - 1.988) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^5	Λ_o (REFERENCE)
ROBINSON-STOKES	4.930 ± 0.016	379.6 (102)
SHEDLOVSKY II	4.928 ± 0.016	379.6 (102)
CLASSICAL	5.790 ± 0.018 (K_c)	357.6
IVES	4.933 ± 0.011	379.1
FUOSS	4.927 ± 0.015	379.9
SHEDLOVSKY I	4.926 ± 0.015	380.1

SOME PREVIOUSLY DETERMINED VALUES

METHOD OF MEASUREMENT (METHOD OF CALCULATION)	EQUILIBRIUM CONSTANT, K_t x 10^5	Λ_o (REFERENCE)
CONDUCTANCE (ROBINSON-STOKES)	4.923 ± 0.015	379.6 (44)
CONDUCTANCE	4.887 ± 0.056	383.7 (83)
CONDUCTANCE (IVES)	4.90 (MOLAR)	--- (103, 104)
ELECTROMOTIVE FORCE	4.928 ± 0.011	--- (105)

TABLE XXIII

EQUILIBRIUM CONSTANTS OF PHENOXYACETIC ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (50.19 - 5.005) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o
ROBINSON-STOKES	7.293 ± 0.0141	380.5*
SHEDLOVSKY II	7.283 ± 0.0144	380.5*
CLASSICAL	8.193 ± 0.0042 (K_c)	370.6
IVES	7.276 ± 0.0144	380.7
FUOSS	7.241 ± 0.0168	381.2
SHEDLOVSKY I	7.235 ± 0.0172	381.3

SOME PREVIOUSLY DETERMINED VALUES

METHOD OF MEASUREMENT	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o (REFERENCE)
CONDUCTANCE	7.59 (MOLAR)	--- (106)
ELECTROMOTIVE FORCE	6.75	--- (90)
ELECTROMOTIVE FORCE	6.58	--- (45)

---

*Shedlovsky IV Λ_0 value, see Table XXXII below.

TABLE XXIV

EQUILIBRIUM CONSTANTS OF PHENOXYACETIC-2,2-d_2 ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (50.55 - 5.059) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o
ROBINSON-STOKES	7.205 ± 0.0180	380.5*
SHEDLOVSKY II	7.195 ± 0.0162	380.5*
CLASSICAL	8.129 ± 0.0046 (K_c)	370.1
IVES	7.219 ± 0.0152	380.2
FUOSS	7.183 ± 0.0176	380.7
SHEDLOVSKY I	7.176 ± 0.0180	380.9

---

*Shedlovsky IV Λ_o value for protium acid, see Table XXXII below.

TABLE XXV

EQUILIBRIUM CONSTANTS OF CHLOROACETIC ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (44.78 - 8.042) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^3	Λ_o
ROBINSON-STOKES	1.399 ± 0.0032	390.1*
SHEDLOVSKY II	1.396 ± 0.0032	390.1*
CLASSICAL	1.572 ± 0.0022 (K_c)	381.0
IVES	1.394 ± 0.0032	390.3
FUOSS	1.388 ± 0.0037	390.8
SHEDLOVSKY I	1.386 ± 0.0037	390.9

SOME PREVIOUSLY DETERMINED VALUES

METHOD OF MEASUREMENT	EQUILIBRIUM CONSTANT, K_t x 10^3	Λ_o (REFERENCE)
CONDUCTANCE	1.396 (MOLAR)	389.5 (107)
CONDUCTANCE	1.396 (MOLAR)	389.6 (108)
CONDUCTANCE	1.359 (MOLAR)	392.0 (42)

---

*Shedlovsky IV Λ_o value, see Table XXXII below.

TABLE XXVI

EQUILIBRIUM CONSTANTS OF CHLOROACETIC-2,2-d_2 ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (44.11 - 7.646) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, $K_t \times 10^3$	Λ_o
ROBINSON-STOKES	1.382 ± 0.0003	390.1*
SHEDLOVSKY II	1.379 ± 0.0014	390.1*
CLASSICAL	1.555 ± 0.0092 (K_C)	380.9
IVES	1.375 ± 0.0042	390.5
FUOSS	1.373 ± 0.0052	390.7
SHEDLOVSKY I	1.371 ± 0.0057	390.8

---

*Shedlovsky IV Λ_o value for protium acid, see Table XXXII below.

TABLE XXVII

EQUILIBRIUM CONSTANTS OF PHENYLTHIOGLYCOLLIC ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (50.08 - 5.027) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o
ROBINSON-STOKES	2.803 ± 0.0040	381.2*
SHEDLOVSKY II	2.799 ± 0.0041	381.2*
CLASSICAL	3.195 ± 0.0050 (K_c)	367.0
IVES	2.799 ± 0.0040	381.3
FUOSS	2.778 ± 0.0048	382.4
SHEDLOVSKY I	2.775 ± 0.0049	382.5

SOME PREVIOUSLY DETERMINED VALUES

METHOD OF MEASUREMENT	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o (REFERENCE)
CONDUCTANCE	2.76 ± 0.04	381.1 (46)
ELECTROMOTIVE FORCE	2.70	--- (45)

---

*Shedlovsky IV Λ_o value, see Table XXXII below.

TABLE XXVIII

EQUILIBRIUM CONSTANTS OF PHENYLTHIOGLYCOLLIC-2,2-d_2 ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (50.08 - 5.023) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, K_t x 10^4	Λ_o
ROBINSON-STOKES	2.752 ± 0.0025	381.2*
SHEDLOVSKY II	2.749 ± 0.0036	381.2*
CLASSICAL	3.114 ± 0.0039 (K_C)	367.8
IVES	2.734 ± 0.0057	381.9
FUOSS	2.706 ± 0.0067	383.4
SHEDLOVSKY I	2.705 ± 0.0068	383.5

---

*Shedlovsky IV Λ_o value for protium acid, see Table XXXII below.

TABLE XXIX

EQUILIBRIUM CONSTANTS OF PHENYLSULFONYLACETIC ACID DERIVED FROM VARIOUS TREATMENTS OF EQUIVALENT CONDUCTANCE DATA OVER A CONCENTRATION RANGE OF (45.33 - 8.094) x 10^{-4} MOLAL

METHOD	EQUILIBRIUM CONSTANT, $K_t \times 10^3$	Λ_o
ROBINSON-STOKES	3.670 ± 0.013	379.7*
SHEDLOVSKY II	3.663 ± 0.012	379.7*
CLASSICAL	4.066 ± 0.0014 (K_C)	373.5
IVES	3.661 ± 0.013	379.8
FUOSS	3.647 ± 0.015	380.1
SHEDLOVSKY I	3.642 ± 0.015	380.2

SOME PREVIOUSLY DETERMINED VALUES

METHOD OF MEASUREMENT	EQUILIBRIUM CONSTANT, $K_t^\circ \times 10^3$	Λ_o (REFERENCE)
CONDUCTANCE	3.63 ± 0.04	379.6 (46)
ELECTROMOTIVE FORCE	3.07	-- (45)

---

*Shedlovsky IV Λ_o value, see Table XXXII below.

3-3. ISOTOPE EFFECTS

Secondary isotope effects of the second kind calculated via the Shedlovsky III Method (described above, pp. 53 - 56) for the isotopic acid pairs RCH_2COOH/RCD_2COOH, where R = PhO, Cl, and PhS, have been tabulated in Appendix III. A summary of these isotope effects is presented in Table XXX.

Isotope effects derived from the appropriate comparisons of thermodynamic equilibrium constants [see Tables XXII to XIX] are listed with those calculated by the Shedlovsky III Method in Table XXXI.

TABLE XXX

ISOTOPE EFFECTS DERIVED FROM SHEDLOVSKY III TREATMENT OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA

ACID PAIR	CELL NUMBER	ISOTOPE EFFECT, $m_t(D)/m_t(H)$
Phenoxyacetic	1	1.0104 ± 0.0009
	2	1.0099 ± 0.0008
	3	1.0104 ± 0.0009
	4	1.0108 ± 0.0009
	5	1.0109 ± 0.0009
Chloroacetic	1	1.0114 ± 0.0008
	2	1.0116 ± 0.0008
	3	1.0116 ± 0.0008
	4	1.0114 ± 0.0008
	5	1.0116 ± 0.0008
Phenylthioglycollic	1	1.0207 ± 0.0006
	2	1.0209 ± 0.0006
	3	1.0205 ± 0.0006
	4	1.0211 ± 0.0007
	5	1.0211 ± 0.0006

TABLE XXXI

A COMPARISON OF ISOTOPE EFFECTS FOR THREE ISOTOPIC ACID PAIRS

METHOD OF	ISOTOPE EFFECTS FOR RCH_2COOH/RCD_2COOH		
CALCULATION	R = PhO	R = Cl	R = PhS
Robinson-Stokes	1.012 ± 0.003	1.012 ± 0.002	1.020 ± 0.001
Shedlovsky II	1.012 ± 0.002	1.012 ± 0.002	1.020 ± 0.001
Ives	1.008 ± 0.002	1.014 ± 0.003	1.024 ± 0.002
Fuoss	1.008 ± 0.003	1.011 ± 0.004	1.027 ± 0.003
Shedlovsky I	1.008 ± 0.002	1.011 ± 0.004	1.026 ± 0.003
Classical	1.011 ± 0.001	1.012 ± 0.001	1.021 ± 0.001
Shedlovsky III	1.011 ± 0.001	1.012 ± 0.001	1.021 ± 0.001

3-4. LIMITING EQUIVALENT CONDUCTANCE (Λ_0) VALUES

Values of Λ_0 used in the Direct Methods of thermodynamic equilibrium constant calculation were obtained from Salt Method values (converted to the molal scale) determined by other workers and from the Shedlovsky IV treatment of the concentration-equivalent conductance data of the acids. The abbreviated results of the Shedlovsky IV treatment of the data are presented in Appendix IV, and the Λ_0 values of the acids determined by this method are summarized in Table XXXII.

TABLE XXXII

Λ_o VALUES DERIVED FROM SHEDLOVSKY IV TREATMENT OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA

ACID	Λ_o VALUE THAT YIELDS MINIMUM ERROR IN SHEDLOVSKY K_t					
	CELL I	CELL II	CELL III	CELL IV	CELL V	AVERAGE Λ_o
Phenoxyacetic	380.5	380.5	380.5	380.6	380.4	380.5
Phenoxyacetic-2,2-d_2	380.0	379.9	380.0	380.1	380.1	380.0
Chloroacetic	390.1	390.1	390.1	390.1	390.1	390.1
Chloroacetic-2,2-d_2	390.6	390.6	390.7	390.5	390.7	390.6
Phenylthioglycollic	381.3	381.1	381.3	381.1	381.2	381.2
Phenylthioglycollic-2,2-d_2	381.7	381.6	381.5	381.8	381.8	381.7
Phenylsulfonylacetic	379.7	379.6	379.7	379.7	379.7	379.7

CHAPTER 4

DISCUSSION

4-1. THERMODYNAMIC EQUILIBRIUM CONSTANTS

4-1a. A COMPARISON WITH THE LITERATURE

The determination of the thermodynamic equilibrium constant of phenylacetic acid in the present study was attempted for comparison with values previously reported. The demonstrated reproducibility of the K_t for this acid, when compared with values previously determined, assures some measure of reliability in the technique.

Values of the K_t of phenylacetic acid calculated via the various methods described above are reported in Table XXII, and, with the exception of the Classical calculation, the values determined by all methods agree to within 0.3%. More significantly, these values are in excellent agreement with those recently determined by both conductance and electromotive force methods (44, 83, 103, 104, 105).

The K_t values of phenylacetic acid calculated by the Direct Methods, namely the Robinson-Stokes and Shedlovsky II Methods, were evaluated using a corrected value of Λ_0. The correction of this parameter was necessitated by an oversight in the bath temperature adjustment (the temperature was actually 25.051°C instead of 25.000°C), and was accomplished using data provided by Laughton and Demayo (104). These authors have proposed the linear variance of the limiting equivalent conductance of phenylacetic acid over the temperature range of 20°C to 40°C according to the equation

$$[65] \qquad \Lambda_o = -1122.08 + 4.9614\ T$$

The increase of 4.9614 Λ_o units per ^oK yields a Λ_o value at 25.051^{o}C some 0.25 equivalent conductance units ($cm^2\ \Omega^{-1}\ mole^{-1}$) higher than the Λ_o value quoted for 25.000^{o}C (102).

In their investigation of the temperature dependence of the thermodynamic equilibrium constant of phenylacetic acid, Laughton and Demayo (104) obtained only a 3.9% decrease in K_t over a temperature range of 20^{o}C to 40^{o}C. On this basis, temperature correction of the K_t values calculated at 25.051^{o}C in the present study was considered unnecessary, as the correction represents about 0.01% of the quoted K_t value.

The thermodynamic equilibrium constants of the other acids investigated (see Tables XXIII to XXIX) indicate that while certain of the evaluative methods appear more precise than others, the discrepancies between the K_t values generated for any one acid by the different evaluative techniques are diminutive. With the exception of chloroacetic acid, the K_t values of the protio acids are in excellent agreement with previously reported values determined by the conductance method.

In the case of chloroacetic acid, although the values of the thermodynamic equilibrium constant reported by Shedlovsky and co-workers (107, 110) and Saxton and Langer (108) are coincident with values determined here, there is considerable discrepancy between the latter and the much lower thermodynamic equilibrium constant reported by Ives and Pryor (42). In their highly precise investigation of monohalogenoacetic acids, Ives and Pryor suggest that erroneous values of Λ_0 obtained via the Salt Method (see above, p. 47) may account for the discrepancies in reported thermodynamic equilibrium constant values of chloroacetic acid. These authors ascribe the error in Λ_0 measurement to hydrolytic decomposition of aqueous sodium chloroacetate which gives rise to inconsistent conductance measurements of the unstable salt solutions. Instability of the salt solutions has not been previously reported however [c.f. (107, 110) and (108)], even in highly alkaline media under moderate conditions (111), nor did the chloroacetic acid solutions in the present study show evidence of instability.

To accommodate the highly precise, yet lower, thermodynamic equilibrium constant reported by Ives and Pryor for chloroacetic acid, speculation must lead to the possibility of a homogeneous impurity present in their acid sample which would lower the K_t value. The two obvious possibilities are bromoacetic acid, an impurity in commercial samples of chloroacetic acid and one which is removed only with great difficulty (111), and water. The notoriously hygroscopic nature of chloroacetic acid necessitated its weighing in a dry atmosphere in the present study, but this was not the procedure followed in the Ives-Pryor study (112).

The thermodynamic equilibrium constant of phenylsulfinylacetic acid has been measured by Crockford and Douglas (46), who employed a conductance technique, and by Pasto and Kent (45), who used an electromotive force method. Although not in agreement as to the absolute value of the ionization constant of phenylsulfinylacetic acid, both groups of workers note that the thermodynamic equilibrium constant of the acid is unusually large in comparison with the values of phenylthioglycollic and phenylsulfonylacetic acids. Indeed, Pasto and co-workers (45, 113) go to some lengths to explain the anomalous behaviour of these three acids in aqueous and non-aqueous media.

The thermodynamic equilibrium constants of the protio and deutero phenylsulfinylacetic acids are not reported in this study, as aqueous phenylsulfinylacetic acid proved unstable to conductance measurement. The change of resistance of the acid solution with time indicated a process of uniform rate was occurring, probably a decomposition of the type originally proposed by Pummerer (114) and recently examined by Walker and Leib (115). This process was accompanied by the deposition of a sparingly soluble material on the cell electrodes, which was removed only after repeated washing.

Aqueous phenylsulfonylacetic acid evidenced no instability to conductance measurement, but a uniform decrease in resistance with time was observed for solutions of the deuterium acid analogue. As the aqueous protio acid appeared stable, this resistance change is attributed to the re-exchange of hydrogen for deuterium at the methylene position of the aqueous deutero acid.

4-1b. UNCERTAINTY IN THE PRESENT RESULTS

A small residual concentration dependence of equilibrium constant values derived from conductance measurements has recently been noted (38, 44, 78, 116, 117). This dependence can be ascribed to errors associated with frequency dependence of measured resistance, significant specific conductance of solvent, hydrogen bonding differences between the isotopic atoms and the solvent, incomplete isotopic substitution in the deutero acids, and the use of inaccurate limiting equivalent conductance values. Each of these sources of error will be discussed in turn.

The frequency dependence of electrolyte solutions continues to be a complex problem of current research interest [c.f. (118)]. The highly precise conductance measurements on substituted acetic acid solutions by Ives et al. (42, 112, 119, 120) using four-lead double cells enabled these workers to confirm the approximate linearity of resistance with reciprocal frequency. Although the function of resistance with frequency appears to depend on the type of electrodes employed (121a), Pryor (112) notes that the frequency dependence of the resistances associated with solutions of monohalogenoacetic acids is insignificant, not exceeding 0.01% of the apparent resistance. This observation was confirmed by Ives and Moseley in a later communication (122) in which these authors waive the double cell advantage of small residual frequency dependence in favour of the statistical advantage of two separate cells. The effect of frequency dependence on apparent resistance in the two separate cells was reported as "almost inconsiderable".

In the present investigation, the frequency dependence of the resistance measurements obtained on the impedance comparator (G.R.I.C.) appeared not to exceed 0.02% of the resistance values. However, resistance measurements on the Tinsley bridge showed some frequency dependence, but subsequent extrapolation of resistance as a function of frequency yielded resistance values within 0.03% of those obtained on the impedance comparator.

The correction of specific conductance values of acid solutions has been advocated by Laughton and Demayo in a recent extensive study of errors associated with conductance measurement (104). This correction requires the subtraction of the specific conductance of the conductivity water from that of the aqueous acid prior to the calculation of equivalent conductance. Apart from conductivity due to its own dissociation, the specific conductance of conductivity water is usually attributed to the presence of dissociated carbonic acid (121b). While it cannot be considered negligible in the case of potassium chloride solutions {c.f. Equation [61]}, this dissociation must be altered in solutions of other acids. The solvent correction factor then becomes extremely difficult to estimate and its application is of questionable necessity.

As current theories of hydrocarbon solubility in water suggest that specific interactions between solute and solvent are weak, the effect of hydrogen bonding differences between the methylene H and D atoms with water is not considered to be a parameter of sufficient magnitude to influence the hydrodynamic properties of the dissolved acids.

Errors associated with the effect of incomplete isotopic substitution on the thermodynamic equilibrium constants of the deuterium acid analogues have been examined by Scott and Benson (79, 117). Incomplete deuteration of the methylene group results from either partial deuteration during preparation or re-exchange (protium for deuterium) during measurement, and it leads to a mixture of RCH_2COOH, $RCHDCOOH$ and RCD_2COOH. Scott and Benson assume $K_t(HD)$ equal to the geometric mean of $K_t(H)$ and $K_t(D)$ in their calculations and treat the problem classically, i.e., they neglect interionic effects on both the activities and mobilities of the ions involved in the equilibria. These authors conclude that the validity of the $K_t(D)$ determination will not be seriously endangered if the deuterium content at the methylene position is not less than 95%.

The errors associated with limiting equivalent conductances produced by the simultaneous generation of Λ_0 and K_t via the Indirect Methods has attracted considerable comment (38, 82, 104, 123). Belcher (82) has compared limiting equivalent conductance values obtained from the Salt Method with those derived from the iterative techniques (see Table XXXIII). He concludes that the iterative-extrapolation techniques of the Indirect Methods are only reliable if the electrolyte has a dissociation constant greater than 1 x 10^{-3}. If the thermodynamic equilibrium constant of the electrolyte is less than 1 x 10^{-5}, then the Λ_o value, and hence the K_t value, will be in serious error. Belcher maintains that even if the theoretical expressions for data treatment are adequate over the complete concentration range investigated, an accurate value of Λ_o will not be determined unless the random errors are small and the number of empirical data points is large.

Belcher's contention is supported by Kilpatrick (123) in her investigation of errors arising from the generation of Λ_o via the Ives Method. The results of extensive data treatment by both Barnes (44) and Demayo (104) provide further confirmation of Belcher's observation. Indeed, in the present work the variation of K_t values with concentration becomes increasingly apparent with changes in Λ_o on either side of the best value (see Table XXXIV).

However, the data of Ives et al. (42, 119, 122, 124, 125, 126), processed by the Ives Method, appear to give excellent results; but this may be partly a consequence of the relative strengths of these acids. As Belcher (82) notes, the data derived from relatively strong acids require only short extrapolation in the generation of Λ_o. The original intention of Ives

TABLE XXXIII

A COMPARISON OF Λ_o AND K_t VALUES OF VARIOUS ACIDS TABULATED BY BELCHER (82)

	FROM ACID AND SALT		FROM ACID ALONE		
ACID	Λ_o	$K_t \times 10^5$	Λ_o	$K_t \times 10^5$	REFERENCE
Carbonic	394.3	0.0431	424	0.0365	(128)
Acetic	390.71	1.753	395.3	1.705	(75)
Propionic	385.47	1.343	386.34	1.337	(82)
Chloroacetic	389.52	139.6	389.5	139.6	(107)
n-Butyric	382.40	1.508	386.05	1.475	(82)
Benzoic	382.21	631.2	382.1	631.2	(129)
o-Chlorobenzoic	380.07	119.7	380.0	119.7	(130)

TABLE XXXIV

A COMPARISON OF K_t AND DEVIATION (δ) VALUES, DETERMINED BY THE ROBINSON-STOKES METHOD EMPLOYING VARIOUS Λ_o VALUES, FOR SOLUTIONS OF CHLOROACETIC ACID IN CELL NUMBER I

CONCENTRATION $\times 10^4$ (MOLAL)	$\Lambda_o = 388.3$, (K_t and δ) $\times 10^5$	$\Lambda_o = 390.1$, (K_t and δ) $\times 10^5$	$\Lambda_o = 390.8$, (K_t and δ) $\times 10^5$
44.782	141.4 + 0.5232	139.6 + 0.1994	138.9 + 0.0753
39.977	141.5 + 0.4175	139.7 + 0.1210	139.0 + 0.0073
35.018	141.9 + 0.1235	140.0 - 0.1382	139.3 - 0.2385
29.870	142.1 + 0.2179	140.1 - 0.1933	139.4 - 0.2756
24.699	142.3 - 0.1022	140.2 - 0.2536	139.4 - 0.3112
20.042	142.2 - 0.0353	140.0 - 0.1051	139.2 - 0.1316
15.121	142.5 - 0.2830	140.2 - 0.2172	139.3 - 0.1920
10.104	142.7 - 0.3897	139.9 - 0.0675	138.9 + 0.0555
8.8361	142.3 - 0.1038	139.4 + 0.3209	138.3 + 0.4827
8.0417	142.3 - 0.1173	139.3 + 0.3897	138.2 + 0.5826
AVERAGE ($K_t \pm \delta$) $\times 10^5$ FOR CELLS I-V	142.1 ± 0.4007	139.9 ± 0.3177	139.0 ± 0.4152

(42, 72) in the development and use of the iterative-extrapolation technique was to safeguard against salt decomposition in aqueous media. A similar situation is encountered in the present work, in as much as the salts of the various deutero acids may be subject to rapid re-exchange in aqueous media (111). Hence, although desirable, direct measurements of Λ_0 by the Salt Method have not been attempted in the present study.

The Shedlovsky IV treatment of concentration-equivalent conductance data (see Appendix IV) developed by Scott et al. (38, 79, 117) provides a useful alternative to the iterative-extrapolation methods of Fuoss (69), Shedlovsky (70, 109) and Ives (72) in the determination of Λ_0. This method does not rely on an extrapolation but rather finds its basis in a linear least squares interpolation (see above, p. 48). Some Λ_0 values produced by this method are compared with those evaluated by the Salt Method and the iterative methods in Table XXXV. In all cases the Λ_0 values calculated by the Shedlovsky IV Method are closer to the Λ_0 values calculated from salt data than those of an iterative-extrapolation technique.

The apparent concentration dependence of the thermodynamic equilibrium constants is undoubtedly influenced by parameters other than those discussed above [c.f. (127)]. Whether, for instance, the theoretical model and the assumptions inherent in the methods of calculation (e.g. the approximations of a definite ion size and the activity of undissociated solute) are valid at the

TABLE XXXV

A COMPARISON OF Λ_0 VALUES DETERMINED BY THE SHEDLOVSKY I ITERATIVE METHOD, THE SHEDLOVSKY IV METHOD AND THE SALT METHOD

R IN RCH_2COOH ACID	SHEDLOVSKY I ITERATIVE METHOD	SHEDLOVSKY IV METHOD	SALT METHOD (REFERENCE)
	Λ_0 (MOLAL) VALUES*		
H	391.9	391.4	389.6 (75)
C_6H_5	386.4	381.7	379.6 (102)
4-MeO-C_6H_4	380.2	377.0	377.3 (81)
4-NO_2-C_6H_4	378.9	378.5	376.6 (80)
Cl	390.9	390.1	389.5 (107)
C_6H_5S	382.5	381.2	381.1 (46)
$C_6H_5SO_2$	380.2	379.7	379.6 (46)

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*The unreferenced values for the first four acids listed are taken from (44), and all others are from this study.

extremities of the concentration range is questionable. Since, however, this presentation is essentially empirical in nature, in the interests of brevity the discussion of theoretical parameters and their uncertainty is left to others [c.f. (47, 48, 51, 104)].

4-2. ISOTOPE EFFECTS

The isotope effects exhibited by the three isotopic acid pairs RCH_2COOH/RCD_2COOH, R = Cl, PhO, and PhS, are compared in Table XXXI. These effects are larger than those measured by Scott and Barnes (38, 44) for the substituted phenylacetic acid pairs (R = C_6H_5, 4-MeO-C_6H_4 and 4-NO_2-C_6H_4) but are less than those reported by Streitweiser and Klein (32) and Bates et al. (40) for the acetic acid pair, CH_3COOH/CD_3COOH.

