The product distributions of all the coupled products except the coupled benzoic acids were carried out using a 12-ft 15% Apiezon N column at 250°. Flow rate was 60 ml/min. The identity of the 2,2′, 3,3′, and 4,4′ bitolyls was determined from vpc by fortification with an authentic sample of each isomer. The identity of the 2,3′, 2,4′, and 3,4′ mixed bitolyls was inferred from their reported order of elution under very similar vpc conditions.[30] Further support for the assignment by vpc retention times was obtained by the ultraviolet spectra of samples collected from the vpc eluent. Because of the small samples and similarities in spectra it was difficult to make positive identification. However, the comparison of these spectra with published spectra[31] of the isomers lent support to the assignments by vpc retention time. The coupled benzoic acids were esterified by diazomethane and the esters analyzed using a 6-ft Apiezon N column at 260°. Flow rate was 60 ml/min.

**Kinetic Runs.**—Quantitative analyses were by polarographic analysis. The wave for monoarylthallium(III) compounds falls between the waves for $Tl^{III}$ and diarylthallium(III) compounds. The kinetic runs were made using a soft-drink bottle stirred with a magnetic stirring bar. The bottle was capped with a metal cap having holes sealed by a rubber liner through which samples for analysis could be withdrawn using a syringe with needle attached. Two-milliliter aliquots were withdrawn and quenched by addition of 1 ml of 4 *M* NaCl. The sample was diluted to 10 ml with water for analysis. These samples were analyzed at 25° using a Sargent Model XXI polarograph. The $E_{1/2}$ for $Tl^{3+}$ occurred at $-0.1$ V *vs.* a standard calomel electrode, the $E_{1/2}$ for phenyl thallium at $-0.2$ V, and the $E_{1/2}$ for diphenylthallium at $-0.5$ V. The $i_d$ for the $Tl^{3+}$ was directly proportional to $Tl^{3+}$ concentration in the bulk of the solution. Control runs showed no disproportion took place in the time required for analysis.

**Registry No.**—Thallic triacetate, 2570-63-0; palladium(II) diacetate, 3375-31-3.

**Acknowledgments.**—The author gratefully acknowledges helpful discussions with Dr. H. G. Tennent and the late Professor S. Winstein, as wel las the capable technical assistance of Mr. Michael Centuolo.

---

[30] E. A. Johnson, *J. Chem. Soc.*, 4155 (1957).

[31] G. H. Beaven and E. A. Johnson, *Spectrochim. Acta*, **14**, 67 (1959).

---

# Substituent Effect Transmission from Heavy Atoms. Microscopic Dissociation Constants of Selenoglycolic Acid

JOSEPH L. KURZ AND JUDITH COBURN HARRIS[1]

*Department of Chemistry, Washington University, St. Louis, Missouri 63130*

*Received February 18, 1970*

An unusual enhancement of the substitutent effect of a negative charge on the $pK_a$ of a carboxyl group has been observed to be present when that charge is located on a selenium atom. A method for preparing solutions of pure selenols from the corresponding diselenides is described, and such solutions have been used in determining the extents of dissociation of the SeH groups in $HSeCH_2CO_2CH_3$ and $HSeCH_2CO_2H$ as functions of pH. Values for the microscopic dissociation constants of the latter acid have been derived from those data, and are: for the SeH groups, $pk_a = 4.7$, $pk_d = 7.3$; for the $CO_2H$ group, $pk_b = 4.1$, $pk_c = 6.7$. Relative to the effect on the acidity of a carboxyl group which is produced by a charge located on nitrogen or oxygen, the substitutent effects of charges located on S and Se in $^-SCH_2CO_2H$ and $^-SeCH_2CO_2H$ are too large by 0.6 and 0.8 pK units, respectively. It is shown that this enhancement of the substituent effect is within the range attributable to a decrease in the effective dielectric constant arising from the increase in atomic radius in the sequence O, S, Se. An uncertain fraction of this increase in ΔpK probably arises from a decrease in the interaction between the charge on $CO_2^-$ and the XH dipole moment as X varies through the same sequence.

The effect of charged substituents on the acidity of carboxylic acids has been studied extensively,[2-4] and for several classes of acids it has been shown[3] that such effects can be predicted from a suitably modified electrostatic model with an uncertainty not exceeding a few tenths of a pK unit. However, tests of such electrostatic predictions, as well as of purely empirical correlations of pK with the distance between the charge and the acidic site,[5-7] have been almost completely restricted to acids in which the charge is borne by a first-row atom, N or O. In connection with other work in these laboratories, it became necessary to make similar estimates for the effect of charges located on heavier atoms.

Very few pK values are available for dibasic acids in which one or both protons are bound to non-first-row atoms, and most which have been reported are apparent values measured at high or unspecified ionic strength. It is known that ΔpK for acids in which two protons are bound to the same basic atom can vary widely as that atom is changed (*e.g.*, $H_3O^+$ *vs.* $H_2O$, $\Delta pK = 17.4$; $H_2S$ *vs.* $HS^-$, $\Delta pK = 7.6$,[8] in at least qualitative agreement with an electrostatic prediction based on the relative size of O and S). However, the scarcity of data makes it uncertain whether any such variation persists when the protons are not bound to the same atom and the nonelectrostatic effects which contribute[8] to those very large differences are therefore no longer operative. That changes in effective dielectric constant, $D_E$, arising from an increase in the radius of the atom bearing the charge might be important is suggested by the observation[4] that the acid-strengthening effect of a positive charge on quaternary nitrogen is greater than that of a charge on less highly substituted nitrogen. (*E.g.*, at 25° (a) for $H_3N^+CH_2CO_2H$ *vs.* $(CH_3)_3N^+$-$CH_2CO_2H$, $\Delta pK = 0.5$,[9] (b) for amine salts derived from the 1,4-diazabicyclo[2.2.2]octane ring system, $HN^+(CH_2CH_2)_3NH^+$ has $pK_a = 2.67$, $CH_3N^+(CH_2$-

---

[1] National Science Foundation Graduate Fellow, 1968–1969.

[2] (a) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); (b) F. H. Westheimer and J. G. Kirkwood, *ibid.*, **6**, 513 (1938); (c) F. H. Westheimer and M. W. Shookhoff, *J. Amer. Chem. Soc.*, **61**, 555 (1939).

[3] C. Tanford, *ibid.*, **79**, 5348 (1957).

[4] C. F. Wilcox, Jr. and J. S. McIntyre, *J. Org. Chem.*, **30**, 777 (1965).

[5] G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Englewood Cliffs, N. J., 1941, Chapter 6.

[6] J. L. Kurz and J. I. Coburn, *J. Amer. Chem. Soc.*, **89**, 3528 (1967).

[7] J. C. McGowan, *J. Appl. Chem.*, **10**, 312 (1960).

[8] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 92.

[9] D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworths, London, 1965.

$CH_2)_3NH^+$ has p$K_a$ = 2.26, and $\Delta$p$K$ (symmetry corrected) = 0