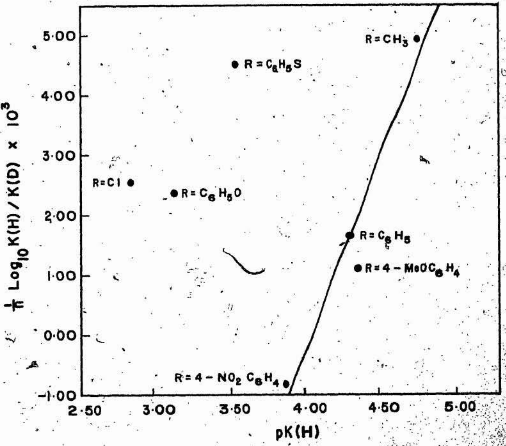
The isotopic ratios reported here are close to the K(H)/K(D) value of 1.02 predicted by the inductive treatment described above, but do not correspond to the inverse isotope effects predicted by Equation [12] for the correlation shown in Figure IV (see Figure IX). The influence of structural variation and the corresponding change in inductive effect on the isotopic ratios indicates that the simple inductive treatment is not an adequate model for the description of isotope effects. This is clearly evident since the model requires, to a first approximation, isotope effects to be independent of the nature of the substituent, i.e. constant with structural change, but the isotope effects reported here and elsewhere (38, 44) are in fact randomly influenced by structural changes.

Although in excellent internal agreement, the isotope effects computed using thermodynamic equilibrium constants derived from the Direct and Indirect Methods show greater

FIGURE IX

A PLOT OF $\frac{1}{n}\log_{10} K(H)/K(D)$ vs. pK(H) FOR THE ISOTOPICALLY SUBSTITUTED ACETIC ACID PAIRS RCH_2COOH/RCD_2COOH

The K(H) and K(D) values for R = CH_3 are taken from (40), the values for R = C_6H_5, 4-$MeOC_6H_4$, 4-$NO_2C_6H_4$ are taken from (44), and the values for R = C_6H_5O, C_6H_5S, Cl are taken from this work. The correlation shown in the Figure represents the linear free energy relationship given by Equation [12].



uncertainty than those calculated by isotopic slope comparison (see Table XXXI). The larger uncertainty associated with isotope effects calculated by the comparison of K_t values may be a consequence of the fact that the Direct and Indirect methods rely heavily on the accuracy of Λ_o.

An examination of Appendix III reveals that a change of 1 equivalent conductance unit in Λ_o will produce a change in slope which does not exceed 1%, but a similar examination of Appendix VI indicates that for the same change in Λ_o the corresponding change in K_t is to the order of 10%. The uncertainty of isotope effects derived from the appropriate K_t comparisons clearly must be greater than the uncertainty associated with those obtained from isotopic slope comparisons.

The uncertainty of the isotope effects derived from the Classical isotopic slopes appears to be comparable in size to the uncertainty associated with calculation by the Shedlovsky III Method, and less than the uncertainty attached to isotope effects obtained via the other methods. The reason for this is not easily discerned in view of the fact that ion activity and mobility effects are ignored in the correlation of the "Classical" variables $1/\Lambda$ and $\Lambda \cdot c$. However, the differences between the contributions of these small, but significant, effects to their respective isotopic slopes must be diminutive, since these differences only reflect the perturbation of isotopic substitution on ion activity and mobility. Although the influence of these isotopic differences on the slopes may not be negligible, the cancelling effect which occurs when the isotopic slopes are compared by ratio probably accounts for their disappearance.

A similar aspect of isotope effect calculation is presented when the same value of Λ_0 is utilized to process the concentration-equivalent conductance data of both protio and deutero acids by the Direct Methods, i.e. $\Lambda_0(H)$ and $\Lambda_0(D)$ are assumed equal. This value of Λ_0 need only be in the region of the true Λ_0 to yield an isotope effect equal, albeit less certain, to that obtained when an accurate value of Λ_0 is employed. Some justification of this empirical observation is offered in the following section.

4-3. THE EQUALITY OF $\Lambda_0(H)$ AND $\Lambda_0(D)$

The calculation of isotope effects by comparison of thermodynamic equilibrium constants, $K_t(H)/K_t(D)$, and isotopic slopes, $m_t(D)/m_t(H)$, relies heavily on the assumption that the limiting equivalent conductances of the protio acid and its isotopically substituted analogue are not significantly different, that is

[66] $$\Lambda_0(D)/\Lambda_0(H) \rightarrow 1$$

By the subtraction of $\Lambda_0(H^+)$ from Equation [66], the approximation may be reduced to a consideration of the isotopically substituted anions, given by

[67] $$\Lambda_0^-(D)/\Lambda_0^-(H) \rightarrow 1$$

This approximation is not without precedent, having been implicitly assumed by Streitweiser and Klein (32) in their consideration of the acetic acid isotopic pair. Robertson and co-workers (36, 43) have also presumably applied this approximation in their investigation of some isotopically substituted tetraalkylammonium ion pairs, as have Bell and Miller (131) in their study of the formic acid isotopic analogues. The isotope ratios reported by Streitweiser and by Bell are in excellent agreement with those determined by other empirical techniques

(40, 132). If Λ_o is a function of isotopic substitution, deuterium for hydrogen, then the limiting equivalent conductances of the CH_3COOH/CD_3COOH and $HCOOH/DCOOH$ acid pairs must be more significantly affected than the isotopically substituted acetic acids examined in the present work.

Nevertheless, by virtue of the diminutive nature of the isotope effects reported here, the assumption implied by Equation [67] necessitates closer scrutiny to insure the integrity of the isotope ratios. In the methods utilizing isotopic slope comparison, the isotope effect was given above as the ratio of Equations [51] and [52] which leads to

$$[68] \qquad \frac{K_t(H)}{K_t(D)} = \frac{m_t(D)\Lambda_o^2(D)}{m_t(H)\Lambda_o^2(H)}$$

where the parameters have their usual significance. Clearly, the uncertainty in the isotope effect is the product of the uncertainties in the ratio of isotopic slopes and the ratio of $[\Lambda_o(D)/\Lambda_o(H)]^2$. The validity of the real but small isotope effects reported here requires that the latter ratio be much closer to unity than the ratio of the isotopic slopes.

Scott <u>et al</u>. (38, 78, 133) have critically examined the approximation in Equation [67] by employing an approach of wider scope. They note that the effect of isotopic substitution on the limiting equivalent conductance of ions may be considered part of the more extensive problem of the variation of Λ_o with structural change.

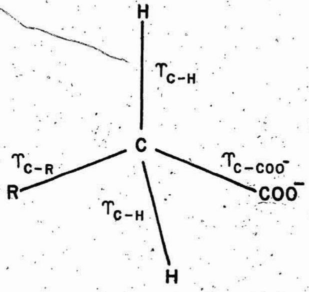
Although the effect of structural variation on the limiting equivalent conductance of simple spherical cations and anions appears complex (47), the problem has been broached by considering ion radius as the significant structural parameter (134, 135). This approach has been adopted by the sophisticated Fuoss-Boyd-Zwanzig theory (136) in the investigation of the hydrodynamic properties of spherical ions. This theory involves the assessment of ion-dipole interactions arising from the frictional forces created by the viscous and dielectric properties of the medium.

However, the molecular anions of the substituted acetic acids are not spherical in shape and hence cannot be adequately defined by an ion radius. The ion-dipole interactions must consequently be replaced by dipole-dipole interactions between the molecular anions and solvent. Differences in limiting equivalent conductance for the isotopically substituted anions would arise from differences in size between the H and D analogues and differences in dipole moments between C-H and C-D bonds.

Scott (133) has correlated the limiting equivalent conductances of some carboxylic anions of the type shown in Figure X with a parameter ($\overline{T}_m$) employed to define anion size (see Table

FIGURE X

A DIAGRAM OF THE TYPE OF CARBOXYLIC ACID ANION CONSIDERED IN EQUATION [69]



XXXVI). The T_m parameter is the mean of the bond distances of the groups tetrahedrally attached to the methylene carbon atom of the carboxylic acid anions, and is given by

$$[69] \qquad \overline{T}_m = \frac{2T_{C\text{-}H} + T_{C\text{-}COO^-} + T_{C\text{-}R}}{4}$$

The trend of the correlation between $\Lambda_0(RCH_2COO^-)$ and $\overline{T}_m$ shown in Figure XI clearly indicates a decrease in limiting equivalent conductance with increasing anion size. More explicitly, the slope of the correlation, -10.4 equivalent conductance units per Å, allows the estimation of the effect of isotopic substitution. Since C-D bonds are shorter than C-H bonds by 0.003 Å to 0.005 Å (139), then the difference in $\overline{T}_m$ between the RCH_2COO^- and RCD_2COO^- anion pairs, $\Delta\overline{T}_m$, will not exceed 2.5 x 10^{-3} Å. This change will yield a reduction of 0.026 equivalent conductance units for $\Lambda_0(D)$ compared to $\Lambda_0(H)$. If the protio compound has a limiting equivalent conductance in the region of 380 equivalent conductance units, then the $[\Lambda_0(D)/\Lambda_0(H)]^2$ ratio will differ from unity by ca. 0.014%. Since this value is small compared to the isotope effects reported for the three isotopic acid pairs, the requirement that $[\Lambda_0(D)/\Lambda_0(H)]^2$ be much closer to unity than $m_t(D)/m_t(H)$ is satisfied, i.e. the isotope effects calculated by isotopic slope comparison are real and significant.

TABLE XXXVI

$\overline{T}_m$ AND Λ_o VALUES FOR SOME CARBOXYLIC ACID ANIONS COMPILED BY SCOTT (133)

R IN RCH_2COO^- ANION	$\overline{T}_m(RCH_2COO^-)$*	$\Lambda_o(RCH_2COO^-)$**
H	1.36	40.9
Cl	1.54	39.8
CH_3	1.75	35.8
CH_3CH_2	2.13	32.6
C_6H_5	2.45	29.8

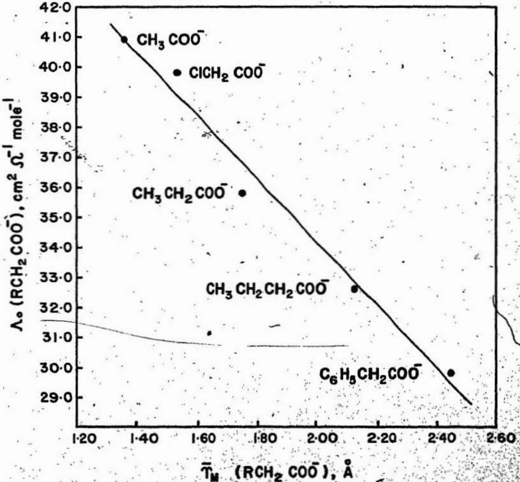
---

*$\overline{T}_m$ is computed from Equation [69]; all contributing bond distances are measured in Å and are taken from (137).

**Λ_o values have units of $cm^2\ \Omega^{-1}\ mole^{-1}$ and are taken from (138), with the exception of $\Lambda_o(C_6H_5CH_2COO^-)$ which is taken from (102).

FIGURE XI

THE CORRELATION OF Λ_0 AND $\bar{T}_m$ FOR SOME CARBOXYLIC ACID ANIONS [TAKEN FROM (133)]



4-4. SUMMARY

One of the original aims of the present study was to furnish further data which would describe the effects of structural variation on isotope effects. In a recent review by Thornton and Thornton (140) the effects of structural variation on isotope effects are regarded as important parameters in the comprehensive study of transition states. The results of the present work provide some base line data for equilibria, where the advantage of relatively well-defined states is in contrast to the speculative nature of transition states.

By way of summation, the following points emerge as important in the present study:

(1) In conjunction with the results of Scott and Barnes (38, 44), the present work clearly demonstrates the inadequacy of the simple inductive model in describing secondary isotope effects of the second kind. The isotope effects are not independent of substituent variation, and hence the requirement of the inductive model, namely that isotope effects remain constant with structural variation, is not satisfied.

(2) The trend of diminishing isotope effect per deuterium atom with increasing acidity correlated by Scott and Barnes (38, 44) appears coincidental for their results alone. The reasonably consistent correlation detailed by these authors requires that monosubstituted acetic acids with pK_a's less than 4 yield inverse isotope effects. The isotope effects reported here appear random

in this respect since these effects are larger than those described by Scott and Barnes (38, 44) but the acids themselves are stronger.

(3) The Shedlovsky III Method, which utilizes the comparison of the Shedlovsky slopes of isotopically substituted acid pairs $[m_t(D)/m_t(H)]$ to calculate isotope effects, is further tested in the present study. As in the earlier work of Barnes (44), the precision of this method of isotope effect calculation is demonstrated to be higher than the precision associated with those methods which rely on the direct comparison of thermodynamic equilibrium constants $[K_t(H)/K_t(D)]$. This method not only avoids the troublesome calculation of thermodynamic equilibrium constants, but also largely eliminates the uncertainty associated with cell constants and limiting equivalent conductance values.

(4) The Shedlovsky IV Method emerges as a useful alternative in the calculation of limiting equivalent conductances. Values of Λ_o determined by this method appear closer to Λ_o values from salt data than those calculated by the Indirect Methods. Theoretical justification of this method lies in the use of a linear least squares interpolation as opposed to the extrapolation techniques of the iterative methods.

In conclusion, it is worthy of note that this study and the earlier one of Barnes (44) were undertaken with the rather large isotope effect determined by Halevi (34) for the phenylacetic acid pair clearly in mind. That this effect of some 12% proved an order of magnitude too large in the light of repeated measurement is difficult to comprehend. The investigation of the isotope effects associated with the acids studied here and elsewhere (44, 104) became an order of magnitude more difficult, as the anticipated isotope effects of about 10% were actually of the order of 1%. Fortunately, the precision of the conductance technique was sufficiently high to partially accommodate the increased demand for accuracy.

The simple inductive model has obviously outgrown its utility in describing secondary isotope effects of the second kind. This, in conjunction with the fact that these isotope effects are not amenable to a linear free energy correlation, leads to the conclusion that any future investigations of these effects must find their theoretical justification based in a rigorous, statistical thermodynamic treatment which can account for frequency-force constant changes between the isotopic acid pairs and their related anions. Also, in view of the diminutive nature of these effects, future studies must be prepared to develop a technique of measurement which is sufficiently precise to allow the satisfactory detection of these effects.

PART II

CHAPTER 5

INTRODUCTION

5-1. ON THE ORIGIN OF THE MAGNETIC NONEQUIVALENCE OF THE METHYLENE PROTONS IN PHENYLSULFINYLACETIC ACID

A factor fundamental to the determination of accurate thermodynamic equilibrium constants by conductimetry is the integrity of the compounds investigated. Consequently, the preparation and purification of the acids and their suitability to conductimetric measurement have been given careful attention in the present study. The preparation of phenylsulfinylacetic-2,2-d_2 and phenylsulfonylacetic-2,2-d_2 acids was accomplished by proton-deuteron exchange at the methylene positions of these acids. The facility of this exchange in acidic deuterium oxide presented the possibility of rapid re-exchange (D → H) in water, which would clearly lead to erroneous conductance results for aqueous solutions of these acids. This possibility prompted further investigation of the exchange reactions which led to some novel observations concerning the chemical reactivity and magnetic nonequivalence of the methylene protons of phenylsulfinylacetic acid (111, 156).

The methylene protons of phenylsulfinylacetic acid and certain of its derivatives were observed to exhibit magnetic nonequivalence when dissolved in various solvents (see Tables XXXVII to XL). This magnetic nonequivalence arises as a consequence of the intrinsic asymmetry of the sulfoxide group adjacent to the methylene, and is displayed as a single AB quartet in the appropriate n.m.r. spectra. In other solvents, however,

TABLE XXXVII

THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF PHENYLSULFINYLACETIC ACID DISSOLVED IN VARIOUS SOLVENTS [TAKEN FROM (111)]

SOLVENT	CHEMICAL SHIFTS (τ)				J_{AB} (Hz)
	C_6H_5	H_A	H_B	CH_2*	
CF_3COOH	2.02 - 2.44	5.67	5.88	-	15.1
CF_3COOH/C_6H_6	-	6.36	6.51	-	15.0
CD_3COOD	2.09 - 2.51	5.88	6.02	-	14.9
CD_3COCD_3	2.09 - 2.49	-	-	6.09	-
D_2O **	2.42 - 2.50	-	-	6.16	-
CD_3SOCD_3	2.15 - 2.52	5.99	6.10	-	14.5

*The methylene protons appear as a singlet.

**The chemical shifts of all solutes in D_2O are not directly related to the τ-scale.

The asterisk and double-asterisk retain these meanings throughout the following tables.

TABLE XXXVIII

THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF PHENYLSULFINYLACETAMIDE DISSOLVED IN VARIOUS SOLVENTS [TAKEN FROM (111)]

SOLVENT	CHEMICAL SHIFTS (τ)			J_{AB} (Hz)
	C_6H_5	CH_2*	NH_2	
CF_3COOH	2.05 - 2.43	5.80	2.50 - 2.65	14.1
CF_3COOH/C_6H_5	- -	6.88	- -	14.0
CD_3COOD	2.13 - 2.53	6.03	2.13 - 2.53	-
CD_3SOCD_3	2.14 - 2.52	6.24	2.68 - 2.72	13.8

TABLE XXXIX

THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF SODIUM PHENYLSULFINYLACETATE AND POTASSIUM PHENYLSELENOXYACETATE DISSOLVED IN DEUTERIUM OXIDE [TAKEN FROM (111)]

COMPOUND	CHEMICAL SHIFTS (τ)			J_{AB} (Hz)
	C_6H_5	H_A	H_B	
$C_6H_5SOCH_2COONa$	2.24 - 2.53	6.05	6.26	14.0
$C_6H_5SeOCH_2COOK$	2.09 - 2.49	5.88	6.14	14.0

TABLE XL

THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN VARIOUS SOLVENTS [TAKEN FROM (111)]

SOLVENT	CHEMICAL SHIFTS (τ)					J_{AB} (Hz)
	C_6H_5	H_A	H_B	CH_2*	CH_3	
CF_3COOH	2.03 - 2.46	5.68	5.80	-	6.13	15.0
$CF_3COOH/C_6H_5NO_2$	-	5.77	5.91	-	6.27	14.6
$(CH_3)_3CCOOH$	2.17 - 2.65	6.08	6.18	-	6.44	14.0
CD_3COOD	2.12 - 2.50	5.89	6.08	-	6.33	14.0
$CDCl_3$	2.19 - 2.59	6.17	6.13	-	6.32	13.6
CH_2Cl_2	2.25 - 2.58	-	-	6.29	6.34	14.2
$C_6H_5NO_2$	-	-	-	6.13	6.34	-
C_6H_6	-	-	-	6.47	6.70	14.2
CCl_4	2.54 - 2.82	-	-	6.47	6.38	11.0
CD_3SOCD_3	2.12 - 2.50	5.90	6.08	-	6.36	14.0
Neat (135°)	2.20 - 2.61	-	-	6.15	6.41	-

the methylene protons appeared as a singlet, indicating their magnetic equivalence. These observations invoked a preliminary examination of some underlying factors which affect the nonequivalence of the methylene protons (111).

On the assumption that "staggered" conformations are more stable than "eclipsed" ones (141), the two enantiomers of phenylsulfinylacetic acid give rise to six rotamers which exist as three pairs of mirror-image conformers (see Figure XII). Theoretically, the methylene protons of each of the conformers are nonequivalent, even under conditions of rapid rotation and equal population (142, 143). Hence, the expected n.m.r. signal for the methylene protons of the six mirror-image conformers would be three AB quartets.

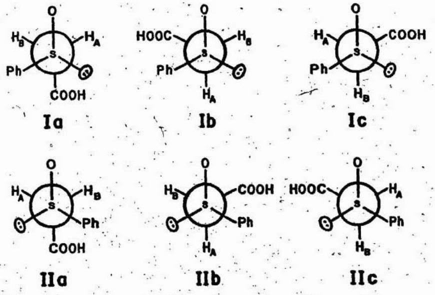
In contrast to the anticipated spectrum, however, only a single AB quartet is observed for the methylene protons of the phenylsulfinylacetic acid conformers in acidic solvents, e.g. trifluoroacetic acid, and in dimethyl sulfoxide-d_6. Moreover, the effective nonequivalence of the observed methylene proton chemical shifts in these solvents is large relative to their apparent equivalence when the acid is solvated by deuterium oxide and acetone-d_6 (see Table XXXVII).

The observation of only a single AB quartet for the methylene protons of the conformers may be explained by one of the following (144):

(1) The energy difference between the conformers of long

FIGURE XII

NEWMAN PROJECTION DIAGRAMS (VIEWED ALONG THE S-C BOND) OF THE THREE PAIRS OF MIRROR-IMAGE CONFORMERS* FOR THE TWO PHENYLSULFINYLACETIC ACID ENANTIOMERS



Ia Ib Ic

IIa IIb IIc

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*Conformers Ia and IIa, Ib and IIb, Ic and IIc are mirror images. The methylene protons are arbitrarily designated as H_A and H_B.

lifetime is so large that only the most stable is present.

(2) An equilibrium exists between the conformers in which each conformer is sufficiently long-lived and abundant to give its own n.m.r. spectrum. That the observed spectrum shows only a single AB quartet implies the spectrum of any one of the conformers is the same as that of any other. The observed spectrum then is a simple superposition which represents all the conformers.

(3) Internal rotation of the methylene group and/or inversion of the electron lone pair at sulfur occur at a sufficiently rapid rate for the effective chemical shifts (screening) and the spin coupling constants to be averaged.

The effective nonequivalence of the methylene protons of phenylsulfinylacetic acid in any solvent at a given temperature is a function of the relative populations of the conformers such that

[70] $$\langle \delta H_A \text{ effective} \rangle = P_1 \delta H_{A_1} + P_2 \delta H_{A_2} + P_3 \delta H_{A_3}$$

[71] $$\langle \delta H_B \text{ effective} \rangle = P_1 \delta H_{B_1} + P_2 \delta H_{B_2} + P_3 \delta H_{B_3}$$

[72] $$\langle (\delta H_A - \delta H_B) \text{ effective} \rangle = P_1(\delta H_{A_1} - \delta H_{B_1}) + P_2(\delta H_{A_2} - \delta H_{B_2}) + P_3(\delta H_{A_3} - \delta H_{B_3})$$

where δH_{A_n} and δH_{B_n} are the respective chemical shifts of the methylene protons of conformer n, $<(\delta H_A - \delta H_B)_{effective}>$ is the observed nonequivalence, and P_1, P_2, and P_3 are the fractional populations of the conformers.

The large effective nonequivalence of the methylene protons displayed when the acid is solvated by acidic solvents or dimethyl sulfoxide-d_6 relative to their apparent equivalence in deuterium oxide and acetone-d_6 (see Table XXXVII) is not readily explained, but may lie in a consideration of the following possibilities:

(1) The nonequivalence of the methylene protons is a consequence of the intrinsic asymmetry of the adjacent sulfoxide group and it may be differentially enhanced by changes in magnetic anisotropy incurred from solute-solvent interactions at specific sites on the solute molecule.

(2) The populations of the three conformers in deuterium oxide and acetone-d_6 may be such that the effective nonequivalence of H_A and H_B appears small, due to a cancelling effect in the terms of the averaged sum {see Equation [72]}. However, specific solute-solvent interactions, which may exist when phenylsulfinylacetic acid is dissolved in acidic media (or dimethyl sulfoxide-d_6), could favour a particular conformer. These interactions could also restrict internal rotation and inversion at sulfur, such that interconversion between the conformers is inhibited. Hence, the cancelling effect exhibited in deuterium oxide and acetone-d_6 may be reduced in acidic media

and dimethyl sulfoxide-d_6 as a consequence of altered conformer populations.

(3) The inherent asymmetry of the sulfoxide group may be destroyed by the formation of symmetrical solute dimers in deuterium oxide and acetone-d_6 in which the methylene protons experience similar or equivalent magnetic environments [c.f. (145)]. Also, solvation by the addition of deuterium oxide may destroy the inherent asymmetry of the sulfoxide group in much the same manner as water is purported to do in the case of analogous selenium and tellurium compounds (146).

The n.m.r. spectra of phenylsulfinylacetamide dissolved in various solvents (see Table XXXVIII) are similar to those of phenylsulfinylacetic acid in deuterium oxide and acetone-d_6. The AB quartet of the methylene protons is unresolved and appears as a singlet, but coupling between H_A and H_B in trifluoroacetic acid (J_{AB} = 14.1 Hz) and dimethyl sulfoxide-d_6 (J_{AB} = 13.8 Hz) is evident.

For the methylene protons of sodium phenylsulfinylacetate dissolved in deuterium oxide at 40°C, the effective nonequivalence is 9.7 Hz (see Table XXXIX). About 94% of the acid is undissociated* in deuterium oxide, but the sodium salt is assumed to be present as ions. The chemical shifts of the

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*Based on pK_a = 2.66 in H_2O (46).

methylene protons in both the acid and the sodium salt are dependent upon the electronic configuration of the solvated species, and the negative charge of the phenylsulfinylacetate anion will certainly perturb the electronic configuration. Hence, any comparison of the nonequivalence of the methylene protons in the acid and sodium salt is not strictly valid. The phenylsulfinylacetate anion could well be a "structure maker" in aqueous solution, analogous to the acetate ion (147) which has a Bingham value* of -21.4. This implies that the phenylsulfinylacetate anion is bound by a more rigid solvent shell in deuterium oxide than the undissociated acid.

The temperature dependence of the chemical shifts for H_A and H_B of sodium phenylsulfinylacetate in deuterium oxide was examined to provide additional information about the solvation of the anion (see Table XLI and Figure XIII). If conformational interconversion is rapid, the chemical shifts for H_A and H_B will be averaged as shown by Equations [70], [71] and [72]; and if the conformers have different energies, the ratio of $P_1:P_2:P_3$ will be given by

$$[73] \quad P_1:P_2:P_3 = a_1e^{-E_1/kT} : a_2e^{-E_2/kT} : a_3e^{-E_3/kT}$$

---

*A measure of molal fluidity elevations of ions proposed by E.C. Bingham (148).

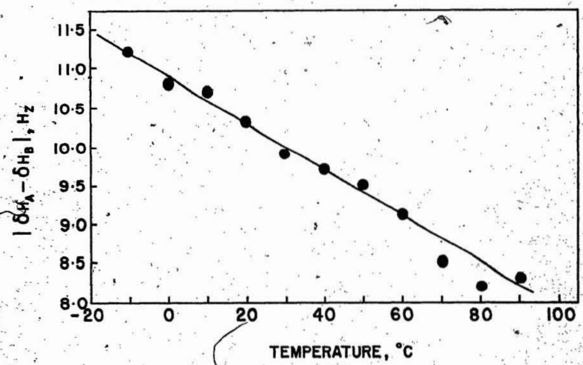
TABLE XLI

THE VARIATION OF THE CHEMICAL SHIFTS FOR THE METHYLENE PROTONS OF SODIUM PHENYLSULFINYLACETATE (30 ± 1% BY WEIGHT IN DEUTERIUM OXIDE) WITH TEMPERATURE [TAKEN FROM (111)]

TEMPERATURE, ^{o}C	$\lvert \delta H_A - \delta H_B \rvert$, Hz
90	8.3
80	8.2
70	8.5
60	9.1
50	9.5
40	9.7
30	9.9
20	10.3
10	10.7
0	10.8
-10	11.2

FIGURE XIII

THE VARIATION OF $|\delta H_A - \delta H_B|$ WITH TEMPERATURE IN A DEUTERIUM OXIDE SOLUTION OF SODIUM PHENYLSULFINYLACETATE [TAKEN FROM (111)]



where a_1, a_2 and a_3 are usually different for each of the conformers, and will be only slightly temperature dependent. Thus, since the effective chemical shifts of H_A and H_B are temperature dependent, i.e., nonequivalence changes with temperature, then conformational interconversion is indicated (144).*

The adoption of a single, favoured conformation by the anion in aqueous media is not unreasonable. The favoured conformer clearly would be the one in which the repulsive tendency between the electron lone pair on sulfur and the negatively charged carboxylate oxygen is satisfied by maximum separation. This additional barrier to conformational interconversion, by internal rotation and/or inversion, provides some explanation of the large effective nonequivalence exhibited by the methylene protons of the aqueous anion relative to their apparent equivalence in aqueous solutions of the largely undissociated acid. Clearly, the barrier to conformational interconversion would be less in the case of the acid, as evidenced by the apparent equivalence of the methylene protons due to chemical shift averaging (see above, p. 149).

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*More detailed analyses of solvent effects on analogous systems have been discussed by Nishio (149, 150, 151, 152) and more generally by Roberts et al. (153).

The spectral temperature dependence of the effective nonequivalence of the methylene protons in the aqueous anion may also be a consequence of specific solute-solvent interactions. If the intrinsic asymmetry of the anion is small, then the large effective nonequivalence exhibited by the methylene protons could result from enhancement of the anion asymmetry by solvation at specific sites. As the temperature is increased these solute-solvent interactions would be diminished, and the effective nonequivalence of the methylene protons would approach a minimum.

The n.m.r. spectra of methyl phenylsulfinylacetate (see Tables XL and XLII to XLVII) indicate that the effective chemical shifts of H_A and H_B, the methylene protons, are very sensitive to the nature of the solvent and the solute-solvent ratio but are only slightly affected by temperature changes.

The significance of specific solvent-solute interactions on the effective chemical shifts of the methylene protons of the ester dissolved in pivalic acid is demonstrated by the fact that magnetic nonequivalence is exhibited only when the mole ratio of solvent to solute is 2:1 or greater. This does not preclude the formation of symmetrical solute dimers at high concentration, but in view of the absence of spectral temperature dependence, dimerization appears unlikely and rapid interconversion of the rotamers is indicated.

TABLE XLII

THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE

(30 ± 2% BY WEIGHT) DISSOLVED IN ACETIC ACID-d_4 [TAKEN FROM (111)]

TEMPERATURE (°C)	CHEMICAL SHIFTS (τ)				J_{AB} (Hz)
	C_6H_5	H_A	H_B	CH_3	
43	2.13 - 2.50	5.90	6.08	6.33	14.2
60	2.13 - 2.52	5.92	6.05	6.33	14.0
80	2.12 - 2.52	5.93	6.05	6.33	14.0
100	2.11 - 2.53	5.93	6.07	6.32	14.0

TABLE XLIII

THE CHEMICAL SHIFTS, COUPLING CONSTANTS, AND DIFFERENCES BETWEEN THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN PIVALIC ACID AT 55°C [TAKEN FROM (111)]

$(CH_3)_3COOH$	$C_6H_5SOCH_2COOCH_3$	MOLE RATIO	CHEMICAL SHIFTS (τ)			$\lvert\delta H_A - \delta H_B\rvert$	J_{AB} (Hz)
MOLES x 10^{-4}, (X)	MOLES x 10^{-4}, (Y)	X/Y	H_A	H_B	CH_2*	(Hz)	
45.06	2.52	17.9	5.95	6.20	-	15.0	14.0
39.16	5.04	7.8	5.99	6.18	-	11.3	13.9
34.27	7.57	4.5	6.00	6.16	-	9.5	13.5
29.37	10.09	2.9	5.99	6.12	-	7.7	13.7
24.48	12.60	1.9	6.08	6.17	-	5.4	14.0
19.58	15.13	1.3	-	-	6.10	-	14.0
14.69	17.65	0.83	-	-	6.07	-	14.0
9.79	20.18	0.49	-	-	6.05	-	14.0
4.90	22.70	0.22	-	-	6.06	-	14.0

TABLE XLIV

THE CHEMICAL SHIFTS, COUPLING CONSTANTS, AND DIFFERENCES BETWEEN THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN PIVALIC ACID AT 65°C

[TAKEN FROM (111)]

$(CH_3)_3CCOOH$	$C_6H_5SOCH_2COOCH_3$	MOLE RATIO	CHEMICAL SHIFTS (τ)			$\|\delta H_A - \delta H_B\|$	J_{AB} (Hz)
MOLES x 10^{-4}, (X)	MOLES ~~x 10^{-4}~~, (Y)	X/Y	H_A	H_B	CH_2*	(Hz)	
45.06	2.52	17.9	5.96	6.21	-	15.1	13.9
39.16	5.04	7.8	5.94	6.13	-	11.4	14.2
34.27	7.57	4.5	6.00	6.16	-	9.4	14.0
29.37	10.09	2.9	6.05	6.18	-	7.8	14.0
24.48	12.60	1.9	-	-	6.09	-	14.2
19.58	15.13	1.3	-	-	6.10	-	14.1
14.69	17.65	0.83	-	-	6.09	-	14.0
9.79	20.18	0.49	-	-	6.09	-	14.0
4.90	22.70	0.22	-	-	6.09	-	14.1

TABLE XLV

THE CHEMICAL SHIFTS, COUPLING CONSTANTS, AND DIFFERENCES BETWEEN THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN PIVALIC ACID AT 75°C

[TAKEN FROM (111)]

$(CH_3)_3COOH$	$C_6H_5SOCH_2COOCH_3$	MOLE RATIO	CHEMICAL SHIFTS (τ)			$\|\delta H_A - \delta H_B\|$	J_{AB} (Hz)
MOLES x 10^{-4}, (X)	MOLES x 10^{-4}, (Y)	X/Y	H_A	H_B	CH_2*	(Hz)	
45.06	2.52	17.9	5.97	6.22	-	14.6	14.0
39.16	5.04	7.8	6.00	6.19	-	11.3	14.0
34.27	7.57	4.5	6.00	6.16	-	9.7	14.0
29.37	10.09	2.9	6.03	6.16	-	7.8	14.0
24.48	12.60	1.9	-	-	6.10	-	14.0
19.58	15.13	1.3	-	-	6.09	-	14.0
14.69	17.65	0.83	-	-	6.09	-	-
9.79	20.18	0.49	-	-	6.10	-	-
4.90	22.70	0.22	-	-	6.09	-	-

TABLE XLVI

THE CHEMICAL SHIFTS, COUPLING CONSTANTS, AND DIFFERENCES BETWEEN THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN PIVALIC ACID AT 85°C

[TAKEN FROM (111)]

$(CH_3)_3COOH$ MOLES x 10^{-4}, (X)	$C_6H_5SOCH_2COOCH_3$ MOLES x 10^{-4}, (Y)	MOLE RATIO X/Y	CHEMICAL SHIFTS (τ)			$\lvert \delta H_A - \delta H_B \rvert$ (Hz)	J_{AB} (Hz)
			H_A	H_B	CH_2*		
45.06	2.52	17.9	6.00	6.23	-	13.9	14.0
39.16	5.04	7.8	5.99	6.18	-	11.2	14.0
34.27	7.57	4.5	6.03	6.19	-	9.7	13.9
29.37	10.09	2.9	6.06	6.20	-	8.2	13.8
24.48	12.60	1.9	-	-	6.09	-	13.9
19.58	15.13	1.3	-	-	6.09	-	14.0
14.69	17.65	0.83	-	-	6.09	-	-
9.79	20.18	0.49	-	-	6.09	-	-
4.90	22.70	0.22	-	-	6.09	-	-

TABLE XLVII

THE CHEMICAL SHIFTS, COUPLING CONSTANTS, AND DIFFERENCES BETWEEN THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF METHYL PHENYLSULFINYLACETATE DISSOLVED IN PIVALIC ACID AT 95°C

[TAKEN FROM (111)]

$(CH_3)_3COOH$	$C_6H_5SOCH_2COOCH_3$	MOLE RATIO	CHEMICAL SHIFTS (τ)			$\lvert\delta H_A - \delta H_B\rvert$	J_{AB} (Hz)
MOLES x 10^{-4}, (X)	MOLES x 10^{-4}, (Y)	X/Y	H_A	H_B	CH_2*	(Hz)	
45.06	2.52	17.9	6.00	6.23	-	13.9	14.0
39.16	5.04	7.8	6.02	6.21	-	11.9	14.0
34.27	7.57	4.5	6.04	6.20	-	9.8	14.0
29.37	10.09	2.9	6.05	6.18	-	7.7	13.9
24.48	12.60	1.9	6.09	6.18	-	5.6	13.5
19.58	15.13	1.3	-	-	6.11	-	13.5
14.69	17.65	0.83	-	-	6.11	-	13.9
9.79	20.18	0.49	-	-	6.10	-	-
4.90	22.70	0.22	-	-	6.09	-	-

In summary, although comparisons of the chemical shifts of the methylene protons of phenylsulfinylacetic acid with those of its amide, methyl ester and sodium salt may not be strictly valid, a generality of their collective magnetic behaviour appears to be that the effective nonequivalence of the methylene protons in each is a function of solute-solvent interactions. The major influence of these interactions is summarized in the following two considerations:

(1) The intrinsic asymmetry of the acid and its derivatives, which may be inherently small [c.f. (154)], is enhanced by specific solute-solvent interactions. This solvation almost certainly lends greater asymmetry to the solute and the resulting changes in magnetic anisotropy are evidenced by corresponding changes in the effective nonequivalence of the methylene protons.

The apparent equivalence of the methylene protons of the acid dissolved in various solvents (acetone-d_6, chloroform-d, benzene-d_6, carbon tetrachloride) is then explained by small solute-solvent interactions which cause no appreciable enhancement of the magnetic anisotropy of the solute and hence the methylene protons appear equivalent.

The apparent equivalence of the methylene protons of the acid dissolved in deuterium oxide, however, is not easily explained in terms of small solute-solvent interactions. Although dimerization has been postulated in other sulfoxide systems (155) to account for the disappearance of magnetic nonequivalence in deuterium oxide, the collapse of the AB quartet n.m.r. signal for the methylene protons may be a consequence of specific solvation which destroys the inherent asymmetry of the sulfoxide group [c. f. (146)].

In view of the insignificant spectral changes with corresponding changes in temperature and concentration, the formation of dimers of the acid (trifluoroacetic acid, acetic acid, and dimethyl sulfoxide-d_6 solutions) appears unlikely. The large effective nonequivalence of the methylene protons of the acid in these solvents is amenable to the generality of increased magnetic anisotropy through solute-solvent interactions*.

(2) The effective nonequivalence of the methylene protons of phenylsulfinylacetic acid and its derivatives is also a function of the relative populations of conformers. The relative populations are in turn dependent upon the barriers to conformational interconversion, and the differences between the respective barriers are undoubtedly influenced by solute-solvent interactions. Since conformational interconversion occurs through

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*These interactions presumably take the form of hydrogen bonding, and although the absence of spectral temperature dependence in the effective nonequivalence of the methylene protons does not preclude the formation of hydrogen bonds, any such bonds formed must be exceptionally strong.

internal rotation and inversion at sulfur, the differences in the rates of these processes must in part be governed by solute-solvent interactions.

This concept is supported by the large effective nonequivalence displayed in highly acidic media and dimethyl sulfoxide-d_6 and the apparent equivalence of the methylene protons in solvents of lower dielectric and hydrogen bonding capacity. Solute-solvent interactions presumably are stronger and more specific in the former than in the latter, and hence increase the barriers to conformational interconversion by inhibiting internal rotation and inversion at sulfur.

5-2. PROTON-DEUTERON EXCHANGE REACTIONS OF PHENYLSULFINYLACETIC ACID

Phenylsulfinylacetic acid-2,2-d_2 has been prepared and a qualitative kinetic investigation of the deuteron to proton re--exchange process at the methylene position of the acid has been examined (156). The n.m.r. spectra of the recovered samples in moist trifluoroacetic acid and dimethyl sulfoxide-d_6 revealed four peaks appropriate to the methylene protons of the protium acid together with two further relatively broad singlets close to, but which did not exactly correspond with, the shifts of the methylene protons of the protium acid (see Figure XIV). The magnitude of the latter varied with time, reaching a maximum and then diminishing as the conversion of the deuterated acid to the protium acid progressed. These two broad absorptions were assigned to the six rotamers of the two diastereoisomers (see Figure XV) formed in the exchange.

Theoretically, six different absorptions should appear for the diastereotopic protons of the rotamers, but only two peaks were observed. This observation is similar to that for the solvated protium acid. The two observed peaks are broadened, presumably by unresolved (triplet) coupling to deuterium in each case, and the unequal magnitude of the two peaks has been ascribed in analogous cases to differing exchange rates for the two methylene deuterons (157).

FIGURE XIV

PORTIONS OF N.M.R. SPECTRA OF PARTIALLY RE-EXCHANGED

PHENYLSULFINYLACETIC-2,2-d_2 ACID AT VARIOUS TIMES

[TAKEN FROM (111)]

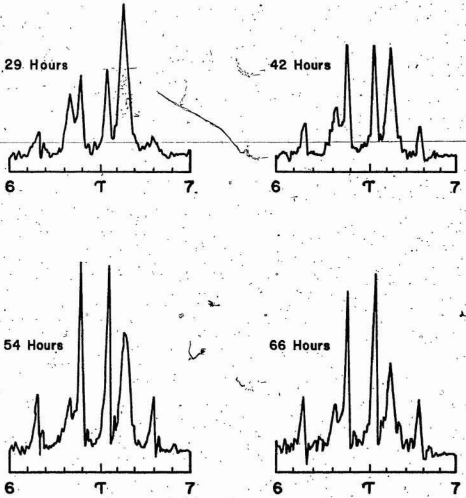
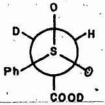
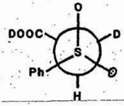


FIGURE XV

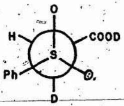
NEWMAN PROJECTION DIAGRAMS (VIEWED ALONG THE S-C BOND) OF SIX DIFFERENT ROTAMERS OF THE TWO PHENYLSULFINYLACETIC-2-d ACID DIASTEREOISOMERS [TAKEN FROM (111)]



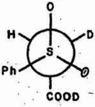
Ia



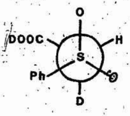
Ib



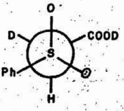
Ic



IIa



IIb



IIc

Rauk, Wolfe, Buncel, and Moir (158, 159) have reported similar observations concerning the reactivity of the methylene protons of benzyl methyl sulfoxide towards isotopic exchange in 1M NaOD/D_2O, and have shown that the methylene protons in this compound differ in reactivity by about a factor of fourteen. The differences in the chemical shifts and the coupling constants for the methylene protons were similar in phenylsulfinylacetic acid and benzyl methyl sulfoxide, and the only significant factor which influenced the observation of the diastereoisomers by n.m.r. was the relative rates of exchange of the two protons or deuterons (156). It was consequently concluded that the methylene protons of phenylsulfinylacetic acid in acidic aqueous media are closer in reactivity than those of benzyl methyl sulfoxide in 1M NaOD/D_2O, since both the diastereoisomers were observed with the former compound, whereas only one absorption representing the diastereotopic proton was observed in the case of benzyl methyl sulfoxide.

An explanation of the preferential exchange process of the methylene protons of benzyl methyl sulfoxide has been offered by Wolfe et al. (158, 159). From dipole moment studies and n.m.r. considerations these workers concluded that the conformation displayed in Figure XVI is favoured in both nonpolar and polar solvents and that H_A is stereospecifically exchanged. This conclusion was further augmented by MO calculations put forward by Wolfe, Rauk and Csizmadia (160) on the relative stability of the

FIGURE XVI

A NEWMAN PROJECTION DIAGRAM OF BENZYL METHYL SULFOXIDE VIEWED ALONG THE C-S BOND

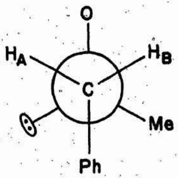
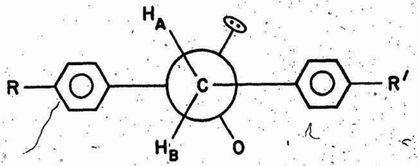


FIGURE XVII

A NEWMAN PROJECTION DIAGRAM OF R'-BENZYL R-PHENYL SULFOXIDE VIEWED ALONG THE C-S BOND



hypothetical carbanion $^{(-)}CH_2$-SO-H. They concluded that the most stable conformation is that with the carbon lone pair orbital gauche to both the sulfoxide-oxygen bond and the sulfur lone pair. Another energy minimum occurred for the carbon lone pair trans to the sulfoxide-oxygen bond and gauche to the sulfur lone pair, but the conformation in which the carbon lone pair is trans to both the sulfoxide-oxygen bond and the sulfur lone pair occurred at an energy maximum. In a further work of wider scope, Wolfe (161) has enunciated a generality which states,"in agreement with the predictions of ab initio molecular orbital calculations, but not with current qualitative and phenomenological concepts, such species exhibit a 'gauche effect', i.e., a tendency to adopt that structure which has the maximum number of gauche interactions between the adjacent electron pairs and/or polar bonds".

Nishio (149, 150, 151, 152) has reported that in compounds of the type R-C_6H_4-SO-CH_2-C_6H_4-R' the proton which is trans to the sulfur lone pair and gauche to the sulfoxide-oxygen bond is less sensitive to change in the electronegativity of the R' substituent than the proton which is cis to the sulfur lone pair. The chemical shift of the proton trans to the sulfur lone pair (H_B) is also more sensitive to acidic solvation, as shown in Figure XVII. From an examination of the stereochemistry and differential solvent effects on the n.m.r. spectra of these types of compounds, Nishio has attempted to unambiguously assign the methylene protons and has predicted that H_B, the proton *gauche* to the sulfoxide-oxygen bond and *trans* to the sulfur lone pair, is preferentially exchanged.

Hutchinson, Andersen, and Katritzky (162) have examined the base-catalyzed hydrogen-deuterium exchange of the α-sulfinyl protons in the conformationally rigid *cis*- and *trans*-4-phenyltetrahydrothiopyran-1-oxides. The order of increasing proton acidity adjacent to a sulfinyl group was concluded to be (a) *trans* to the sulfur-oxygen bond and *gauche* to the sulfur lone pair, (b) *gauche* to the sulfur-oxygen bond and to the sulfur lone pair, and (c) *gauche* to the sulfur-oxygen bond and *trans* to the sulfur lone pair.

This order of acidity is not in agreement with the conclusions of Nishio and only partially confirms the theoretical arguments of Wolfe, Rauk and Csizmadia (160, 163, 164)*. Katritzky and co-workers agree there are two possible energy minima, but that the order of acidity of the α-sulfinyl protons postulated by Wolfe *et al.* for these minima should be interchanged, i.e., the "fast-exchange" proton is located *trans* to the sulfur-oxygen bond and *gauche* to the sulfur lone pair, rather than *gauche* to both the asymmetric contributors.

In a study concurrent with that of Katritzky and co-workers, Baldwin, Hackler, and Scott (165) have reported that deuterium

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*See, however, the later comments of Wolfe *et al.* (166).

exchange of the kinetically more labile proton in (S)-benzyl methyl sulfoxide yields the (R)-configuration at the benzylic carbon atom, an observation opposite to that of Wolfe *et al*. The results of Baldwin, Hackler, and Scott appear to confirm the observations of Katritzky and co-workers, in that the more labile proton of the methylene group in benzyl methyl sulfoxide is apparently *gauche* to the sulfur-oxygen bond and *trans* to the sulfur lone pair.

In view of the above, speculation might lead to the conclusion that the more labile proton of the methylene group of phenylsulfinylacetic acid is *gauche* to the sulfur-oxygen bond and *trans* to the sulfur lone pair. However, the exchange process has thus far only been considered as a pseudo-first order reaction in alkaline media (166), in which the formation of the most stable carbanion represents the least energetic transition state on the potential energy pathway. Wolfe, Rauk and Csizmadia (160, 163, 164) have based their *ab initio* MO calculations on unsolvated species and Katritzky *et al*. (162) have only considered solvation in a general qualitative statement. In the case of the hydrogen-deuterium exchange reaction at the methylene group of phenylsulfinylacetic acid this simple approach to the reaction may not be entirely justified, since specific solvent participation in the reaction is possible (145, 146) and may be indicated by the following:

(1) The apparent equivalence of the methylene protons when phenylsulfinylacetic acid is dissolved in water may indicate the formation of a solvated species in which the intrinsic asymmetry of the sulfoxide group is destroyed.

(2) The difference in the rates of exchange of the two methylene protons appears much smaller for phenylsulfinylacetic acid than for those of sulfoxides previously reported. This may reflect a simple dependence upon the acidity of the exchange media but does not exclude specific deuteron/deuterium oxide participation.

5-3. N.M.R. SPECTRA OF PARTIALLY EXCHANGED PHENYLSULFINYLACETIC ACID

From an examination of n.m.r. spectra of partially exchanged phenylsulfinylacetic acid, it has been noted that the shifts of the two broad peaks representing the phenylsulfinylacetic-2-d acid diastereoisomers are interchanged when dissolved in dimethyl sulfoxide-d_6 relative to their positions in trifluoroacetic acid (156). This change in position was evident since the shifts were of unequal magnitude, a consequence of unequal reactivity. N.m.r. measurements on solutions of phenylsulfinylacetic acid in varying amounts of trifluoroacetic acid and dimethyl sulfoxide-d_6 were recorded (see Table XLVIII and Figure XVIII), and the following were proposed to account for the observed phenomenon:

(1) The chemical shifts of H_A and H_B actually coalesce, cross, and then interchange positions as the amount of one solvent (CF_3COOH) increases relative to the amount of the other (CD_3SOCD_3). This "crossing" of chemical shifts may result from the change of one preferred conformer in CF_3COOH to another in CD_3SOCD_3. Although equivalence of H_A and H_B is theoretically impossible, coincidental equivalence of H_A and H_B may occur due to a cancelling effect in the n.m.r. signal {see Equation [72]} as the relative populations of the conformers are altered by a gradual change in solvation.

(2) The chemical shifts of H_A and H_B are interchanged in trifluoroacetic acid relative to their positions in dimethyl sulfoxide-d_6 due to specific solvation differences which result

TABLE XLVIII

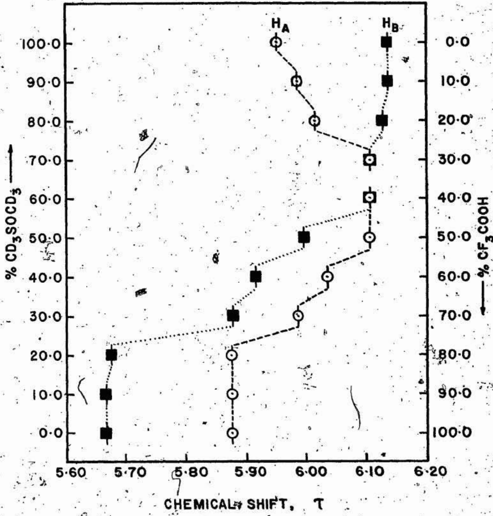
THE CHEMICAL SHIFTS AND COUPLING CONSTANTS OF THE METHYLENE PROTONS OF PHENYLSULFINYLACETIC ACID (25 ± 1% BY WEIGHT) DISSOLVED IN MIXTURES OF TRIFLUOROACETIC ACID AND DIMETHYL SULFOXIDE-d_6 [TAKEN FROM (111)]

SOLVENT COMPOSITION			CHEMICAL SHIFTS (τ)			
%CD_3SOCD_3	%CF_3COOH	MULTIPLICITY	H_A	H_B	CH_2*	J_{AB} (Hz)
100	0	quartet	5.96	6.14	-	14.2
90	10	quartet	5.99	6.14	-	14.2
80	20	quartet	6.02	6.13	-	14.2
70	30	singlet	-	-	6.11	14.2
60	40	singlet	-	-	6.11	-
50	50	quartet	6.00	6.11	-	14.1
40	60	quartet	5.92	6.04	-	14.1
30	70	quartet	5.88	5.99	-	14.0
20	80	quartet	5.68	5.88	-	15.2
10	90	quartet	5.67	5.88	-	15.1
0	100	quartet	5.67	5.88	-	15.1

FIGURE XVIII

THE CHEMICAL SHIFTS OF THE METHYLENE PROTONS OF PHENYLSULFINYLACETIC ACID IN MIXTURES OF TRIFLUOROACETIC ACID AND DIMETHYL SULFOXIDE-d_6

[TAKEN FROM (111)]



in different magnetic anisotropies for each of the solvated species. Assuming that dimethyl sulfoxide-d_6 is more "basic" than phenylsulfinylacetic acid, solute-solute and solute-solvent interactions, in the form of intramolecular and intermolecular hydrogen bonding [c.f. Pasto et al. (45, 113)], may well be significant in the molecular description of the solute in this solvent.

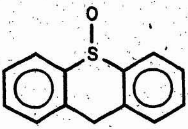
As the concentration of trifluoroacetic acid is increased in a solution of phenylsulfinylacetic acid and dimethyl sulfoxide-d_6, the latter may be removed from the sphere of solvation. As this occurs the observed differences in the chemical shifts of H_A and H_B will tend to a minimum, exhibiting apparent coalescence if the asymmetric contribution of the sulfoxide group is inherently small [c.f. (154)]. At this point the phenylsulfinylacetic acid is presumably solvated by a trifluoroacetic acid-dimethyl sulfoxide-d_6 complex, which must be quite different in magnetic susceptibility and dipole moment than either of the parent solvents.

As the trifluoroacetic acid becomes more abundant than the dimethyl sulfoxide-d_6, specific solvation of undissociated phenylsulfinylacetic acid by the former predominates, and probably takes the form of hydrogen bonding to the carboxylate and sulfoxide oxygens as described by Oae et al. (145). Hence, the apparent coalescence disappears and the chemical shifts of H_A and H_B exhibit nonequivalence relevant to their new molecular environments.

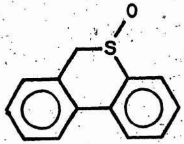
Further investigation of this "chemical shift interchange" effect due to solvation is attempted in the present work through the syntheses and partial proton-deuteron exchange of two conformationally restricted sulfoxides, namely thioxanthene-10-oxide and 9-thia-9,10-dihydrophenanthrene-9-oxide (see Figure XIX).

FIGURE XIX

TWO CONFORMATIONALLY RESTRICTED SULFOXIDES



thioxanthene-10-oxide



9-thia-9,10-dihydrophenanthrene-9-oxide

CHAPTER 6

EXPERIMENTAL

6-1. INSTRUMENTATION

Nuclear magnetic resonance (n.m.r.) spectra were recorded on Varian A-60 and HA-100 instruments at 60 MHz and 100 MHz respectively, with probe temperatures ca. 40°C unless otherwise specified. Chemical shifts are reported on the τ scale, i.e., relative to the internal standard signal of tetramethylsilane. Infrared (i.r.) spectra were recorded on Perkin-Elmer 237B or 225 spectrometers. Each i.r. spectrum was calibrated against a portion of a polystyrene spectrum. An Hitachi/Perkin-Elmer RMU-6E mass spectrometer recorded the mass spectra (m.s.) at an ionization voltage of 70 ev. Gas-liquid chromatographic (g.l.c.) analyses were carried out on a Beckman GC-2A instrument with a Carbowax-4000 dioleate column (2.5 ft) at 190°C with 20 lb per in^2 pressure of helium carrier gas. Melting points (m.p.) were determined on a Fisher-Johns melting point apparatus. Melting points and boiling points (b.p.) are uncorrected. Chemical microanalyses were carried out by the Alfred Bernhardt Mikroanalytisches Laboratorium, West Germany.

6-2. MATERIALS

o-Nitrobenzyl phenyl sulfide. - Sodium (17.2 g; 0.747 mole) was dispersed in anhydrous xylene (500 ml), and thiophenol (88 g; 0.800 mole) was added dropwise to the refluxing solution. After the complete evolution of hydrogen, the solution was allowed to cool slightly below the reflux temperature, and a mixture* of o- and p-nitrobenzyl chlorides (125 g; 0.729 mole; technical grade) in anhydrous xylene (400 ml) was added dropwise over 1 h. After the exothermic reaction was complete, the hot solution was filtered immediately.

The residue was washed with diethyl ether (100 ml), and solvents were removed from the respective filtrates by distillation under reduced pressure. The reddish-brown residues were combined and taken up in hot absolute ethanol. On cooling, yellow plates (152.1 g; 85.2% yield) of o- and p-nitrobenzyl phenyl sulfides crystallized. The product was recrystallized four times from absolute ethanol, m.p. 64-65°C [lit. m.p. 64°C (167)] [Found: C, 63.51; H, 4.59; N, 5.59; O, 13.21; S, 13.24. $C_{13}H_{11}NO_2S$ requires C, 63.67; H, 4.52; N, 5.71; O, 13.05; S, 13.05%].

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*The mixture of nitrobenzyl chlorides was supplied by Aldrich Chemicals as technical grade o-nitrobenzyl chloride. Later analyses (n.m.r. and g.l.c.) indicated the mixture was 65% o-nitrobenzyl chloride and 35% p-nitrobenzyl chloride.

An n.m.r. spectrum (CCl_4) had three absorptions, a singlet at 5.61 τ (CH_2) and two multiplets, 2.93 τ to 2.47 τ and 2.19 τ to 1.90 τ (protons attached to aromatic rings). The integration of the singlet to that of the multiplets was in the ratio of 2:9. An i.r. spectrum (CCl_4) showed absorptions at 3060 cm^{-1} (medium) for the aromatic CH stretch, 2930 cm^{-1} and 2855 cm^{-1} (small) for the CH_2-S asymmetric and symmetric stretches, 1520 cm^{-1} and 1350 cm^{-1} (strong) for the asymmetric and symmetric aromatic NO_2 stretches, 1435 cm^{-1} (medium) for the CH_2 deformation, and 1090 cm^{-1} (small) for the aryl-S stretch. A mass spectrum showed the molecular ion at an m/e value of 245.

o-Aminobenzyl phenyl sulfide. A mixture of o- and p-nitrobenzyl phenyl sulfides (28.8 g; 0.117 mole) dissolved in methanol (2000 ml) was added to Pd/C (5%; 9.8 g) and H_2O (100 ml). Hydrazine (85%; 300 ml) was cautiously added to the solution and the mixture was refluxed for 36 h. The hot solution was filtered through Celite, and the solvent removed by distillation under reduced pressure. The residue was dissolved in hot ligroin (b.p. 100-115°C) and white prisms (21.8 g; 86.8% yield) of o- and p-aminobenzyl phenyl sulfides formed on cooling, m.p. 80-82°C [lit. m.p. 81°C (167)] [Found: C, 72.57; H, 6.08; N, 6.38; S, 14.93. $C_{13}H_{13}NS$ requires C, 72.54; H, 6.09; N, 6.51; S, 14.86%]. The product was recrystallized three times from ligroin (b.p. 100-115°C).

An n.m.r. spectrum (CCl_4) showed three absorptions, a broad singlet at 6.30 - 5.99 τ (NH_2), a singlet at 6.00 τ (CH_2), and a multiplet from 3.60 to 2.61 τ having two major peaks at 2.79 τ and 2.77 τ (protons attached to the aromatic rings). The ratio of the respective integrations was 2:2:9. An i.r. spectrum (CCl_4) showed absorptions at 3440 cm^{-1} and 3345 cm^{-1} (medium) for the asymmetric and symmetric NH_2 stretches, 3060 cm^{-1} and 3020 cm^{-1} (medium) for the aromatic CH stretch, 2950 cm^{-1} with a shoulder at 2920 cm^{-1} (small) for the CH_2-S stretch, 1620 cm^{-1} (strong) for the NH_2 deformation, 1495 cm^{-1} and 1480 cm^{-1} (medium) for the CH_2 deformation and wag and 1090 cm^{-1} (medium) for the aryl-S stretch. A mass spectrum showed the molecular ion had an m/e value of 215.

9-Thia-9,10-dihydrophenanthrene: the Pschorr Reaction.

(i) A mixture of o- and p-aminobenzyl phenyl sulfides (8.6 g; 0.040 mole) dissolved in HCl (3M; 300 ml) was cooled to -5°C. Solid sodium nitrite (3.0 g; 0.0435 mole) was slowly added with stirring over 0.25 h, and the resulting diazonium salt was stirred for 0.5 h after the addition. Copper powder (3.0 g; 0.047 mole) was slowly added to the cold solution.

The gas which evolved (983 ml) was collected over water and its volume exceeded the theoretical amount of nitrogen by 24 ml. This excess was tentatively attributed to nitrogen dioxide, the reddish-brown color and pungent odor of which were readily detected. The solution was allowed to come to room temperature with stirring over 18 h, and finally warmed to <u>ca.</u> 40°C until the evolution of gas was complete (0.5 h).

Diethyl ether (100 ml) was added to the cooled solution and the mixture was filtered through Celite. The residue was washed with water (100 ml) and two portions of diethyl ether (50 ml). The layers were separated and the aqueous layer was washed with three portions of diethyl ether (150 ml). The combined ethereal extracts were dried over anhydrous magnesium sulfate, and the solvent was removed by distillation under reduced pressure.

The residue was extracted with petroleum ether (b.p. 30 - 60°C) and the extract was placed on a neutral alumina column (300 g) developed by petroleum ether (b.p. 30 - 60°C). After an initial 300 ml of eluent, a light yellow oil began to issue from the column. Elution with a further 400 ml of solvent appeared to completely wash the oil from the column. Attempts to crystallize (CH_3OH) or sublime the oily residue (3.30 g) after solvent evaporation failed to separate the products.

A mass spectrum of the material showed at least three molecular ions at m/e values of 198, 200 and 234. A g.l.c. analysis showed five separate peaks (see Table XLIX). A sample of the residue on a thin-layer chromatographic plate developed with petroleum ether (b.p. 30 - 60°C) showed five spots, confirming the g.l.c. analysis.

TABLE XLIX

A GAS-LIQUID CHROMATOGRAPHIC ANALYSIS* OF THE PETROLEUM ETHER (b.p. 30 - 60°C) SOLUBLE PRODUCTS FROM THE PSCHORR REACTION

PEAK NUMBER	RETENTION TIME (MIN)	STRUCTURE ASSIGNED	% OF MIXTURE
1	8.6	C_6H_5-CH_2-S-C_6H_5	27.2
2	14.1	C_6H_5-S-S-C_6H_5	1.9
3	17.1	o-Cl-C_6H_4-CH_2-S-C_6H_5	18.9
4	21.4	p-Cl-C_6H_4-CH_2-S-C_6H_5	12.8
5	27.2	unidentified**	39.2

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*The column used was a 2.5 ft Carbowax 4000-dioleate column at 190°C with a helium carrier gas flow of 1.25 ml/sec.

**This was identified as 9-thia-9,10-dihydrophenanthrene below.

The residue was distilled under reduced pressure (0.05 - 0.03 mm Hg) and four fractions were collected. A g.l.c. analysis of the first fraction (96 - 103°C) showed the major component had a retention time of 8.6 min. The fraction was taken up in hot methanol and on cooling (-5°C) crystals of benzyl phenyl sulfide were isolated, m.p. 39 - 40°C [lit. m.p. 39 - 40°C (168)] [Found: C, 77.94; H, 6.05; S, 16.05. $C_{13}H_{12}S$ requires C, 77.94; H, 6.04; S, 16.02%]. The g.l.c. retention time of recrystallized benzyl phenyl sulfide was 8.6 min, and this coincided with the retention time of an authentic sample of benzyl phenyl sulfide.

An n.m.r. spectrum (CCl_4) showed two absorptions, a singlet at 5.99 τ (CH_2) and a multiplet from 3.00 τ to 2.67 τ, the major peak appearing at 2.80 τ (protons attached to the aromatic rings). The ratio of the respective integrations was 2:10. An i.r. spectrum (CCl_4) showed absorptions at 3055 cm^{-1} and 3020 cm^{-1} (strong) for the aromatic CH stretches, 2910 cm^{-1} (medium) for the CH_2 stretch, 1589 cm^{-1} and 1608 cm^{-1} (strong) for the monosubstituted benzene ring stretches, a series at 1498 cm^{-1}, 1485 cm^{-1}, 1458 cm^{-1} and 1445 cm^{-1} (all strong) for the various CH_2 deformations and wags, 1095 cm^{-1} and 1073 cm^{-1} (both medium) for the aryl-S stretch. A mass spectrum showed the molecular ion at an m/e value of 200.

The second fraction (110 - 113°C) was analyzed by g.l.c. and the major peak had a retention time of 17.1 min. The fraction was a mixture of benzyl phenyl sulfide (16.1%), o-chlorobenzyl phenyl sulfide (62.6%)*, and p-chlorobenzyl phenyl sulfide (21.3%)**. This analysis was confirmed by an n.m.r. spectrum (neat) which had four absorptions, three singlets at 6.52 τ (CH_2 of p-chlorobenzyl phenyl sulfide), 6.41 τ (CH_2 of benzyl phenyl sulfide) and 6.27 τ (CH_2 of o-chlorobenzyl phenyl sulfide), and a multiplet from 3.62 τ to 2.96 τ (protons attached to the various aromatic rings). The ratio of the respective methylene integrations indicated that the mixture was 62.5% o-chlorobenzyl phenyl sulfide, 15.9% benzyl phenyl sulfide, and 21.6% p-chlorobenzyl phenyl sulfide. The assignments of the latter two methylene singlets were confirmed by the corresponding rise in intensity of the respective signals with the addition of authentic samples of each to the mixture.

An i.r. spectrum (CCl_4) of the mixture had absorptions at 3050 cm^{-1} (medium) for the aromatic CH stretches, 2920 cm^{-1} (weak) for the CH_2-S stretches, 1580 cm^{-1} (medium) for the aromatic ring stretches, 1478 cm^{-1} (medium) and 1437 cm^{-1} (medium) for the CH_2 deformations, 1090 cm^{-1} (medium) for the aryl-S stretches, 740 cm^{-1} (medium) and 690 cm^{-1} (medium) for the C-Cl stretches

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*This is a tentative structural assignment [lit. b.p. 114°C at 0.03 mm Hg (169)].

**This is a tentative structural assignment; proven correct below.

[Found: C, 68.4; H, 5.0; Cl, 11.6; S, 15.3. The mixture, if correctly determined, requires C, 68.3; H, 4.9; Cl, 11.5; S, 15.3%].

The third fraction (113 - 116°C) was taken up in hot methanol, and on cooling, white prisms of p-chlorobenzyl phenyl sulfide crystallized, m.p. 77.5 - 78.5°C [lit. m.p. 77.5 - 78°C (169)] [Found: C, 66.68; H, 4.86; Cl, 15.03; S, 13.51. $C_{13}H_{11}ClS$ requires C, 66.50; H, 4.73; Cl, 15.11; S, 13.66%].

A g.l.c. analysis showed a single peak at a retention time of 21.4 min. A mass spectrum showed a molecular ion at an m/e value of 234. An n.m.r. spectrum (CCl_4) had three absorptions, a singlet at 6.00 τ (CH_2) and two singlets at 2.80 τ and 2.79 τ (protons attached to aromatic rings). The ratio of the integrations was 2:9, the integrations of the latter two absorptions being combined. An i.r. spectrum ($CHCl_3$) showed absorptions at 3060 cm^{-1} (medium) for the aromatic CH stretches, 2980 cm^{-1} (medium) and 2920 cm^{-1} (small) for the CH_2-S stretches, 1585 cm^{-1} with a shoulder at 1595 cm^{-1} (medium) for the aromatic ring stretches, 1480 cm^{-1} (strong) for the CH_2 deformation, and 1093 cm^{-1} (strong) for the aryl-S stretch.

The fourth fraction (121 - 125°C) was examined by g.l.c. and showed only two major peaks at retention times of 21.4 min and 27.2 min. The former corresponded to that of p-chlorobenzyl phenyl sulfide. The components of this fraction could not be separated.

A g.l.c. analysis showed that the retention time ([illegible].1 min) of an authentic sample of diphenyl disulfide, when compared with the retention times of the components of the Pschorr reaction mixture, corresponded with that of peak number 2, Table XLIX.

An n.m.r. spectrum (CCl_4) of the complete Pschorr reaction mixture indicated the unidentified compound (g.l.c. retention time 27.2 min) had eight aromatic protons. This datum was deduced by identification of the other components and their subtraction from the spectrum, while assuming the contribution of diphenyl disulfide was negligible.

A Sandmeyer reaction (170) was carried out using the mixture of o- and p-aminobenzyl phenyl sulfides. Both o- and p-chlorobenzyl phenyl sulfides were isolated, and their respective retention times (17.1 min and 21.4 min) corresponded to the retention times assigned to o- and p-chlorobenzyl phenyl sulfides produced in the Pschorr reaction.

(ii) A mixture of o- and p-aminobenzyl phenyl sulfides (7.1 g; 0.033 mole) was added to acetone (1000 ml) and sulfuric acid (conc; 18 ml). The resulting hydrogen sulfates were diazotized at 0°C by the addition of isopentyl nitrite (9 ml). Solid sodium iodide (20 g; 0.133 mole) was added to the cold solution, and a gas was spontaneously evolved. The solution was warmed to 80°C and poured into hot water, whereupon an oily organic layer separated but did not crystallize (171).

The free iodine was taken up with sodium thiosulfate (6N; 50 ml) and the solution was washed with diethyl ether (150 ml). The ethereal extract was dried over anhydrous magnesium sulfate, and the solvent was then removed by distillation under reduced pressure. The residue was taken up in hot methanol and on cooling white prisms of p-iodobenzyl phenyl sulfide formed (2.1 g; 19.5% yield). The product was recrystallized (CH_3OH) and sublimed, m.p. 87.5 - 88.5°C [lit. m.p. 88°C, (172)] [Found: C, 47.83; H, 3.50; I, 38.83; S, 9.90. $C_{13}H_{11}IS$ requires C, 47.85; H, 3.40; I, 38.92; S, 9.83%].

A mass spectrum of the product showed a molecular ion at an m/e value of 326. An n.m.r. spectrum (CCl_4) had four absorptions, a singlet at 6.04 τ (CH_2), a doublet at 3.03 τ coupled to a doublet at 2.43 τ (A_2B_2 system for protons attached to benzylic aryl ring; $J_{A_2B_2}$ = 8.4 Hz), and a singlet at 2.80 τ (protons attached to the phenyl ring). The respective integrations were in the ratio of 2:2:2:5. An i.r. spectrum (CCl_4) had absorptions at 3065 cm^{-1} and 3010 cm^{-1} (both medium) for the aromatic CH stretches, 2915 cm^{-1} (weak) for the CH_2-S stretch, 1588 cm^{-1} (medium) for the aromatic ring stretches, 1490 cm^{-1} and 1445 cm^{-1} (both strong) for the CH_2 deformations, 1095 cm^{-1} (medium) for the aryl-S stretch and 1065 cm^{-1} (strong) for the aryl-I stretch.

(iii) A mixture of o- and p-aminobenzyl phenyl sulfides (21.5 g; 0.100 mole) in sulfuric acid (3M; 200 ml) and ethanol (95%; 400 ml) at 0°C was diazotized by the addition of solid sodium nitrite (7.1 g; 0.103 mole). The solution was stirred for 1 h at 0°C and then copper powder (10.0 g; 0.158 mole) was slowly added. The solution was allowed to come to room temperature with stirring over 20 h. The volume of gas evolved from the reaction was 2530 ml, slightly exceeding the theoretical amount of nitrogen possible.

The solution was refluxed for an additional 0.2 h on a steam bath. After cooling, diethyl ether (300 ml) was added, and the solution was filtered through Celite. The filtrate was separated and the aqueous layer was washed with three portions of diethyl ether (300 ml total). The combined ethereal extracts were dried over anhydrous magnesium sulphate, and the solvent was then removed by distillation under reduced pressure. The residue was extracted with petroleum ether (b.p. 30 - 60°C) and the solvent removed in similar fashion to the latter.

A g.l.c. of the residue (temperature at 220°C and the flow of helium carrier gas at 0.714 ml/sec) showed two peaks at retention times of 2.05 min and 6.0 min. The compound ascribed to the former was benzyl phenyl sulfide, and under new conditions (temperature at 190°C and the flow of helium carrier gas at 1.25 ml/sec) the retention time of the latter was 27.2 min, corresponding to that of the unidentified compound from the dilute HCl-Pschorr reaction (see Table XLIX).

The residue was distilled under reduced pressure (0.05 - 0.03 mm Hg), and two fractions were collected. The first fraction (2.8 g; 14.0% yield) collected at 104 - 106°C gave a single g.l.c. peak at a retention time of 8.6 min. It was recrystallized twice (CH_3OH), m.p. 38 - 40°C, and its n.m.r., i.r., and mass spectra were similar in all respects to an authentic sample of benzyl phenyl sulfide. The second fraction (2.6 g; 13.1% yield) collected at 122 - 124°C was identified as 9-thia-9,10-dihydrophenanthrene and it had a single g.l.c. peak at a retention time of 27.2 min. It was recrystallized twice (CH_3OH) and sublimed, m.p. 75.5 - 76.0°C [lit. m.p. 75.5°C (167)] [Found: C, 78.70; H, 5.21; S, 16.05. $C_{13}H_{10}S$ requires C, 78.73; H, 5.09; S, 16.18%].

A mass spectrum of the compound had a molecular ion at an m/e value of 198. An n.m.r. spectrum (CCl_4) showed two absorptions, a singlet at 6.29 τ (CH_2) and a multiplet from 2.99 τ to 2.20 τ (protons attached to the aromatic rings). The respective integrations were in the ratio of 2:8. An i.r. spectrum ($CHCl_3$) had absorptions at 3045 cm^{-1} (medium) for the aromatic CH stretches, 2890 cm^{-1} and 2800 cm^{-1} (both weak) for the CH_2-S stretch, 1587 cm^{-1} (medium) for the aromatic ring stretches, a series of (strong) peaks at 1485 cm^{-1}, 1468 cm^{-1}, 1445 cm^{-1} and 1422 cm^{-1} for the CH_2 deformations, and 1075 cm^{-1} (medium) for the aryl-S stretch.

9-Thia-9,10-dihydrophenanthrene-9-oxide. - (i) 9-Thia-9,10-dihydrophenanthrene (2.62 g; 0.0132 mole) dissolved in glacial acetic acid (50 ml) and methylene chloride (50 ml) was cooled to -5°C, and 30% hydrogen peroxide (1.79 g; 0.0132 mole) was added dropwise to the stirred solution. The reaction mixture was allowed to come to room temperature over 48 h. The methylene chloride was removed by distillation under reduced pressure and the solution was lyophilized. The residue was taken up in hot benzene-hexane (1:4) and on cooling white prisms of 9-thia-9,10-dihydrophenanthrene-9-oxide (1.61 g; 57.1% yield) precipitated from the solution. The material was recrystallized three times from benzene-hexane (1:4) and washed with petroleum ether (b.p. 30 - 60°C), m.p. 101 - 102°C [Found: C, 72.83; H, 4.72; O, 7.47; S, 14.92. $C_{13}H_{10}OS$ requires C, 72.87; H, 4.70; O, 7.47; S, 14.96%].

A mass spectrum of the compound had a molecular ion at an m/e value of 214. An n.m.r. spectrum (CD_3COCD_3) showed two doublets of an AB quartet at 5.79 τ and 5.51 τ (nonequivalent methylene protons; J_{AB} = 14.0 Hz) and a multiplet from 2.72 τ to 1.90 τ (protons attached to aromatic rings).

(ii) 9-Thia-9,10-dihydrophenanthrene (1.98 [illegible]; 0.0100 mole) in methanol (200 ml) was added to sodium metaperiodate (2.14 g; 0.0100 mole) dissolved in methanol (2500 ml) at 0°C and the solution was stirred at this temperature for 5 days.

The solid material was subsequently removed by filtration and washed with diethyl ether (200 ml). The solvent was removed from the filtrate by distillation under reduced pressure and the residue was taken up in diethyl ether (200 ml) and filtered. The combined ethereal solutions were dried over anhydrous magnesium sulfate, and the solvent removed by distillation under reduced pressure.

The residue dissolved in benzene (2 ml) was placed on a silica gel G (47.8 g) chromatography column which was developed by the eluents detailed in TABLE L. Each fraction collected (50 ml) was examined subsequent to solvent removal by distillation under reduced pressure. The residue of the combined chloroform fractions was taken up in hot benzene-hexane (1:4) and on cooling white prisms of 9-thia-9,10-dihydrophenanthrene-9-oxide (1.42 g; 50.4% yield) precipitated, m.p. 101 - 102°C [Found: C, 72.75; H, 4.80; O, 7.57; S, 14.82. $C_{13}H_{10}OS$ requires C, 72.87; H, 4.70; O, 7.47; S, 14.96%]. The n.m.r. (CD_3COCD_3) and mass spectra of the material were similar in all respects to those of 9-thia-9,10-dihydrophenanthrene-9-oxide prepared above.

Thioxanthene-10-oxide. - Thioxanthene (25.0 g; 0.126 mole; Aldrich Chemicals) dissolved in chloroform (20 ml) was placed on a silica gel G (500 g) chromatography column developed by petroleum ether (b.p. 30 - 60°C; 4000 ml). The petroleum ether was removed from the collected fractions by distillation under reduced

TABLE L

THE ELUTION OF THE 9-THIA-9,10-DIHYDROPHENANTHRENE AND SODIUM METAPERIODATE REACTION MIXTURE ON A SILICA GEL G CHROMATOGRAPHIC COLUMN

FRACTION NUMBER	ELUENT COMPOSITION	VOLUME OF ELUENT (ml)
1 - 6	petroleum ether (b.p. 30 - 60°C)	300
7 - 10	benzene-petroleum ether (1:9)	200
11 - 12	benzene-petroleum ether (1:3)	100
13 - 15	benzene-petroleum ether (1:1)	150
16 - 20	benzene	250
21 - 24	benzene-chloroform (3:1)	200
25 - 27	benzene-chloroform (1:1)	150
28 - 30	benzene-chloroform (1:3)	150
31 - 80	chloroform	2500

pressure, and the residue was recrystallized three times from chloroform-ethanol (1:3). The resulting white needles of thioxanthene (23.1 g; 92.4% yield) were collected and air dried, m.p. 130 - 131°C [lit. m.p. 128 - 131°C (173)] [Found: C, 78.70; H, 5.12; S, 16.03. $C_{13}H_{10}S$ requires C, 78.75; H, 5.08; S, 16.17%].

Purified thioxanthene (14.37 g; 0.0725 mole) dissolved in glacial acetic acid (100 ml) and methylene chloride (200 ml) was cooled to -5°C, and 30% hydrogen peroxide (8.21 g; 0.0725 mole) was added dropwise to the solution. The reaction mixture was gradually allowed to come to room temperature with stirring over 48 h and the solvents were subsequently removed by lyophilization. The residue was taken up in boiling hexane and white crystals (13.86 g) precipitated from the cold solution. An n.m.r. spectrum ($CDCl_3$) indicated that this material was a mixture of 5% thioxanthene (CH_2 at 6.17 τ), 92% thioxanthene-10-oxide (two AB doublets at 6.23 τ and 5.85 τ; J_{AB} = 16.8 Hz) and 3% thioxanthene-10,10-dioxide (CH_2 at 5.78 τ).

The mixture (5.21 g) dissolved in chloroform (2 ml) was placed on a dry neutral alumina (Fluka; 500 g) chromatography column. The column was initially eluted with petroleum ether (b.p. 30 - 60°C; 4100 ml), and each fraction (100 ml) was collected and weighed subsequent to solvent removal. The weights of the material from the initial 20 fractions did not increase or decrease appreciably with fraction numbers, but remained between

0.145 g and 0.120 g for each fraction. The total weight of the material recovered from these fractions was 2.65 g, representing slightly more than 50% of the material placed on the column. The material was recrystallized from chloroform-ethanol (1:3) and identified as thioxanthene, m.p. 130.3 - 131.0°C [lit. m.p. 128 - 131°C (173)]. An n.m.r. spectrum (CD_3COCD_3) and a mass spectrum were similar in all respects to those of purified thioxanthene prepared above.

Material (0.160 g; 3% of reaction mixture) recovered from subsequent elution of the column with benzene-petroleum ether (1:1; 2000 ml) and neat benzene (1000 ml) was recrystallized from ethanol. It was identified as thioxanthene-10,10-dioxide, m.p. 173.5 - 174.5°C [lit. m.p. 174 - 175°C (173)].

The column was then eluted with benzene-chloroform (1:1; 2000 ml), neat chloroform (2000 ml) and chloroform-diethyl ether (9:1; 2000 ml). The material (2.38 g; 45.6% of reaction mixture) recovered from the final eluent was recrystallized three times from chloroform and was identified as thioxanthone, m.p. 213 - 214°C [lit. m.p. 213 - 214°C (173)] [Found: C, 73.52; H, 3.82; O, 7.52; S, 15.05. $C_{13}H_8OS$ requires C, 73.56; H, 3.80; O, 7.54; S, 15.10%]. A mass spectrum of the compound showed a molecular ion at an m/e value of 212, and an n.m.r. spectrum (CD_3COCD_3) indicated only the presence of protons attached to aromatic rings.

This chromatography procedure was repeated using material

(5.52 g) from the initial reaction mixture and similar results were obtained, i.e. 53% thioxanthene, 4% thioxanthene-10,10-dioxide and 41% thioxanthone. In both experiments, thioxanthene-10-oxide could not be recovered.

The remaining material (3.13 g) from the reaction mixture was recrystallized three times from hexane. The resulting white crystals of thioxanthene-10-oxide, m.p. 117 - 118°C [lit. m.p. 116 - 117°C (174)], were then sublimed (90°C; 1 mm Hg) and recrystallized from hexane, m.p. 110 - 111°C [lit. m.p. 109 - 110°C (173)].

The reaction procedure was repeated using purified thioxanthene (5.22 g; 0.0264 mole) and 30% hydrogen peroxide (2.95 g; 0.0264 mole). Following lyophilization, thioxanthene-10-oxide (4.75 g; 84% yield) was isolated by recrystallization (C_6H_{14}) and sublimation, m.p. 110 - 111°C [lit. m.p. 109 - 110°C (173)] [Found: C, 72.79; H, 4.75; O, 7.38; S, 14.93. $C_{13}H_{10}OS$ requires C, 72.87; H, 4.70; O, 7.47; S, 14.96%]. A mass spectrum of the compound indicated a molecular ion at an m/e value of 214, and an n.m.r. spectrum ($CDCl_3$) of the compound showed two doublets of an AB quartet at 6.23 τ and 5.85 τ (nonequivalent protons of CH_2; J_{AB} = 16.8 Hz), and two multiplets, 2.67 τ to 2.48 τ and 2.18 τ to 1.83 τ (protons attached to aromatic rings).

The reaction procedure was repeated a third time using purified thioxanthene (1.98 g; 0.0100 mole) and 30% hydrogen peroxide

(1.13 g; 0.0100 mole). Following lyophilization, the reaction mixture dissolved in chloroform (2 ml) was placed on a silica gel G (200 g) chromatography column developed with petroleum ether (b.p. 30 - 60^{o}C). Material recovered from the petroleum ether fraction (500 ml) was identified as thioxanthene, and subsequent elution of the column with benzene (500 ml) led to the isolation of thioxanthene-10,10-dioxide. The column was then eluted with chloroform-benzene (1:1) and finally neat chloroform. Thioxanthene-10-oxide, representing 81% of the reaction mixture, was isolated from the combined chloroform fractions.

Proton-deuteron exchange at the cyclic methylene of 9-thia-9,10-dihydrophenanthrene-9-oxide. - 9-Thia-9,10-dihydrophenanthrene-9-oxide (0.550 g; 2.57 x 10^{-3} mole) dissolved in acetone-d_6 (3.85 g; 6.02 x 10^{-2} mole), deuterium oxide (0.275 g; 1.38 x 10^{-2} mole) and triethylamine (0.550 g; 5.45 x 10^{-3} mole) was allowed to stand at room temperature for ca. 0.5 h. The solution was then lyophilized and the residue was recrystallized twice from benzene-hexane (1:4), m.p. 101 - 102^{o}C.

Proton-deuteron exchange at the cyclic methylene of thioxanthene-10-oxide. - (i) Thioxanthene-10-oxide (0.750 g; 3.50 x 10^{-3} mole) dissolved in acetone-d_6 (2.45 g; 3.83 x 10^{-2} mole), deuterium oxide (0.375 g; 1.88 x 10^{-2} mole) and triethylamine (0.750 g; 7.43 x 10^{-3} mole) was allowed to stand at room temperature for ca. 5 min. The solution was subsequently lyophilized and the residue was recrystallized twice from hexane, m.p. 117 - 118°C [lit. m.p. 116 - 117°C (174)].

(ii) To thioxanthene-10-oxide (0.050 g; 2.34×10^{-4} mole) a drop of aqueous sodium hydroxide (6N) was added. Within 10 min at ca. 40°C the methylene protons could not be detected in an n.m.r. spectrum. The yellow solution began to turn blue within 15 min after the addition of base, but reverted to a clear yellow color upon shaking. The recurrence of the blue color persisted for several hours after several repetitions of the shaking procedure.

CHAPTER 7

RESULTS AND DISCUSSION

7-1. 9-THIA-9,10-DIHYDROPHENANTHRENE-9-OXIDE

The synthetic route to 9-thia-9,10-dihydrophenanthrene-9-oxide (TDPO), illustrated by Figure XX, has been partially investigated by Lüttringhaus and Kolb (167) in their study of 9-thia-phenanthrenium-perchlorate. Although the present synthesis of TDPO followed a similar route, the yields of intermediate products and the properties of these products were not always in agreement with those described by Lüttringhaus and Kolb. The integrity of the 9-thia-9,10-dihydrophenanthrene (TDP) prepared in the present study has also been verified by Dewer, Forrester and Thomson (175), who have concurrently synthesized TDP in an alternate manner but describe a similar melting point.

Although Rabideau, Harvey, and Stothers (176) have calculated the free energy barriers for conformational interconversions of various 9,10-dihydrophenanthrene derivatives, no such barrier was observed in the case of TDPO. N.m.r. spectra (CS_2; CD_3SOCD_3) at temperatures ranging from -85°C to 100°C did not indicate any coalescence of the AB quartet nor the appearance of another duplicate quartet. Although the possibility of a large free energy barrier to conformational interconversion may exist such that solvated TDP occurs only in one preferred form, rapid interconversion between the two stable conformers (177, 178) probably represents a more correct interpretation of n.m.r. spectral temperature independence (see Figure XXI).

FIGURE XX

A SYNTHETIC ROUTE TO

9-THIA-9,10-DIHYDROPHENANTHRENE-9-OXIDE

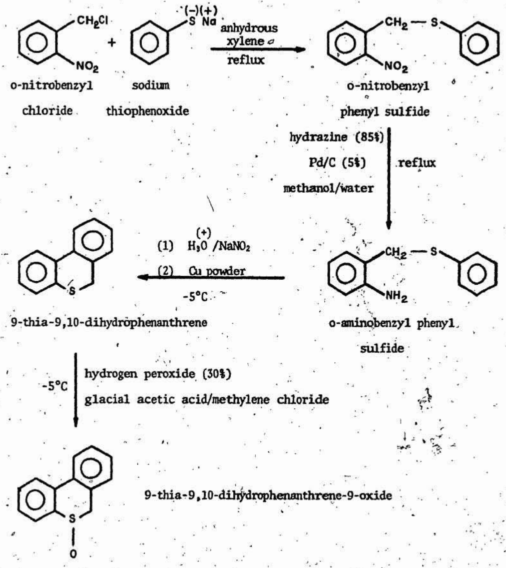
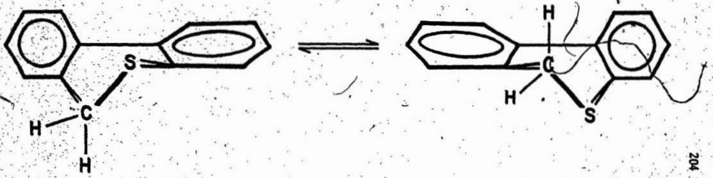


FIGURE XXI

INTERCONVERSION OF THE TWO STABLE CONFORMERS

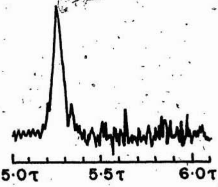
OF 9-THIA-9,10-DIHYDROPHENANTHRENE



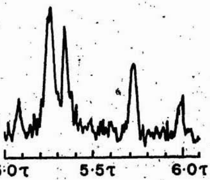
N.m.r. spectra of TDPO which has undergone partial hydrogen-deuterium exchange at the cyclic methylene position indicate that the methylene proton represented by the upfield doublet of the AB quartet is more labile in basic media than the proton represented by the downfield doublet. It is equally evident that the chemical shifts of H_A and H_B, the methylene protons, do not interchange positions when the partially deuterated TDPO is dissolved in trifluoroacetic acid with respect to their chemical shifts in dimethyl sulfoxide-d_6 (see Figures XXII and XXIII). This is implied by the n.m.r. spectral shift of the "slow-exchange" proton, labelled by the downfield unresolved -CHD- triplet representing one of the two diastereoisomeric forms, which remains downfield in both trifluoroacetic acid and dimethyl sulfoxide-d_6, i.e., the two AB doublets of the quartet do not interchange n.m.r. spectral positions with respect to each other when TDPO is solvated respectively by trifluoroacetic acid and dimethyl sulfoxide-d_6.

FIGURE XXII

PORTIONS OF N.M.R. SPECTRA OF PARTIALLY DEUTERATED TDPO DISSOLVED IN TRIFLUOROACETIC ACID



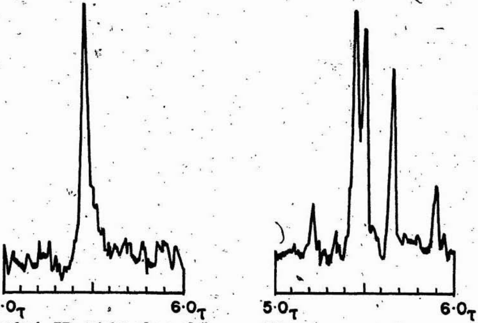
(a) the unresolved -CHD- triplet of one of the TDPO diastereoisomers generated in the proton--deuteron exchange reactions at the methylene position



(b) the spectrum shown in (a) with the AB quartet resulting from added protium TDPO

FIGURE XXIII

PORTIONS OF N.M.R. SPECTRA OF PARTIALLY DEUTERATED TDPO DISSOLVED IN DIMETHYL SULFOXIDE-d_6



(a) the unresolved -CHD- triplet of one of the TDPO diastereoisomers generated in the proton-deuteron exchange reactions at the methylene position

(b) the spectrum shown in (a) with the AB quartet resulting from added protium TDPO

7-2. THIOXANTHENE-10-OXIDE

Thioxanthene-10-oxide (TXO) was prepared by the simple oxidation of thioxanthene (see Figure XXIV). The reaction of TXO in aprotic solvent media (petroleum ether, benzene, chloroform, diethyl ether) on a neutral alumina column appears to be a novel disproportionation in which the TXO is converted to thioxanthene and thioxanthone (see Figure XXV). Although the oxidation of the methylene group to the corresponding alcohol may occur via an intramolecular mechanism due to intramolecular hydrogen bonding, the fact that thioxanthene and thioxanthone are probably produced in equal proportions suggests that the second oxidation step occurs via an intermolecular mechanism.

In a study of TXO and numerous derivatives, Ternay and coworkers (179, 180, 181, 182, 183) argue that the polymorphism exhibited by two different melting species of TXO (176), which appear to have different infrared spectra in the SO stretching region (173, 183), corresponds to the two stable conformational forms of TXO (see Figure XXVI). Although this is in empirical agreement with the present work, Ternay et al. have not as yet published evidence of a more conclusive nature to substantiate the existence of the two conformers as separate crystalline entities.

Ternay and Chasar (181) have proposed that the pseudoaxial proton of TXO is coupled to the aryl protons of the adjacent

FIGURE XXIV

THE OXIDATION OF THIOXANTHENE

TO THIOXANTHENE-10-OXIDE

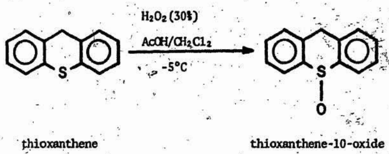


FIGURE XXV

THE REACTION OF THIOXANTHENE-10-OXIDE

ON NEUTRAL ALUMINA

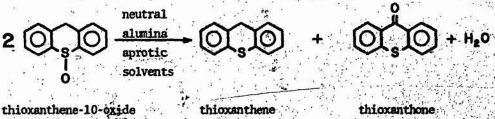
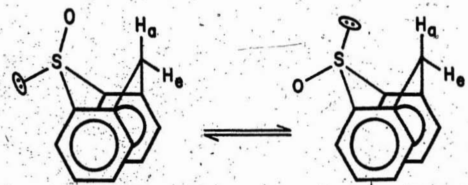


FIGURE XXVI

TWO STABLE CONFORMERS OF THIOXANTHENE-10-OXIDE



pseudoaxial array

pseudoequatorial array

H_a and H_e represent the pseudoaxial and pseudoequatorial protons, respectively, in each of the conformers.

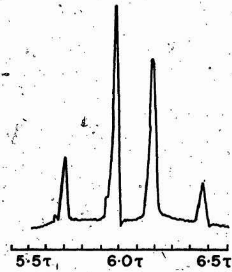
phenyl rings (see Figure XXVI). Their proposal is supported by the observation that the n.m.r. signal for the upfield doublet of the AB quartet is considerably broadened (based on width at half-height) compared to the downfield doublet when TXO is dissolved in chloroform-d [see Figure XXVII(a)]. This observation is further supported by decoupling experiments described by Ternay, Ens, Herrmann, and Evans (183) in which irradiation of the aryl protons (2.61 τ) sharpened the signal of the broadened upfield doublet almost three times more than that of the downfield doublet.

From this and other evidence arising from an extensive investigation of conformationally restricted derivatives of TXO, Ternay et al. have proposed that TXO prefers the pseudoequatorial array in chloroform-d (see Figure XXVI). These workers have observed, however, that if TXO is dissolved in trifluoroacetic acid the broadened doublet signal of the AB quartet lies downfield to that of a sharper doublet [see Figure XXVII(b)]. This apparent interchange of shift positions for the doublets has been interpreted as evidence for a conformational change such that TXO now occupies the pseudoaxial array (see Figure XXVI), while the broadened doublet signal continues to represent the pseudoaxial proton of the methylene group (183).

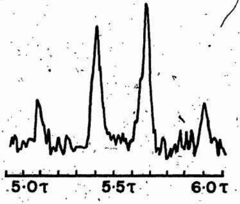
The hydrogen-deuterium exchange reactions for the methylene protons of TXO occur rather rapidly in the slightly alkaline

FIGURE XXVII

PORTIONS OF N.M.R. SPECTRA OF TXO SHOWING THE AB QUARTET OF THE METHYLENE PROTONS



(a) TXO dissolved in $CDCl_3$

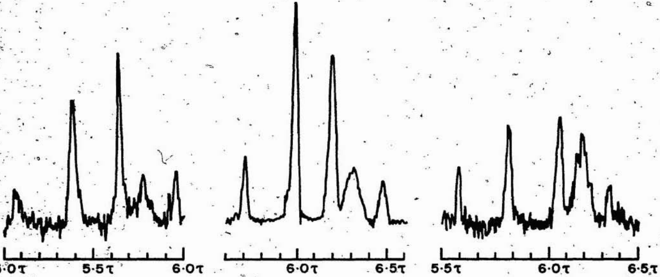


(b) TXO dissolved in CF_3COOH

media of deuterium oxide and triethylamine, with the more labile methylene proton being represented by the downfield doublet of the AB quartet in the n.m.r. spectra (c.f. Figure XXVII). This "fast-exchange" proton corresponds to the methylene proton Ternay et al. have cited as occupying the pseudoequatorial position when TXO is dissolved in chloroform-d. In the initial stage of the exchange reactions, an unresolved triplet signal located slightly to high field of the upfield doublet shift of the methylene quartet (see Figure XXVIII) increases rapidly with time. This signal represents the -CHD- of a diastereoisomer, the proton of which corresponds to the methylene proton which is represented by the upfield doublet of the AB quartet in the n.m.r. spectrum of unreacted protium TXO. The location of the unresolved triplet arising from the -CHD- of the diastereoisomer then, in effect, labels the upfield doublet of the methylene, such that the two doublets of the AB quartet are distinguishable in n.m.r. spectra of partially deuterated TXO. Since the n.m.r. absorption signal for the -CHD- of the diastereoisomer does not change shift position with respect to the A and B doublets of the quartet, i.e., remains upfield, when samples of TXO and partially deuterated TXO are solvated by trifluoroacetic acid, chloroform-d and dimethyl sulfoxide-d_6, respectively (see Figure XXVIII), it can then be assumed that the methylene protons of protium TXO do not interchange n.m.r. shift positions with respect to each other in these solvents.

FIGURE XXVIII

PORTIONS OF N.M.R. SPECTRA OF TXO WHICH SHOW THE AB QUARTET OF THE PROTIUM METHYLENE AND THE UNRESOLVED TRIPLET OF ONE OF THE PARTIALLY DEUTERATED TXO DIASTEREOISOMERS



(a) protium TXO and partially deuterated TXO dissolved in CF_3COOH

(b) protium TXO and partially deuterated TXO dissolved in $CDCl_3$

(c) protium TXO and partially deuterated TXO dissolved in CD_3SOCD_3

This observation is directly opposed to the supposition of Ternay et al. (173, 183) which states that the n.m.r. signal of the proton occupying the pseudoaxial position is downfield to that of the pseudoequatorial proton when TXO is solvated by trifluoroacetic acid, but is upfield when TXO is dissolved in chloroform-d and carbon tetrachloride. If the conformational change proposed by Ternay and co-workers for TXO is correct, namely that TXO changes from a pseudoequatorial array in chloroform-d to a pseudoaxial array in trifluoroacetic acid (as evidenced by an interchange of n.m.r. shift positions for the pseudoaxial and pseudoequatorial protons), then the present results can only be interpreted to mean that an extremely rapid exchange process occurs in which all the diastereoisomer, represented by the upfield unresolved triplet, must be converted exactly and only to the other diastereoisomer. The requirements of this exchange are doubtful under any conditions, but are even more unlikely when the hypothetically exchanging species are subjected to the highly acidic medium of trifluoroacetic acid.

Regardless of whether the aforementioned conformational change of TXO occurs or does not occur with the appropriate change in solvation, the present work would appear to suggest that the broadened doublet of the AB quartet does not always represent the same methylene proton, but indeed can represent the n.m.r. signal of either the pseudoaxial or pseudoequatorial proton. Since the effects of n.m.r. signal broadening are not likely to be experienced by the pseudoequatorial proton as a result of aryl proton coupling [c.f. (184)], and in view of the fact that the decoupling experiment described by Ternay et al. (183) could not be satisfactorily reproduced in the present work, the explanation given by Ternay, Ens, Herrmann, and Evans, namely that n.m.r. signal broadening of one of the methylene doublets of TXO is a result of aryl proton coupling, must be suspect.

7-3. SUMMARY

From the present investigation of two conformationally restricted sulfoxides, namely 9-thia-9,10-dihydrophenanthrene-9-oxide and thioxanthene-10-oxide, the following may be concluded:

(1) The methylene protons adjacent to the sulfoxide group in each compound retain their n.m.r. shift positions with respect to each other regardless of whether the compounds are solvated by dimethyl sulfoxide-d_6 or trifluoroacetic acid. This observation is contrary to that noted for the methylene protons of phenylsulfinylacetic acid, but is in agreement in this respect with prior investigations of other sulfoxide systems.

(2) Although a preferred conformation has been previously reported for thioxanthene-10-oxide (183), the results of the present investigation do not lend substantiation to the existence of preferential conformers in solutions of thioxanthene-10-oxide or 9-thia-9,10-dihydrophenanthrene-9-oxide, but rather imply that the conformers of each compound are in rapid equilibrium.

(3) The downfield doublet of the AB quartet in n.m.r. spectra of thioxanthene-10-oxide represents the more labile methylene proton of the compound, while the more acidic methylene proton of 9-thia-9,10-dihydrophenanthrene-9-oxide is signalled by the upfield doublet of the AB quartet in n.m.r. spectra of the latter.

(4) When dissolved in aprotic solvents and exposed to alumina, thioxanthene-10-oxide appears to undergo a novel

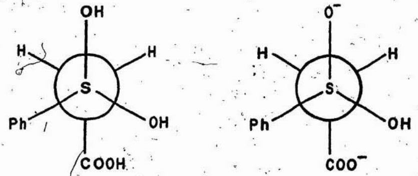
disproportionation to yield thioxanthone and thioxanthene. Preliminary experiments indicate that a similar reaction may occur in the presence of dilute aqueous sodium hydroxide [c.f. (182)].

Further quantitative empirical examination of the phenylsulfinylacetic acid system may be warranted. Investigation of specific proton/water participation in the solvation of the acid, and the corresponding role played by deuteron/deuterium oxide in the hydrogen-deuterium exchange process at the methylene position remains a priority. As stated above, the factor previously considered to predominant in the exchange process was the effect of the intrinsic asymmetry of the sulfoxide group on the relative chemical reactivity of the adjacent methylene protons in conjunction with competitive conformer stability. This notwithstanding, solvent participation may also be a significant factor in the proton-deuteron exchange process at the methylene position of phenylsulfinylacetic acid.

The intrinsic asymmetry of the sulfoxide group of the acid may be destroyed by solvation in aqueous media [c.f. (146); see Figure XXIX], but the solvated carbanions will lead to diastereotopic selectivity only if the rate of conformational interconversion, through internal rotation and inversion, is slow compared to the rate of proton-deuteron

FIGURE XXIX

NEWMAN PROJECTION DIAGRAMS (VIEWED ALONG THE S-C BOND) OF POSSIBLE SOLVATED STRUCTURES FOR PHENYLSULFINYLACETIC ACID AND ANION IN AQUEOUS ACIDIC AND ALKALINE MEDIA



solvated phenylsulfinylacetic acid in aqueous acidic media

solvated phenylsulfinylacetate anion in aqueous alkaline media *exchange [see Figure XXX].* Since stereoselectivity is evidenced* by unequal populations of the diastereoisomers arising from proton-deuteron exchange, the rate of interconversion and, hence the rate of inversion, must be less than the rate of exchange. The implication that inversion significantly affects the product ratio of the diastereoisomers, however, only requires that the rate of oxygen exchange at sulfur be competitive with that of proton-deuteron exchange.

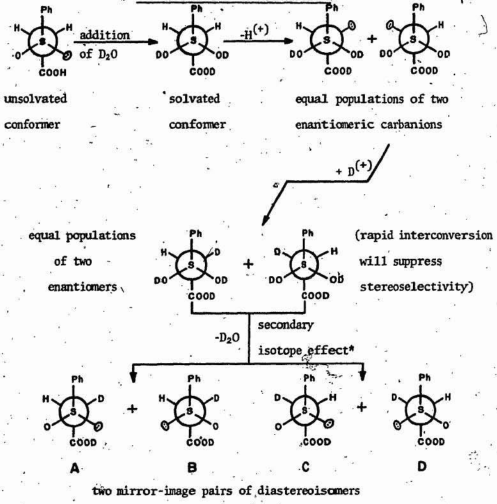
In one of a series of papers Oae (145) has reported the rate of oxygen exchange at sulfur for three sulfoxides in the presence of carboxylic acids of varying acidity. Although quantitative measurements were not recorded for phenylsulfinylacetic acid, an approximation of the rate of the sulfoxide oxygen exchange at 25°C would yield a value not less than 10^{-7} sec^{-1} to within one order of magnitude. *If the deuterium* exchange reaction at the adjacent methylene carbon is assumed to be pseudo-first order, the rate of exchange is also

---

*Irrespective of the rate of interconversion, unequal populations of the diastereoisomers may arise as a consequence of a secondary isotope effect which would produce stereoselective collapse of the solvated acid subsequent to deuteration as shown in Figure XXX. It is doubtful, however, whether the difference in the populations of the diastereoisomers can be totally accounted for by a secondary isotope effect.

FIGURE XXX

NEWMAN PROJECTION DIAGRAMS (VIEWED ALONG THE S-C BOND) OF PROTON-DEUTERON EXCHANGE IN A SOLVATED PHENYLSULFINYLACETIC ACID CONFORMER UNDER CONDITIONS OF RAPID CONFORMATIONAL INTERCONVERSION



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*Irrespective of the rate of interconversion, unequal populations of the diastereoisomers may arise as a consequence of a secondary isotope effect. On this basis, the populations of A and D might be expected to differ from those of B and C.

approximately 10^{-7} sec^{-1} at room temperature.

Recently, Durst and co-workers (185) have shown that the differential kinetic acidities of the diastereotopic protons in benzyl methyl sulfoxide depend on the nature of the base and the solvent system, indicating that proton-deuteron exchange rates are not solely intrinsic properties of the unsolvated sulfoxide and related carbanions. D'Amore and Brauman (186) have also questioned the validity of the assumption [see Wolfe et al. (158)] that the product ratios of the monodeuterated conformers of benzyl methyl sulfoxide obtained via quenching techniques reflect the relative stabilities of the corresponding carbanions. From their kinetic study of the rates of proton-deuteron exchange and epimerization of methyl 1-phenylethyl sulfoxide, D'Amore and Brauman conclude that the rate of interconversion between the diastereoisomers may be comparable to the rate of quenching. Hence, the resulting product ratios are not necessarily a measure of relative carbanion stability nor are they indicative of proton lability. This conclusion is supported by Nishihawa and Nishio (187), who report a similar finding from studies of the effect of quenching on proton-deuteron exchange in benzyl methyl sulfoxide dissolved in tetrahydrofuran.

Hence, an analysis of the possible effects of solute-solvent interactions on the reactivity of the methylene protons of phenylsulfinylacetic acid would necessitate the determination of the rate of racemization of an enantiomer of the acid in aqueous media and the rate of ^{18}O exchange at sulfur. A comparison of these values with the rate of proton-deuteron exchange at the methylene position would then perhaps offer some indication of the significance of solute--solvent interactions in aqueous media and suggest the relative importance of solvated species in the proton-deuteron exchange process.

APPENDIX I

A DESCRIPTION OF THE TINSLEY AND GENERAL RADIO IMPEDANCE COMPARATOR BRIDGES AND THE CONSTANT TEMPERATURE BATHS

A simplified block diagram of the 4896 Tinsley Bridge with auxiliary equipment is shown in Figure XXXI. The bridge and accessories were assembled according to the description of Robertson (188), but minor modifications in this design were necessary because of the commercial unavailability of some of the components described.

A Hewlett Packard oscillator (model 200 AB) supplied the alternating current (AC) at 1000 cycles per second (cps) to the bridge. A constant voltage power source (117 ± 1 volt) for the oscillator was supplied by a Sorensen AC regulator (ARC 5000 model) connected to a 120 volt mains output.

Balancing of the bridge was obtained by observing a Lissajous pattern on the oscilloscope (Hewlett Packard 120B model) which derived its signal from a 1000 cps high gain amplifier (see Figure XXXII). This amplifier was connected to the bridge output through a 578-A transformer, and the amplifier output was fed through shielded leads to the vertical input plates of the oscilloscope [For a more detailed discussion, see (44)].

The G.R.I.C., type 1605-A, is designed to measure the magnitude and phase angle difference between two external impedances. The instrument essentially consists of a special self-contained bridge measurement system, composed of a signal source, a bridge and a detecting circuit (see Figure XXXIII).

FIGURE XXXI

A BLOCK DIAGRAM OF THE TINSLEY CONDUCTANCE BRIDGE CIRCUIT

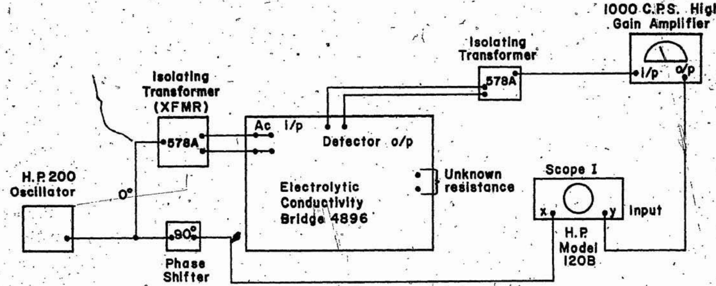
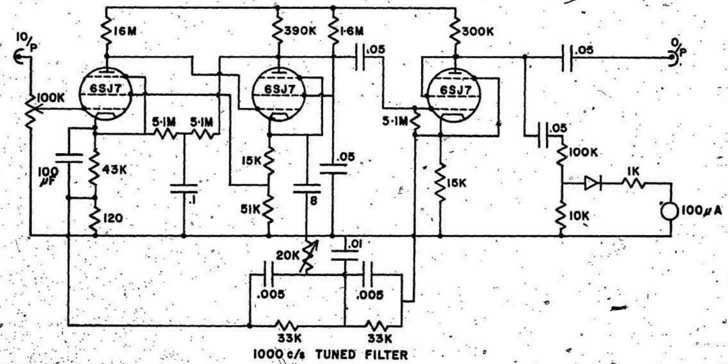


FIGURE XXXII

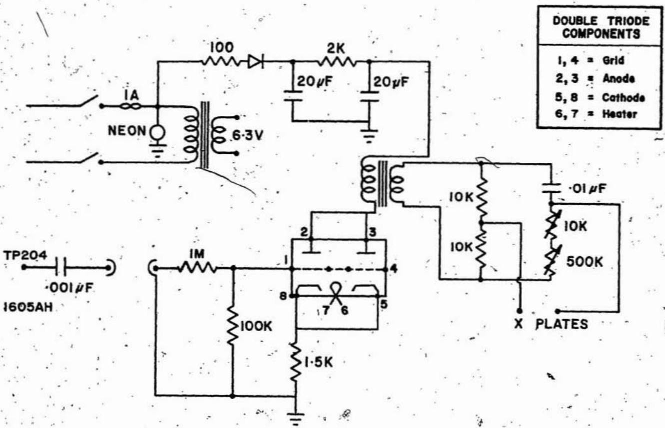
A DIAGRAM OF THE 1000 CPS AMPLIFIER CIRCUIT



GAIN AT 1000 c/s 20,000
NOISE 100MV.

FIGURE XXXIII

A DIAGRAM OF THE IMPEDANCE BRIDGE CIRCUIT FOR THE G.R.I.C. (TYPE 1605-A)



The bridge proper has two external impedances to be compared and two highly precise 1:1 ratio arms. Since these arms are equal to within 0.0001%, the accuracy of the impedance measurements depends largely upon the precision of the external standard, a General Radio resistance box, type 1432. This decade box has a resistance range of 0.1-111,111 Ω and the accuracy of the resistance increments was given as ± 0.05%. The bridge was calibrated against a Leeds and Northrup (model 4756-S) standard resistance box with low frequency dependance, and the resulting discrepancy was less than 0.01% between 100 Ω and 50,000 Ω.

A detailed description of the oscillator, amplifier and bridge circuit is given in the General Radio operating instructions for an Impedance Comparator, type 1605-A.

Constant Temperature Bath. - The bath assembly consisted of a 39" x 29" x 24" metal-framed unit which supported two stainless steel tanks (each 28" x 13" x 18"), one mounted above the other, which were insulated by a 1" coating of styrofoam on the outside. As constant cooling and continuous heating were necessary to maintain temperature control, the lower tank was used as a cooling bath and the upper tank served as the constant temperature bath.

Cooling coils constructed from *ca.* 25 ft of copper tubing (3/8" diameter) wound in five spirals (*ca.* 2" apart) were installed 3/8" above the bottom of the upper bath. These coils were connected to the lower cooling bath with heavy, insulated rubber tubing. The flow of coolant (water at 21°C) circulated by a centrifugal pump (maximum rate, 1.5 l/min) from the cooling bath through the cooling coils in the upper bath was regulated by a bypass arrangement with a dual control valve system set in the tubing.

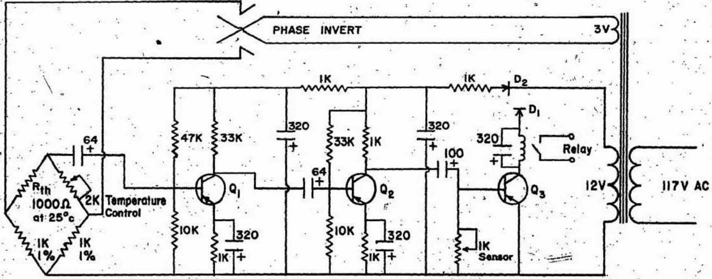
The temperature of the water in the cooling bath was maintained by the cooling coils from a Tecumseh refrigerator (¼ hp). These coils were constructed of ca. 100 ft of copper tubing (3/8" diameter) wound in six spirals about 8" apart and were supported in the lower bath by a metal frame. The water in this bath was circulated over the refrigeration coils by means of a stirrer (Redmond, type T, model 9407; 1/10 hp) mounted on the side of the bath. The temperature of the water was regulated to 21.00 ± 0.25°C by means of a Fenwal Electronics thermistor (GB32J2) in a modified Wheatstone Bridge circuit (see Figure XXXIV).

The constant temperature bath was filled with Voltesso transformer oil (189) which was agitated by means of a Cenco Centrifugal Electric stirrer (1/20 hp; rated circulating capacity for water, 105 gallons/min) mounted at one end of the bath. The temperature of the oil was controlled by a Tronac Regulator (PTC - 1000A).

This regulator essentially consists of a background heater (250 watts) and an intermittent knife heater (250 watts). The latter is controlled by a thermistor probe and temperature

FIGURE XXXIV

A DIAGRAM OF THE TEMPERATURE SENSOR AND REGULATOR CIRCUIT



Q_1, Q_2, Q_3. = SK3060

D_1, D_2 = IN5060

Relay = 130 Ω, 15ma. (DC)

controls set in a Wheatstone Bridge circuit which is excited by a stabilized AC source. The Tronac is capable of regulation to ± 0.001°C, with long term drift of less than ± 0.005°C per week. A full description of its specifications and operation is detailed in a manual supplied by Tronac, Inc.

The temperature of the bath was maintained at 25.000 ± 0.005°C for long periods of time. Over several hours the temperature varied less than ± 0.0024°C. Temperature control of the bath was facilitated by its location in a constant temperature, air-conditioned room.

APPENDIX II

FORTRAN IV COMPUTER PROGRAMS EMPLOYED IN THE CALCULATION OF THERMODYNAMIC EQUILIBRIUM CONSTANTS AND ISOTOPE EFFECTS

```
C                    ROBINSON AND STOKES METHOD
      DIMENSION C(100),EC(100),ALF(100),Y(100),DENOM(100),ALI(
     1100),BLF(100),YY(100),DENON(100),GOLE(100),Z(100),EP(100)
     2,S(100),AKA(100),DEV(100),ADEV(100)
    5 PRINT 3
    3 FORMAT (1X,26HMACINNES-SHEDLOVSKY METHOD)
      READ 2,ALO,BETA,BA,B1,B2
    2 FORMAT (6X,F6.1,F7.4,F8.5,F7.4,F8.4)
      L=0
   20 L=L+1
      READ 1,C(L),EC(L),LAST
    1 FORMAT (6X,E11.4,F9.4,I2)
      IF(LAST)20,20,30
   30 K=L
      EL=L
      PRINT 18
   18 FORMAT (1X,13HCONCENTRATION,3X,8HEQUIVCON,3X,8HLAMBDA I,5
     1X,11HEQUIL.CONST,3X,9HDEVIATION)
      SUMK=0.0
      DO 9 L=1,K
   13 ALF(L)=EC(L)/ALO
      X=B1*ALO+B2
      Y(L)=SQRT(ALF (L)*C(L))
      DENOM(L)=1.+BA*Y(L)
   21 ALI(L)=ALO-(X*Y(L))/DENOM(L)
```

```
      BLF(L)=EC(L)/ALI(L)
      YY(L)=SQRT(BLF(L)*C(L))
      DENON(L)=1.+BA*YY(L)
      GOLE(L)=-BETA*YY(L)/DENON(L)
      Z(L)=2.30259*GOLE(L)
      EP(L)=EXP(Z(L))
      S(L)=(BLF(L)**2)*EP(L)**2*C(L)
      AKA(L)=S(L)/(1.0-BLF(L))
      SUMK=SUMK+AKA(L)
9     CONTINUE
      AVKA=SUMK/EL
      SUMD=0.0
      DO 4 L=1,K
      ADEV(L)=(AVKA-AKA(L))**2
      SUMD=SUMD+ADEV(L)
      DEV(L)=((AVKA-AKA(L))/AVKA)*100.
      PRINT 14,C(L),EC(L),ALI(L), AKA(L), DEV(L)
14    FORMAT (1X,E11.4,5X,F9.4,4X,F7.2,3X,E11.4,3X,E11.4)
4     CONTINUE
      EDEV=SQRT(SUMD/(EL-2.))
      PRINT 92,EDEV
92    FORMAT (1X,22HAVERAGE DEVIATION IS   ,E11.4)
      PRINT 91,AVKA
91    FORMAT (1X,15HAVERAGE KA IS  ,E11.4)
      CALL EXIT
      END
```

```
C                         IVES METHOD
      DIMENSION C(100),EC(100),ALF(100),CI(100),Y(100),X(100),CAL
     1CY(100),DIB(100),AKA(100),DEV(100),ADEV(100),Z(100),ZZ(100)
5     PRINT 4
4     FORMAT (1X,11HIVES METHOD)
      READ 2,ALO,BETA,BA,B1,B2
2     FORMAT (6X,F6.1,F7.4,F8.5,F7.4,F8.4)
      PRINT 31,ALO
31    FORMAT (1X,12HLAMBDA(0) =    ,F6.1)
      L=0
20    L=L+1
      READ 1,C(L),EC(L),LAST
1     FORMAT (6X,E11.4,F9.4,I2)
      IF(LAST)20,20,30
30    K=L
      OK=K
      EL=L
      PRINT 88
88    FORMAT (1X,8H   SLOPE,6X,11H  INTERCEPT,3X,10HERROR IN B,3X
     1,14HERROR IN SLOPE)
60    SUMK=0.0
      SUMX=0.0
      SUMXY=0.0
      SUMXX=0.0
```

```
      DO 25 L=1,K
      ALF(L)=EC(L)/ALO
      A=B1*ALO+B2
      CI(L)=SQRT(ALF(L)*C(L))
      Y(L)=EC(L)+A*CI(L)
      Z(L)=2.*BETA*CI(L)
      ZZ(L)=10.**Z(L)
      X(L)=(C(L)*EC(L)**2)/(ZZ(L)*(ALO-A*CI(L)))
      SUMX=SUMX+X(L)
      SUMY=SUMY+Y(L)
      SUMXY=SUMXY+X(L)*Y(L)
25    SUMXX=SUMXX+X(L)**2
      DENOM=SUMX**2-OK*SUMXX
      SLOPE=(SUMX*SUMY-OK*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      SUMD=0.0
      DO 3 L=1,K
      CALCY(L)=SLOPE*X(L)+B
      DIB(L)=(Y(L)-CALCY(L))**2
3     SUMD=SUMD+DIB(L)
      RE=0.6745*SQRT(SUMD/(EL-2.))
      ERROR=RE*SQRT(SUMXX/(-DENOM))
      ERB=RE*SQRT(OK/(-DENOM))
      PRINT 6,SLOPE,B,ERROR,ERB
6     FORMAT (1X,E11.4,3X,F9.4,3X,E11.4,5X,E11.4)
      DIF=ABS(ALO-B)
```

```
      PRINT 50,DIF
50    FORMAT (1X,37HDIFFERENCE,LAMBDA(0)-1/INTERCEPT IS   ,F7.2)
      IF(DIF-0.01)15,15,17
17    IF(DIF-20.)16,16,95
16    ALO=B
      GO TO 60
15    SAKA=-1./SLOPE
      PRINT 23,SAKA
23    FORMAT (1X,19H KA FROM SLOPE IS   ,E11.4)
      DO 29 L=1,K
      AKA(L)=X(L)/(B-Y(L))
29    SUMK=SUMK+AKA(L)
      AVKA=SUMK/OK
      PRINT 93,AVKA
93    FORMAT (1X,15HAVERAGE KA IS  ,E11.4)
      PRINT 33
33    FORMAT (1X,13HCONCENTRATION,3X,11HEQUIL.CONST,3X,13H    DEVI
     1ATION)
      SUMB=0.0
      DO 45 L=1,K
      DEV(L)=AVKA-AKA(L)
      ADEV(L)=(AVKA-AKA(L))**2
      SUMB=SUMB+ADEV(L)
      PRINT 42,C(L),AKA(L),DEV(L)
42    FORMAT (1X,E11.4,5X,E11.4,4X,E11.4)
45    CONTINUE
```

```
      EDEV=SQRT(SUMB/(EL-2.))
      PRINT 92,EDEV
   92 FORMAT (1X,22HAVERAGE DEVIATION IS  ,E11.4)
   95 CONTINUE
      CALL EXIT
      END
```

```
C                        FUOSS METHOD
      DIMENSION C(100),EC(100),AC(100),ALF(100),Z(100),F1(100),F
     12(100),F3(100),GOLE(100),Q(100),EP(100),Y(100),S(100),XX(1
     200),AKA(100),CALCY(100),DIB(100),DEV(100),ADEV(100)
 5    PRINT 4
 4    FORMAT (1X,22HFUOSS ITERATION METHOD)
      READ 2,ALO,BETA,BA,B1,B2
 2    FORMAT (6X,F6.1,F7.4,F8.5,F7.4,F8.4)
      PRINT 31,ALO
 31   FORMAT (1X,12HLAMBDA(0)=     ,F6.1)
 21   L=0
 20   L=L+1
      READ 1,C(L),EC(L),LAST
 1    FORMAT (6X,E11.4,F9.4,I2)
      IF(LAST)20,20,30
 30   K=L
      EL=L
      PRINT 88
 88   FORMAT (1X,8H   SLOPE,6X,11H1/INTERCEPT,3X,10HERROR IN B,3
     1X,14HERROR IN SLOPE)
 60   CONTINUE
      SUMX=0.0
      SUMY=0.0
      SUMXY=0.0
      SUMXX=0.0
      DO 9 L=1,K
      AC(L)=EC(L)*C(L)
```

```
      X=B1*ALO+B2
      Z(L)=X*SQRT(AC(L)/ALO**3)
      F1(L)=1.-Z(L)
      F2(L)=1.-Z(L)*SQRT(1./F1(L))
      F3(L)=1.-Z(L)*SQRT(1./F2(L))
      ALF(L)=EC(L)/(ALO*F3(L))
      GOLE(L)=-BETA*SQRT(ALF(L)*C(L))
      Q(L)=2.30259*GOLE(L)
      EP(L)=EXP(Q(L))
      Y(L)=F3(L)/EC(L)
      XX(L)=C(L)*EC(L)*EP(L)**2/F3(L)
      SUMX=SUMX+XX(L)
      SUMY=SUMY+Y(L)
      SUMXX=SUMXX+XX(L)**2
    9 SUMXY=SUMXY+XX(L)*Y(L)
      OK=K
      DENOM=SUMX**2-OK*SUMXX
      SLOPE=(SUMX*SUMY-OK*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      F=1.0/B
      SUMD=0.0
      DO 91 L=1,K
      CALCY(L)=SLOPE*XX(L)+B
      DIB(L)=(Y(L)-CALCY(L))**2
   91 SUMD=SUMD+DIB(L)
   22 RE=0.6745*SQRT(SUMD/(EL-2.))
      ERROR=RE*SQRT(SUMXX/(-DENOM))
```

```
      ERB=RE*SQRT(OK/(-DENOM))
      PRINT 6,SLOPE,F,ERROR,ERB
6     FORMAT (1X,E11.4,3X,F9.4,3X,E11.4,5X,E11.4)
      DIF=ABS(ALO-F)
      PRINT 50,DIF
50    FORMAT (1X,37HDIFFERENCE,LAMBDA(0)-1/INTERCEPT IS   ,F8.4)
      IF(DIF-0.01)15,15,17
17    IF(DIF-20.0)16,16,95
16    ALO=F
      GO TO 60
15    SAKA=1./(SLOPE*F**2)
      PRINT 23,SAKA
23    FORMAT (1X,19H KA FROM SLOPE IS  ,E11.4)
      PRINT 33
33    FORMAT (1X,13HCONCENTRATION,3X,11HEQUIL.CONST,3X,14H     DE
     1VIATION)
      SUMK=0.0
      DO 29 L=1,K
      S(L)=(ALF(L)**2)*(EP(L)**2)*C(L)
      AKA(L)=S(L)/(1.0-ALF(L))
29    SUMK=SUMK+AKA(L)
      AVKA=SUMK/OK
      SUMB=0.0
      DO 45 L=1,K
      DEV(L)=AVKA-AKA(L)
      ADEV(L)=(AVKA-AKA(L))**2
```

```
      SUMB=SUMB+ADEV(L)
      PRINT 42,C(L),AKA(L),DEV(L)
42    FORMAT (1X,E11.4,5X,E11.4,4X,E11.4)
45    CONTINUE
      PRINT 93,AVKA
93    FORMAT (1X,15HAVERAGE KA IS   ,E11.4)
      EDEV=SQRT(SUMB/(EL-2.))
      PRINT 92,EDEV
92    FORMAT (1X,22HAVERAGE DEVIATION IS  ,E11.4)
95    CONTINUE
      CALL EXIT
      END
```

```
C                        SHEDLOVSKY 1 METHOD
      DIMENSION C(100),AC(100),EC(100),Z(100),F1(100),F3(100),AL
     1F(100),GOLE(100),Q(100),EP(100),Y(100),XX(100),S(100),AKA(
     2100),DEV(100),CALCY(100),DIB(100)
  100 PRINT 26
   26 FORMAT (1X,17HSHEDLOVSKY METHOD)
      READ 2,ALO,BETA,BA,B1,B2
    2 FORMAT (6X,F6.1,F7.4,F8.5,F7.4,F8.4)
      L=0
   20 L=L+1
      READ 1,C(L),EC(L),LAST
    1 FORMAT (6X,E11.4,F9.4,I2)
      IF(LAST)20,20,30
   30 K=L
      EL=L
      PRINT 88
   88 FORMAT (1X,8H   SLOPE,6X,11H1/INTERCEPT,3X,10HERROR IN B,
     13X,14HERROR IN SLOPE)
   60 CONTINUE
      SUMX=0.0
      SUMXX=0.0
      SUMY=0.0
      SUMXY=0.0
      DO 40 L=1,K
      AC(L)=EC(L)*C(L)
      X=B1*ALO+B2
      Z(L)=X*SQRT(AC(L)/(ALO**3))
```

```
      F1(L)=0.5*Z(L)
      F3(L)=(F1(L)+SQRT(1.+F1(L)**2))**2
      ALF(L)=EC(L)*F3(L)/ALO
      GOLE(L)=-BETA*SQRT(ALF(L)*C(L))
      Q(L)=2.30259*GOLE(L)
      EP(L)=EXP(Q(L))
      Y(L)=1./(F3(L)*EC(L))
      XX(L)=C(L)*EC(L)*EP(L)**2*F3(L)
      SUMX=SUMX+XX(L)
      SUMY=SUMY+Y(L)
      SUMXX=SUMXX+XX(L)**2
3     SUMXY=SUMXY+Y(L)*XX(L)
40    CONTINUE
      OK=K
      DENOM=SUMX**2-OK*SUMXX
      SLOPE=(SUMX*SUMY-OK*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      F=1.0/B
      DIF=ABS(ALO-F)
      SUMD=0.0
      DO 91 L=1,K
      CALCY(L)=SLOPE*XX(L)+B
      DIB(L)=(Y(L)-CALCY(L))**2
91    SUMD=SUMD+DIB(L)
22    RE=0.6745*SQRT(SUMD/(EL-2.))
      ERROR=RE*SQRT(SUMXX/(-DENOM))
```

```
      ERB=RE*SQRT(OK/(-DENOM))
      PRINT 6,SLOPE,F,ERROR,ERB
6     FORMAT (1X,E11.4,3X,F9.4,3X,E11.4,5X,E11.4)
      PRINT 50,DIF
50    FORMAT (1X,37HDIFFERENCE,LAMBDA(0)-1/INTERCEPT IS  ,F8.4)
      IF(DIF-0.01)15,15,17
17    IF(DIF-20.)16,16,95
16    ALO=F
      GO TO 60
15    SAKA=1./(SLOPE*F**2)
      PRINT 23,SAKA
23    FORMAT (1X,19H KA FROM SLOPE IS  ,E14.4)
24    PRINT 5
5     FORMAT (1X,13HCONCENTRATION,3X,11HEQUIL.CONST,3X,13HO/O DE
     1VIATION)
      SUMK=0.0
70    TDEV=0.0
      DO 29 L=1,K
      S(L)=(ALF(L)**2)*(EP(L)**2)*C(L)
      AKA(L)=S(L)/(1.0-ALF(L))
29    SUMK=SUMK+AKA(L)
      AVKA=SUMK/OK
      DO 45 L=1,K
      DEV(L)=(AVKA-AKA(L))*100./AVKA
      PRINT 42,C(L),AKA(L),DEV(L)
42    FORMAT (1X,E11.4,5X,E11.4,4X,F6.2)
45    TDEV=TDEV+(AVKA-AKA(L))**2
```

```
      ADEV=SQRT(TDEV/(OK-2.))
      PRINT 46,ADEV
46    FORMAT (1X,23H AVERAGE DEVIATION IS ',E14.4)
95    CONTINUE
      CALL EXIT
      END
```

```
C                         CLASSICAL METHOD
      DIMENSION C(100),EC(100),AC(100),X(100),CALCY(100),DIF(100
     1),AIF(100)
      L=0
 20   L=L+1
      READ 1,C(L),EC(L),LAST
 1    FORMAT (6X,E11.4,F9.4,I2)
      IF(LAST)20,20,30
 30   K=L
      PRINT 35
 35   FORMAT (1X,13HCONCENTRATION,3X,10HLAMBDA X C,4X,11HREC. LA
     1MBDA)
      SUMX=0.0
      SUMXX=0.0
      SUMY=0.0
      SUMXY=0.0
      DO 3 L=1,K
      AC(L)=EC(L)*C(L)
      X(L)=1.0/EC(L)
      PRINT 14,C(L),AC(L),X(L)
 14   FORMAT (1X,E11.4,5X,E11.4,3X,E11.4)
      SUMX=SUMX+AC(L)
      SUMY=SUMY+X(L)
      SUMXX=SUMXX+AC(L)**2
 3    SUMXY=SUMXY+X(L)*AC(L)
      OK=K
      DENOM=SUMX**2-OK*SUMXX
```

```
      SLOPE=(SUMX*SUMY-OK*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      F=1.0/B
      PRINT 6,SLOPE,F
 6    FORMAT (1X,10HSLOPE IS  ,E11.4,3X,16H1/INTERCEPT IS  ,F7.2)
15    SAKA=1./(SLOPE*F**2)
      PRINT 23,SAKA
23    FORMAT (1X,19H KA FROM SLOPE IS  ,E11.4)
      PRINT 33
33    FORMAT (1X,10H CALC. 1/L,5X,10HDIFFERENCE)
      SUMD=0.0
      DO 5 L=1,K
      CALCY(L)=SLOPE*AC(L)+B
      DIF(L)=X(L)-CALCY(L)
      AIF(L)=DIF(L)**2
      SUMD=SUMD+AIF(L)
      PRINT 7,CALCY(L),DIF(L)
 7    FORMAT (1X,E11.4,3X,E11.4)
 5    CONTINUE
      RE=0.6745*SQRT(SUMD/(OK-2.))
      ERROR=RE*SQRT(SUMXX/(-DENOM))
      ERB=RE*SQRT(OK/(-DENOM))
      PRINT 91,ERROR
91    FORMAT (1X,23HERROR IN INTERCEPT IS  ,E11.4)
      PRINT 92,ERB
92    FORMAT (1X,19HERROR IN SLOPE IS  ,E11.4)
      CALL EXIT
      END
```

```
C                      SHEDLOVSKY 3 METHOD
      DIMENSION C(100),AC(100),EC(100),Z(100),F1(100),F3(100),AL
     1F(100),GOLE(100),Q(100),EP(100),Y(100),XX(100),S(100),AKA(
     2100),CALCY(100),DIB(100)
      PRINT 70
70    FORMAT (1X,12HSHEDLOVSKY 3)
      J=1
60    PRINT 100,J
100   FORMAT (1X,12HCELL NUMBER ,I2)
      J=J+1
      READ 42,ALO,BLO,CLO
42    FORMAT (6X,F7.2,F6.2,F7.2)
      READ 2,BETA,BA,B1,B2
2     FORMAT (6X,F7.4,F8.5,F7.4,F8.4)
      L=0
20    L=L+1
      READ 1,C(L),EC(L),LAST,FINAL
1     FORMAT (6X,E11.4,F9.4,I2,F4.1)
      IF(FINAL)20,20,30
30    K=L
      OK=K
      PRINT 88
88    FORMAT (1X,8H   SLOPE,6X,11H1/INTERCEPT,3X,10HERROR IN B,3
     1X,14HERROR IN SLOPE,3X,9HLAMBDA(0))
31    EL=L
      DO 40 L=1,K
      AC(L)=EC(L)*C(L)
```

```
      X=B1*ALO+B2
      Z(L)=X*SQRT(AC(L)/(ALO**3))
      F1(L)=0.5*Z(L)
      F3(L)=(F1(L)+SQRT(1.+F1(L)**2))**2
      ALF(L)=EC(L)*F3(L)/ALO
      GOLE(L)=-BETA*SQRT(ALF(L)*C(L))
      Q(L)=2.30259*GOLE(L)
      EP(L)=EXP(Q(L))
      Y(L)=1./(F3(L)*EC(L))
      XX(L)=C(L)*EC(L)*EP(L)**2*F3(L)
   40 CONTINUE
      SUMX=0.0
      SUMXX=0.0
      SUMY=0.0
      SUMXY=0.0
      DO 3 L=1,K
      SUMX=SUMX+XX(L)
      SUMY=SUMY+Y(L)
      SUMXX=SUMXX+XX(L)**2
    3 SUMXY=SUMXY+Y(L)*XX(L)
      DENOM=SUMX**2-OK*SUMXX
      SLOPE=(SUMX*SUMY-OK*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      F=1.0/B
      SUMD=0.0
      DO 91 L=1,K
      CALCY(L)=SLOPE*XX(L)+B
```

```
      DIB(L)=(Y(L)-CALCY(L))**2
 91   SUMD=SUMD+DIB(L)
      RE=0.6745*SQRT(SUMD/(OK-2.))
      ERROR=RE*SQRT(SUMXX/(-DENOM))
      ERB=RE*SQRT(OK/(-DENOM))
      PRINT 6,SLOPE,F,ERROR,ERB,ALO
 6    FORMAT (1X,E11.4,3X,F9.4,3X,E11.4,5X,E11.4,2X,F7.2)
      IF(CLO-ALO)8,8,5
 5    ALO=ALO+BLO
      GO TO 31
 8    IF(LAST)9,9,10
 9    GO TO 60
 10   CONTINUE
      CALL EXIT
      END
```

```
C                         SHEDLOVSKY 4 METHOD
      DIMENSION C(100),EC(100),AC(100),Z(100),F1(100),F3(100),AL
     1F(100),GOLE(100),Q(100),EP(100),S(100),AKA(100),ADEV(100)
      PRINT 26
26    FORMAT (1X,12HSHEDLEVSKY 4)
      J=1
60    PRINT 100,J
100   FORMAT (1X,12HCELL NUMBER ,I2)
      J=J+1
      READ 42,ALO,BLO,CLO
42    FORMAT (6X,F7.2,F6.2,F7.2)
      READ 2,BETA,BA,B1,B2
2     FORMAT (6X,F7.4,F8.5,F7.4,F8.4)
      L=0
20    L=L+1
      READ 1,C(L),EC(L),LAST,FINAL
1     FORMAT (6X,E11.4,F9.4,I2,F4.1)
      IF(FINAL)20,20,30
30    K=L
      OK=K
      PRINT 75
75    FORMAT (1X,9HLAMBDA(O),3X,10HAVERAGE KA,3X,17HAVERAGE DEVI
     1ATION)
31    EL=L
      SUMK=0.0
      DO 40 L=1,K
      AC(L)=EC(L)*C(L)
```

```
      X=B1*ALO+B2
      Z(L)=X*SQRT(AC(L)/(ALO**3))
      F1(L)=0.5*Z(L)
      F3(L)=(F1(L)+SQRT(1.+F1(L)**2))**2
      ALF(L)=EC(L)*F3(L)/ALO
      GOLE(L)=-BETA*SQRT(ALF(L)*C(L))
      Q(L)=2.30259*GOLE(L)
      EP(L)=EXP(Q(L))
      S(L)=(ALF(L)**2)*(EP(L)**2)*C(L)
      AKA(L)=S(L)/(1.0-ALF(L))
      SUMK=SUMK+AKA(L)
40    CONTINUE
      AVKA=SUMK/OK
      SUMD=0.0
      DO 45 L=1,K
      ADEV(L)=(AVKA-AKA(L))**2
45    SUMD=SUMD+ADEV(L)
      EDEV=SQRT(SUMD/(EL-2.))
      PRINT 91,ALO,AVKA,EDEV
91    FORMAT (1X,F7.2,4X,E11.4,5X,E11.4)
      IF(CLO-ALO)8,8,5
5     ALO=ALO+BLO
      GO TO 31
8     IF(LAST)9,9,10
9     GO TO 60
10    CONTINUE
      CALL EXIT
      END
```

APPENDIX III

ISOTOPE EFFECTS FOR THE THREE ISOTOPIC ACID PAIRS RCH_2COOH/RCD_2COOH, WHERE R = PhO, Cl, AND PhS, CALCULATED BY THE SHEDLOVSKY III METHOD

PHENOXYACETIC ACID PAIR

CELL I

Λ_o	SLOPE, $m_t(H) \times 10^2$	SLOPE, $m_t(D) \times 10^2$	ISOTOPE EFFECT
370.0	.9513 ± .0008	.9612 ± .0008	1.0104 ± .0009
371.0	.9512 ± .0008	.9611 ± .0008	1.0104 ± .0009
372.0	.9512 ± .0008	.9611 ± .0008	1.0104 ± .0009
373.0	.9511 ± .0008	.9610 ± .0008	1.0104 ± .0009
374.0	.9511 ± .0008	.9610 ± .0008	1.0104 ± .0009
375.0	.9510 ± .0008	.9609 ± .0008	1.0104 ± .0009
376.0	.9510 ± .0008	.9609 ± .0008	1.0104 ± .0009
377.0	.9510 ± .0008	.9608 ± .0008	1.0103 ± .0009
378.0	.9510 ± .0008	.9608 ± .0008	1.0103 ± .0009
379.0	.9509 ± .0008	.9607 ± .0008	1.0103 ± .0009
380.0	.9508 ± .0008	.9607 ± .0008	1.0104 ± .0009
381.0	.9508 ± .0008	.9607 ± .0008	1.0104 ± .0009
382.0	.9507 ± .0008	.9606 ± .0008	1.0104 ± .0009
383.0	.9506 ± .0008	.9605 ± .0008	1.0104 ± .0009
384.0	.9506 ± .0008	.9605 ± .0008	1.0104 ± .0009
385.0	.9506 ± .0008	.9605 ± .0008	1.0104 ± .0009
386.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
387.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
388.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
389.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0008
390.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0008
391.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0008
392.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0008
393.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0008
394.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0008
395.0	.9502 ± .0008	.9601 ± .0008	1.0104 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0104 ± .0009

PHENOXYACETIC ACID PAIR

CELL II

Λ_o	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.9514 ± .0008	.9608 ± .0008	1.0098 ± .0009
371.0	.9513 ± .0008	.9608 ± .0008	1.0099 ± .0009
372.0	.9513 ± .0008	.9608 ± .0008	1.0099 ± .0009
373.0	.9512 ± .0008	.9607 ± .0008	1.0099 ± .0009
374.0	.9512 ± .0008	.9607 ± .0008	1.0099 ± .0009
375.0	.9511 ± .0008	.9606 ± .0008	1.0099 ± .0009
376.0	.9511 ± .0008	.9606 ± .0008	1.0099 ± .0009
377.0	.9510 ± .0008	.9605 ± .0008	1.0099 ± .0009
378.0	.9510 ± .0008	.9605 ± .0008	1.0099 ± .0009
379.0	.9510 ± .0008	.9604 ± .0008	1.0098 ± .0009
380.0	.9509 ± .0008	.9603 ± .0008	1.0098 ± .0008
381.0	.9508 ± .0008	.9603 ± .0008	1.0099 ± .0008
382.0	.9508 ± .0008	.9603 ± .0008	1.0099 ± .0008
383.0	.9508 ± .0008	.9603 ± .0008	1.0099 ± .0008
384.0	.9507 ± .0008	.9602 ± .0008	1.0099 ± .0008
385.0	.9507 ± .0008	.9602 ± .0008	1.0099 ± .0008
386.0	.9507 ± .0008	.9602 ± .0008	1.0099 ± .0008
387.0	.9506 ± .0008	.9601 ± .0007	1.0099 ± .0008
388.0	.9506 ± .0008	.9601 ± .0007	1.0099 ± .0008
389.0	.9506 ± .0008	.9601 ± .0007	1.0099 ± .0008
390.0	.9505 ± .0008	.9600 ± .0007	1.0099 ± .0008
391.0	.9505 ± .0008	.9600 ± .0007	1.0099 ± .0008
392.0	.9505 ± .0008	.9600 ± .0007	1.0099 ± .0008
393.0	.9504 ± .0008	.9599 ± .0007	1.0099 ± .0008
394.0	.9504 ± .0008	.9599 ± .0007	1.0099 ± .0008
395.0	.9504 ± .0008	.9599 ± .0007	1.0099 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0099 ± .0008

PHENOXYACETIC ACID PAIR

CELL III

Λ_0	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.9511 ± .0008	.9610 ± .0008	1.0104 ± .0009
371.0	.9511 ± .0008	.9610 ± .0008	1.0104 ± .0009
372.0	.9510 ± .0008	.9609 ± .0008	1.0104 ± .0009
373.0	.9510 ± .0008	.9609 ± .0008	1.0104 ± .0009
374.0	.9509 ± .0008	.9608 ± .0008	1.0104 ± .0009
375.0	.9509 ± .0008	.9608 ± .0008	1.0104 ± .0009
376.0	.9508 ± .0008	.9607 ± .0008	1.0104 ± .0009
377.0	.9508 ± .0008	.9607 ± .0008	1.0104 ± .0009
378.0	.9507 ± .0008	.9606 ± .0008	1.0104 ± .0009
379.0	.9507 ± .0008	.9606 ± .0008	1.0104 ± .0009
380.0	.9506 ± .0008	.9605 ± .0008	1.0104 ± .0009
381.0	.9506 ± .0008	.9605 ± .0008	1.0104 ± .0009
382.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
383.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
384.0	.9505 ± .0008	.9604 ± .0008	1.0104 ± .0009
385.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0009
386.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0009
387.0	.9504 ± .0008	.9603 ± .0008	1.0104 ± .0009
388.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0009
389.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0009
390.0	.9503 ± .0008	.9602 ± .0008	1.0104 ± .0009
391.0	.9502 ± .0008	.9601 ± .0008	1.0104 ± .0009
392.0	.9502 ± .0008	.9601 ± .0008	1.0104 ± .0009
393.0	.9502 ± .0008	.9601 ± .0008	1.0104 ± .0009
394.0	.9501 ± .0007	.9600 ± .0008	1.0104 ± .0008
395.0	.9501 ± .0007	.9600 ± .0008	1.0104 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0104 ± .0009

PHENOXYACETIC ACID PAIR

CELL IV

Λ_o	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.9512 ± .0008	.9615 ± .0008	1.0108 ± .0009
371.0	.9511 ± .0008	.9615 ± .0008	1.0109 ± .0009
372.0	.9511 ± .0008	.9615 ± .0008	1.0109 ± .0009
373.0	.9510 ± .0008	.9614 ± .0008	1.0109 ± .0009
374.0	.9510 ± .0008	.9614 ± .0008	1.0109 ± .0009
375.0	.9509 ± .0008	.9613 ± .0008	1.0109 ± .0009
376.0	.9509 ± .0008	.9613 ± .0008	1.0109 ± .0009
377.0	.9508 ± .0008	.9612 ± .0008	1.0109 ± .0009
378.0	.9508 ± .0008	.9612 ± .0008	1.0109 ± .0009
379.0	.9508 ± .0008	.9611 ± .0008	1.0108 ± .0009
380.0	.9507 ± .0008	.9611 ± .0008	1.0109 ± .0009
381.0	.9507 ± .0008	.9610 ± .0008	1.0108 ± .0009
382.0	.9507 ± .0008	.9610 ± .0008	1.0108 ± .0009
383.0	.9506 ± .0008	.9609 ± .0008	1.0108 ± .0009
384.0	.9506 ± .0008	.9609 ± .0008	1.0108 ± .0009
385.0	.9505 ± .0007	.9609 ± .0008	1.0109 ± .0009
386.0	.9505 ± .0007	.9608 ± .0008	1.0108 ± .0009
387.0	.9505 ± .0007	.9608 ± .0008	1.0108 ± .0009
388.0	.9504 ± .0007	.9607 ± .0008	1.0108 ± .0009
389.0	.9504 ± .0007	.9607 ± .0008	1.0108 ± .0009
390.0	.9504 ± .0007	.9607 ± .0008	1.0108 ± .0009
391.0	.9503 ± .0007	.9606 ± .0008	1.0108 ± .0008
392.0	.9503 ± .0007	.9606 ± .0008	1.0108 ± .0008
393.0	.9503 ± .0007	.9606 ± .0008	1.0108 ± .0008
394.0	.9502 ± .0007	.9605 ± .0008	1.0108 ± .0009
395.0	.9502 ± .0007	.9605 ± .0008	1.0108 ± .0009

AVERAGE ISOTOPE EFFECT = 1.0108 ± .0009

PHENOXYACETIC ACID PAIR

CELL V

Λ_o	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.9511 ± .0008	.9616 ± .0009	1.0110 ± .0009
371.0	.9511 ± .0008	.9615 ± .0009	1.0109 ± .0009
372.0	.9511 ± .0008	.9615 ± .0009	1.0109 ± .0009
373.0	.9510 ± .0008	.9614 ± .0009	1.0109 ± .0009
374.0	.9510 ± .0008	.9614 ± .0009	1.0109 ± .0009
375.0	.9509 ± .0008	.9613 ± .0009	1.0109 ± .0009
376.0	.9509 ± .0008	.9613 ± .0009	1.0109 ± .0009
377.0	.9509 ± .0008	.9613 ± .0009	1.0109 ± .0009
378.0	.9508 ± .0008	.9612 ± .0009	1.0109 ± .0009
379.0	.9508 ± .0008	.9612 ± .0009	1.0109 ± .0009
380.0	.9507 ± .0008	.9611 ± .0009	1.0109 ± .0009
381.0	.9507 ± .0008	.9611 ± .0009	1.0109 ± .0009
382.0	.9506 ± .0008	.9610 ± .0009	1.0109 ± .0009
383.0	.9506 ± .0008	.9610 ± .0009	1.0109 ± .0009
384.0	.9505 ± .0008	.9609 ± .0009	1.0109 ± .0009
385.0	.9505 ± .0008	.9609 ± .0009	1.0109 ± .0009
386.0	.9505 ± .0008	.9609 ± .0009	1.0109 ± .0009
387.0	.9504 ± .0008	.9608 ± .0009	1.0109 ± .0009
388.0	.9504 ± .0008	.9608 ± .0009	1.0109 ± .0009
389.0	.9503 ± .0008	.9608 ± .0009	1.0110 ± .0009
390.0	.9503 ± .0008	.9607 ± .0009	1.0109 ± .0009
391.0	.9503 ± .0008	.9607 ± .0009	1.0109 ± .0009
392.0	.9502 ± .0008	.9606 ± .0009	1.0109 ± .0009
393.0	.9502 ± .0008	.9606 ± .0009	1.0109 ± .0009
394.0	.9501 ± .0008	.9605 ± .0009	1.0109 ± .0009
395.0	.9501 ± .0008	.9605 ± .0009	1.0109 ± .0009

AVERAGE ISOTOPE EFFECT = 1.0109 ± .0009

CHLOROACETIC ACID PAIR

CELL I

Λ_o	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
371.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
372.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
373.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
374.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
375.0	.4725 ± .0003	.4778 ± .0003	1.0112 ± .0008
376.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
377.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
378.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
379.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
380.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
381.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
382.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
383.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
384.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
385.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
386.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
387.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
388.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
389.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
390.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
391.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
392.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
393.0	.4721 ± .0003	.4774 ± .0003	1.0112 ± .0008
394.0	.4720 ± .0003	.4774 ± .0003	1.0114 ± .0008
395.0	.4720 ± .0003	.4774 ± .0003	1.0114 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0114 ± .0008

CHLOROACETIC ACID PAIR

CELL II

Λ_0	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
371.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
372.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
373.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
374.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
375.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
376.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
377.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
378.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
379.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
380.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
381.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
382.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
383.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
384.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
385.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
386.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
387.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
388.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
389.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
390.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
391.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
392.0	.4721 ± .0003	.4775 ± .0003	1.0114 ± .0008
393.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008
394.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008
395.0	.4720 ± .0003	.4774 ± .0003	1.0114 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0116 ± .0008

CHLOROACETIC ACID PAIR

CELL III

Λ_o	SLOPE, m_t(H) x 10^2	SLOPE, m_t(D) x 10^2	ISOTOPE EFFECT
370.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
371.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
372.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
373.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
374.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
375.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
376.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
377.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
378.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
379.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
380.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
381.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
382.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
383.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
384.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
385.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
386.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
387.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
388.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008
389.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008
390.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008
391.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008
392.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008
393.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008
394.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008
395.0	.4720 ± .0003	.4775 ± .0003	1.0116 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0116 ± .0008

CHLOROACETIC ACID PAIR

CELL IV

Λ_0	SLOPE, $m_t(H) \times 10^2$	SLOPE, $m_t(D) \times 10^2$	ISOTOPE EFFECT
370.0	.4727 ± .0003	.4781 ± .0003	1.0114 ± .0008
371.0	.4727 ± .0003	.4781 ± .0003	1.0114 ± .0008
372.0	.4727 ± .0003	.4781 ± .0003	1.0114 ± .0008
373.0	.4727 ± .0003	.4781 ± .0003	1.0114 ± .0008
374.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
375.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
376.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
377.0	.4726 ± .0003	.4780 ± .0003	1.0114 ± .0008
378.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
379.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
380.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
381.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
382.0	.4725 ± .0003	.4779 ± .0003	1.0114 ± .0008
383.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
384.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
385.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
386.0	.4724 ± .0003	.4778 ± .0003	1.0114 ± .0008
387.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
388.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
389.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
390.0	.4723 ± .0003	.4777 ± .0003	1.0114 ± .0008
391.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
392.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
393.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
394.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008
395.0	.4722 ± .0003	.4776 ± .0003	1.0114 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0114 ± .0008

CHLOROACETIC ACID PAIR

CELL V

Λ_o	SLOPE, $m_t(H) \times 10^2$	SLOPE, $m_t(D) \times 10^2$	ISOTOPE EFFECT
370.0	.4724 ± .0003	.4782 ± .0003	1.0116 ± .0008
371.0	.4727 ± .0003	.4782 ± .0003	1.0116 ± .0008
372.0	.4726 ± .0003	.4781 ± .0003	1.0116 ± .0008
373.0	.4726 ± .0003	.4781 ± .0003	1.0116 ± .0008
374.0	.4726 ± .0003	.4781 ± .0003	1.0116 ± .0008
375.0	.4726 ± .0003	.4781 ± .0003	1.0116 ± .0008
376.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
377.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
378.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
379.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
380.0	.4725 ± .0003	.4780 ± .0003	1.0116 ± .0008
381.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
382.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
383.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
384.0	.4724 ± .0003	.4779 ± .0003	1.0116 ± .0008
385.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
386.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
387.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
388.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
389.0	.4723 ± .0003	.4778 ± .0003	1.0116 ± .0008
390.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
391.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
392.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
393.0	.4722 ± .0003	.4777 ± .0003	1.0116 ± .0008
394.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008
395.0	.4721 ± .0003	.4776 ± .0003	1.0116 ± .0008

AVERAGE ISOTOPE EFFECT = 1.0116 ± .0008

PHENYLTHIOGLYCOLLIC ACID PAIR

CELL I

Λ_o	SLOPE, m_t(H) x 10	SLOPE, m_t(D) x 10	ISOTOPE EFFECT
370.0	.2465 ± .0001	.2515 ± .0001	1.0202 ± .0006
371.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
372.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
373.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
374.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
375.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
376.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
377.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
378.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
379.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
380.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
381.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
382.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
383.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
384.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
385.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
386.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
387.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
388.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
389.0	.2463 ± .0001	.2513 ± .0001	1.0203 ± .0006
390.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
391.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
392.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
393.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
394.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
395.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006

AVERAGE ISOTOPE EFFECT = 1.0207 ± .0006

PHENYLTHIOGLYCOLLIC ACID PAIR

CELL II

λ_o	SLOPE, m_t(H) x 10	SLOPE, m_t(D) x 10	ISOTOPE EFFECT
370.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
371.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
372.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
373.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
374.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
375.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
376.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
377.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
378.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
379.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
380.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
381.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
382.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
383.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
384.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
385.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
386.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
387.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
388.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
389.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
390.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
391.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
392.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
393.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
394.0	.2461 ± .0001	.2513 ± .0001	1.0211 ± .0006
395.0	.2461 ± .0001	.2513 ± .0001	1.0211 ± .0006

AVERAGE ISOTOPE EFFECT = 1.0209 ± .0006

PHENYLTHIOGLYCOLLIC ACID PAIR

CELL III

Λ_o	SLOPE, m_t(H) x 10	SLOPE, m_t(D) x 10	ISOTOPE EFFECT
370.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
371.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
372.0	.2464 ± .0001	.2515 ± .0001	1.0206 ± .0006
373.0	.2464 ± .0001	.2514 ± .0001	1.0202 ± .0006
374.0	.2464 ± .0001	.2514 ± .0001	1.0202 ± .0006
375.0	.2464 ± .0001	.2514 ± .0001	1.0202 ± .0006
376.0	.2464 ± .0001	.2514 ± .0001	1.0202 ± .0006
377.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
378.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
379.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
380.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
381.0	.2463 ± .0001	.2514 ± .0001	1.0207 ± .0006
382.0	.2463 ± .0001	.2513 ± .0001	1.0203 ± .0006
383.0	.2463 ± .0001	.2513 ± .0001	1.0203 ± .0006
384.0	.2463 ± .0001	.2513 ± .0001	1.0203 ± .0006
385.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
386.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
387.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
388.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
389.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
390.0	.2462 ± .0001	.2513 ± .0001	1.0207 ± .0006
391.0	.2462 ± .0001	.2512 ± .0001	1.0203 ± .0006
392.0	.2462 ± .0001	.2512 ± .0001	1.0203 ± .0006
393.0	.2462 ± .0001	.2512 ± .0001	1.0203 ± .0006
394.0	.2462 ± .0001	.2512 ± .0001	1.0203 ± .0006
395.0	.2462 ± .0001	.2512 ± .0001	1.0203 ± .0006

AVERAGE ISOTOPE EFFECT = 1.0205 ± .0006

PHENYLTHIOGLYCOLLIC ACID PAIR

CELL IV

Λ_0	SLOPE, m_t(H) x 10	SLOPE, m_t(D) x 10	ISOTOPE EFFECT
370.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
371.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
372.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
373.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
374.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
375.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
376.0	.2464 ± .0001	.2516 ± .0002	1.0211 ± .0007
377.0	.2463 ± .0001	.2516 ± .0001	1.0215 ± .0007
378.0	.2463 ± .0001	.2516 ± .0001	1.0215 ± .0007
379.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
380.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
381.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
382.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
383.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
384.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
385.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
386.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0007
387.0	.2462 ± .0001	.2515 ± .0001	1.0215 ± .0007
388.0	.2462 ± .0001	.2515 ± .0001	1.0215 ± .0007
389.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
390.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
391.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
392.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
393.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
394.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007
395.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0007

AVERAGE ISOTOPE EFFECT = 1.0211 ± .0007

PHENYLTHIOGLYCOLLIC ACID PAIR

CELL V

Λ_0	SLOPE, $m_t(H)$ x 10	SLOPE, $m_t(D)$ x 10	ISOTOPE EFFECT
370.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
371.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
372.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
373.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
374.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
375.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
376.0	.2464 ± .0001	.2516 ± .0001	1.0211 ± .0006
377.0	.2463 ± .0001	.2516 ± .0001	1.0215 ± .0006
378.0	.2463 ± .0001	.2516 ± .0001	1.0215 ± .0006
379.0	.2463 ± .0001	.2516 ± .0001	1.0215 ± .0006
380.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
381.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
382.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
383.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
384.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
385.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
386.0	.2463 ± .0001	.2515 ± .0001	1.0211 ± .0006
387.0	.2462 ± .0001	.2515 ± .0001	1.0215 ± .0006
388.0	.2462 ± .0001	.2515 ± .0001	1.0215 ± .0006
389.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
390.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
391.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
392.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
393.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
394.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006
395.0	.2462 ± .0001	.2514 ± .0001	1.0211 ± .0006

AVERAGE ISOTOPE EFFECT = 1.0211 ± .0006

APPENDIX IV

ABBREVIATED RESULTS OF THE SHEDLOVSKY IV TREATMENT OF CONCENTRATION-EQUIVALENT CONDUCTANCE DATA OF $PhSO_2CH_2COOH$ AND THE ISOTOPICALLY SUBSTITUTED ACETIC ACID PAIRS RCH_2COOH/RCD_2COOH, WHERE R = PhO, Cl, AND PhS

PHENYLSULFONYLACETIC ACID

(AVERAGE $K_t \pm \delta$) x 10^4

Λ_0	CELL I	CELL II	CELL III	CELL IV	CELL V
379.0	36.98 ± .1802	36.98 ± .1746	36.98 ± .1740	36.98 ± .1805	36.98 ± .1801
379.1	36.93 ± .1695	36.93 ± .1643	36.93 ± .1631	36.93 ± .1697	36.93 ± .1696
379.2	36.88 ± .1600	36.88 ± .1553	36.88 ± .1534	36.88 ± .1601	36.88 ± .1602
379.3	36.83 ± .1521	36.83 ± .1479	36.83 ± .1454	36.83 ± .1521	36.83 ± .1526
379.4	36.78 ± .1458	36.78 ± .1422	36.78 ± .1390	36.78 ± .1458	36.78 ± .1465
379.5	36.73 ± .1414	36.73 ± .1387	36.74 ± .1346	36.73 ± .1413	36.73 ± .1423
379.6	36.68 ± .1391	36.69 ± .1371	36.69 ± .1325	36.68 ± .1389	36.68 ± .1403
379.7	36.63 ± .1387	36.64 ± .1378	36.64 ± .1324	36.63 ± .1385	36.63 ± .1402
379.8	36.58 ± .1407	36.59 ± .1404	36.59 ± .1346	36.58 ± .1403	36.58 ± .1422
379.9	36.53 ± .1445	36.54 ± .1450	36.54 ± .1388	36.53 ± .1440	36.53 ± .1462
380.0	36.48 ± .1501	36.49 ± .1514	36.49 ± .1448	36.49 ± .1496	36.48 ± .1519
380.1	36.44 ± .1572	36.44 ± .1592	36.44 ± .1524	36.44 ± .1567	36.43 ± .1592
380.2	36.39 ± .1656	36.39 ± .1683	36.39 ± .1613	36.39 ± .1651	36.39 ± .1677
380.3	36.34 ± .1754	36.34 ± .1785	36.35 ± .1715	36.34 ± .1749	36.34 ± .1775
380.4	36.29 ± .1859	36.30 ± .1894	36.30 ± .1825	36.29 ± .1853	36.29 ± .1880

PHENOXYACETIC ACID

(AVERAGE $K_t \pm \delta$) x 10^5

Λ_o	CELL I	CELL II	CELL III	CELL IV	CELL V
379.8	73.28 ± .1818	73.26 ± .1801	73.28 ± .1788	73.29 ± .1796	73.27 ± .1758
379.9	73.21 ± .1762	73.20 ± .1744	73.22 ± .1733	73.22 ± .1732	73.21 ± .1704
380.0	73.15 ± .1713	73.14 ± .1695	73.15 ± .1686	73.16 ± .1676	73.14 ± .1658
380.1	73.09 ± .1672	73.07 ± .1654	73.09 ± .1648	73.10 ± .1627	73.08 ± .1622
380.2	73.02 ± .1640	73.01 ± .1622	73.03 ± .1618	73.04 ± .1587	73.02 ± .1599
380.3	72.96 ± .1617	72.95 ± .1599	72.96 ± .1598	72.97 ± .1557	72.95 ± .1576
380.4	72.90 ± .1604	72.89 ± .1586	72.90 ± .1587	72.91 ± .1536	72.89 ± .1567
380.5	72.84 ± .1600	72.82 ± .1582	72.84 ± .1585	72.85 ± .1525	72.83 ± .1568
380.6	72.77 ± .1607	72.76 ± .1589	72.78 ± .1595	72.78 ± .1523	72.77 ± .1580
380.7	72.71 ± .1622	72.70 ± .1605	72.71 ± .1613	72.72 ± .1532	72.70 ± .1601
380.8	72.65 ± .1647	72.64 ± .1630	72.65 ± .1641	72.66 ± .1551	72.64 ± .1631
380.9	72.59 ± .1681	72.57 ± .1664	72.59 ± .1676	72.60 ± .1579	72.58 ± .1668
381.0	72.52 ± .1721	72.51 ± .1704	72.53 ± .1720	72.54 ± .1616	72.52 ± .1715
381.1	72.46 ± .1770	72.45 ± .1753	72.46 ± .1771	72.47 ± .1662	72.45 ± .1767
381.2	72.40 ± .1825	72.39 ± .1810	72.40 ± .1829	72.41 ± .1715	72.39 ± .1826

PHENOXYACETIC-2,2-d_2 ACID

(AVERAGE K_t ± δ) x 10^5

Λ_o	CELL I	CELL II	CELL III	CELL IV	CELL V
379.3	72.70 ± .1830	72.71 ± .1820	72.72 ± .1810	72.72 ± .1984	72.70 ± .1986
379.4	72.64 ± .1775	72.64 ± .1771	72.65 ± .1757	72.65 ± .1921	72.64 ± .1929
379.5	72.58 ± .1728	72.58 ± .1730	72.59 ± .1711	72.59 ± .1865	72.58 ± .1879
379.6	72.52 ± .1688	72.52 ± .1697	72.53 ± .1673	72.53 ± .1816	72.52 ± .1836
379.7	72.45 ± .1657	72.46 ± .1673	72.47 ± .1643	72.47 ± .1774	72.45 ± .1801
379.8	72.39 ± .1635	72.39 ± .1657	72.40 ± .1624	72.40 ± .1741	72.39 ± .1774
379.9	72.33 ± .1622	72.33 ± .1651	72.34 ± .1613	72.34 ± .1717	72.33 ± .1756
380.0	72.27 ± .1619	72.27 ± .1655	72.28 ± .1612	72.28 ± .1700	72.27 ± .1745
380.1	72.20 ± .1625	72.21 ± .1667	72.22 ± .1620	72.22 ± .1692	72.20 ± .1744
380.2	72.14 ± .1641	72.15 ± .1689	72.15 ± .1637	72.15 ± .1693	72.14 ± .1751
380.3	72.08 ± .1665	72.08 ± .1718	72.09 ± .1663	72.09 ± .1703	72.08 ± .1766
380.4	72.02 ± .1697	72.02 ± .1755	72.03 ± .1696	72.03 ± .1721	72.02 ± .1790
380.5	71.96 ± .1736	71.96 ± .1799	71.97 ± .1737	71.97 ± .1748	71.96 ± .1821
380.6	71.90 ± .1783	71.90 ± .1850	71.91 ± .1787	71.91 ± .1783	71.90 ± .1860
380.7	71.83 ± .1838	71.84 ± .1907	71.85 ± .1843	71.85 ± .1825	71.83 ± .1906

CHLOROACETIC ACID

(AVERAGE $K_t \pm \delta$) x 10^5

Λ_0	CELL I	CELL II	CELL III	CELL IV	CELL V
389.4	140.5 ± .3864	140.5 ± .3966	140.5 ± .3865	140.5 ± .4017	140.5 ± .3998
389.5	140.3 ± .3753	140.4 ± .3860	140.4 ± .3750	140.3 ± .3900	140.4 ± .3884
389.6	140.2 ± .3660	140.2 ± .3770	140.2 ± .3647	140.2 ± .3796	140.2 ± .3782
389.7	140.1 ± .3582	140.1 ± .3695	140.1 ± .3562	140.1 ± .3708	140.1 ± .3697
389.8	140.0 ± .3522	140.0 ± .3638	140.0 ± .3495	140.0 ± .3636	140.0 ± .3629
389.9	139.8 ± .3477	139.9 ± .3597	139.9 ± .3444	139.8 ± .3580	139.9 ± .3576
390.0	139.7 ± .3451	139.7 ± .3576	139.7 ± .3412	139.7 ± .3543	139.7 ± .3542
390.1	139.6 ± .3445	139.6 ± .3574	139.6 ± .3399	139.6 ± .3521	139.6 ± .3523
390.2	139.5 ± .3459	139.5 ± .3587	139.5 ± .3407	139.5 ± .3522	139.5 ± .3527
390.3	139.4 ± .3489	139.4 ± .3618	139.4 ± .3433	139.4 ± .3540	139.4 ± .3548
390.4	139.2 ± .3537	139.2 ± .3665	139.2 ± .3475	139.2 ± .3574	139.2 ± .3584
390.5	139.1 ± .3601	139.1 ± .3730	139.1 ± .3535	139.1 ± .3625	139.1 ± .3639
390.6	139.0 ± .3683	139.0 ± .3812	139.0 ± .3612	139.0 ± .3694	139.0 ± .3710
390.7	138.9 ± .3780	138.9 ± .3905	138.9 ± .3704	138.9 ± .3775	138.9 ± .3796
390.8	138.7 ± .3886	138.7 ± .4014	138.8 ± .3809	138.7 ± .3874	138.7 ± .3895

CHLOROACETIC-2,2-d_2 ACID

(AVERAGE K_t ± δ) x 10^5

Λ_o	CELL I	CELL II	CELL III	CELL IV	CELL V
389.9	138.3 ± .2043	138.3 ± .2118	138.3 ± .2187	138.2 ± .2336	138.2 ± .2326
390.0	138.1 ± .1776	138.1 ± .1852	138.1 ± .1920	138.1 ± .2064	138.1 ± .2056
390.1	138.0 ± .1515	138.0 ± .1593	138.0 ± .1658	138.0 ± .1794	138.0 ± .1791
390.2	137.9 ± .1262	137.9 ± .1343	137.9 ± .1404	137.9 ± .1527	137.9 ± .1529
390.3	137.8 ± .1017	137.8 ± .1103	137.8 ± .1157	137.7 ± .1263	137.7 ± .1274
390.4	137.6 ± .0794	137.6 ± .0884	137.6 ± .0928	137.6 ± .1001	137.6 ± .1027
390.5	137.5 ± .0611	137.5 ± .0700	137.5 ± .0724	137.5 ± .0753	137.5 ± .0799
390.6	137.4 ± .0516	137.4 ± .0593	137.4 ± .0585	137.4 ± .0529	137.4 ± .0605
390.7	137.3 ± .0554	137.3 ± .0601	137.3 ± .0553	137.2 ± .0371	137.2 ± .0500
390.8	137.1 ± .0697	137.1 ± .0714	137.1 ± .0641	137.1 ± .0379	137.1 ± .0524
390.9	137.0 ± .0901	137.0 ± .0898	137.0 ± .0816	137.0 ± .0541	137.0 ± .0665
391.0	136.9 ± .1129	136.9 ± .1114	136.9 ± .1027	136.9 ± .0764	136.9 ± .0869
391.1	136.8 ± .1372	136.8 ± .1349	136.8 ± .1262	136.7 ± .1008	136.7 ± .1100
391.2	136.6 ± .1620	136.6 ± .1591	136.6 ± .1505	136.6 ± .1206	136.6 ± .1342
391.3	136.5 ± .1873	136.5 ± .1839	136.5 ± .1753	136.5 ± .1516	136.5 ± .1589

PHENYLTHIOGLYCOLLIC ACID

(AVERAGE $K_t \pm \delta$) x 10^6

Λ_0	CELL I	CELL II	CELL III	CELL IV	CELL V
380.6	281.1 ± .4506	281.1 ± .4443	281.1 ± .4439	281.1 ± .4853	281.1 ± .4625
380.7	280.9 ± .4441	280.9 ± .4393	280.9 ± .4371	280.9 ± .4808	280.9 ± .4573
380.8	280.7 ± .4382	280.7 ± .4356	280.7 ± .4317	280.7 ± .4772	280.7 ± .4529
380.9	280.5 ± .4337	280.5 ± .4330	280.5 ± .4271	280.5 ± .4749	280.5 ± .4496
381.0	280.3 ± .4296	280.3 ± .4314	280.3 ± .4236	280.3 ± .4734	280.3 ± .4474
381.1	280.1 ± .4273	280.1 ± .4307	280.2 ± .4212	280.1 ± .4726	280.1 ± .4460
381.2	279.9 ± .4259	279.9 ± .4314	280.0 ± .4200	280.0 ± .4730	279.9 ± .4456
381.3	279.8 ± .4255	279.8 ± .4331	279.8 ± .4199	279.8 ± .4745	279.8 ± .4466
381.4	279.6 ± .4265	279.6 ± .4360	279.6 ± .4210	279.6 ± .4772	279.6 ± .4487
381.5	279.4 ± .4278	279.4 ± .4396	279.4 ± .4227	279.4 ± .4807	279.4 ± .4515
381.6	279.2 ± .4308	279.2 ± .4442	279.2 ± .4260	279.2 ± .4848	279.2 ± .4553
381.7	279.0 ± .4349	279.0 ± .4500	279.0 ± .4303	279.0 ± .4899	279.0 ± .4601
381.8	278.8 ± .4400	278.8 ± .4568	278.8 ± .4358	278.8 ± .4962	278.8 ± .4662
381.9	278.6 ± .4457	278.6 ± .4644	278.6 ± .4416	278.6 ± .5031	278.6 ± .4730
382.0	278.4 ± .4525	278.4 ± .4724	278.5 ± .4488	278.4 ± .5106	278.4 ± .4800

PHENYLTHIOGLYCOLLIC-2,2-d_2 ACID

(AVERAGE $K_t \pm \delta$) x 10^6

Λ_o	CELL I	CELL II	CELL III	CELL IV	CELL V
381.0	275.0 ± .6158	275.0 ± .6194	275.0 ± .6134	275.0 ± .6594	275.0 ± .6383
381.1	274.8 ± .6114	274.8 ± .6157	274.8 ± .6101	274.8 ± .6544	274.8 ± .6333
381.2	274.6 ± .6077	274.6 ± .6125	274.6 ± .6076	274.6 ± .6505	274.6 ± .6291
381.3	274.4 ± .6049	274.4 ± .6103	274.5 ± .6059	274.4 ± .6470	274.4 ± .6254
381.4	274.3 ± .6025	274.3 ± .6084	274.3 ± .6045	274.2 ± .6444	274.2 ± .6224
381.5	274.1 ± .6011	274.1 ± .6076	274.1 ± .6042	274.0 ± .6419	274.0 ± .6200
381.6	273.9 ± .6001	273.9 ± .6074	273.9 ± .6042	273.9 ± .6403	273.8 ± .6184
381.7	273.7 ± .6000	273.7 ± .6077	273.7 ± .6052	273.7 ± .6395	273.7 ± .6175
381.8	273.5 ± .6008	273.5 ± .6090	273.5 ± .6069	273.5 ± .6394	273.5 ± .6174
381.9	273.3 ± .6017	273.3 ± .6105	273.4 ± .6091	273.3 ± .6397	273.3 ± .6177
382.0	273.1 ± .6040	273.1 ± .6132	273.2 ± .6122	273.1 ± .6409	273.1 ± .6189
382.1	273.0 ± .6065	273.0 ± .6163	273.0 ± .6157	272.9 ± .6426	272.9 ± .6206
382.2	272.8 ± .6100	272.8 ± .6202	272.8 ± .6203	272.8 ± .6452	272.7 ± .6232
382.2	272.6 ± .6137	272.6 ± .6243	272.6 ± .6248	272.6 ± .6484	272.6 ± .6262
382.3	272.4 ± .6186	272.4 ± .6296	272.4 ± .6306	272.4 ± .6520	272.4 ± .6300

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ERRATA

p. 35, Line 5.

Equation [24] is obtained from a consideration of Equations [13], [21] and [22], and is given by

[24] $$K_t = \frac{\alpha^2 \cdot c \cdot f_{\pm}^2}{(1-\alpha) f_u}$$

This Equation may, however, be obtained from simpler assumptions. The classical equilibrium constant, K_c, given by Equation [29] as

[29] $$K_c = \frac{\alpha^2 c}{(1-\alpha)}$$

is dependent only upon the concentrations of the various species present, expressed in the form of a general equilibrium for weak carboxylic acids in aqueous media, i.e.,

$$HA + H_2O \rightleftharpoons H_3O^{(+)} + A^{(-)}$$

such that

$$K_c = \frac{[H_3O^{(+)}][A^{(-)}]}{[HA]}$$

However, since activities (a) rather than concentrations are appropriate to thermodynamic equilibria, the expression may be rewritten as

$$K_t = \frac{a_{H_3O^{(+)}} \cdot a_{A^{(-)}}}{a_{HA}}$$

Since the respective activities are equal to the products of the concentrations of the species and their appropriate activity coefficients, the expression for K_t can be reduced to

$$K_t = \frac{\alpha^2 \cdot c \cdot f_\pm^2}{(1-\alpha) f_u}$$

which is Equation [24] as stated.

pp. 35-36.

It should be noted that besides the electrophoretic and relaxation effects, the original Onsager formulation also includes a "viscous drag effect" which arises from a consideration of Stokes' Law. Equation [26] is stated in the text as Onsager's expression for the case of weak electrolytes only. A discussion of this point is presented more fully in reference 116.

p. 37, lines 6-9.

References to support the statement which reads, "Indeed, the validity of their application to acid solutions has been questioned in as much as these treatments consider ionic migration as "submarine-like" motion, whereas "proton jumps" might be anticipated for the migration of hydronium ions.", are provided by the following:

(a) E.J. King. Acid-base equilibria. In The international encyclopedia of physical chemistry and chemical physics. Vol. 4. Edited by R.A. Robinson. Pergamon Press, London. 1965. p. 28.

(b) R.A. Robinson and R.H. Stokes. Electrolyte solutions. 2nd ed. Butterworths, London. 1970. p. 121.

p. 39, line 17.

Equation [31], which is given as

$$[31] \qquad F(z) = 1\text{-}z\{1\text{-}z[1\text{-}z(\text{etc.})^{-\frac{1}{2}}]^{-\frac{1}{2}}\}^{-\frac{1}{2}}$$

is supported by the following reference:

E.J. King. Acid-base equilibria. In The international encyclopedia of physical chemistry and chemical physics. Vol. 4. Edited by R.A. Robinson. Pergamon Press, London. 1965. p. 35.

pp. 65-66.

The final step in the preparation of the cells for conductance measurements, prior to the determination of the various cell constants, was the seasoning of the cells with a solution of purified phenylacetic acid. It should be noted that the cells were subsequently seasoned with solutions of the other acids examined in the study prior to the redetermination of the cell constants and the investigation of the conductivity of solutions of these acids.

It is also noteworthy that following the cell cleaning process, the observed resistances of the solution of purified phenylacetic acid used to season the cells were significantly larger than the anticipated resistances. These differences in resistance coincided with a loss in ionic concentration which approximately corresponded to a monolayer deposit of the acid on the clean surfaces of the solution flask and cells.

p. 120, lines 4-6.

The frequency dependence of the resistances of solutions of phenoxyacetic and phenoxyacetic-2,2-d_2 acids was examined. Using the G.R.I.C. resistances of ca. 5000 Ω were recorded for the most dilute solutions of these acids (hence, the most susceptible to frequency dependence), and the resistances recorded at 100 cps differed by not more than 0.9 Ω from those recorded at 1000 cps.

pp. 182-183.

The initial steps in the synthesis of 9-thia-9,10-dihydrophenanthrene-9-oxide are described and the isolation of pure o-nitrobenzyl phenyl sulfide and o-aminobenzyl phenyl sulfide is claimed, even though in each reaction step mixtures of the respective o- and p- isomers were used. This apparent anomaly is explained by the fact that the reaction steps were carried out using the mixtures as stated, but small samples were set aside for analyses. These samples gave reasonably sharp melting points and yielded spectra (i.r., n.m.r. and m.s.) from which it was extremely difficult to discern the fact that they were impure. Investigation of the integrity of the starting material was not initiated until after the Pschorr reaction products were examined. In the course of the investigation, pure samples of the respective o- and p- isomers of nitrobenzyl phenyl sulfide and aminobenzyl phenyl sulfide were isolated. Consequently, although the initial reactions were carried out on material, the bulk of which proved to be a mixture, the pure o- isomers were isolated and their properties appropriately recorded.

pp. 184-193.

The notation "CH_2-S" in the Thesis is used to represent the vibrational stretching modes of hydrogen atoms attached to carbon in methylene groups adjacent to unoxidized sulfur atoms. This follows the notation used in

N.B. Colthup, L.H. Daly, and S.E. Wiberley. Introduction to infrared and raman spectroscopy. Academic Press, Inc., New York. 1964. p. 306.

This notation may be misleading and these vibrational modes are perhaps better represented by "C-H of CH_2-S". The erroneous notation occurs on the following pages in the text:

p. 184, line 9;
p. 187, line 16;
p. 188, line 17;
p. 189, line 16;
p. 191, line 19;
p. 193, line 20.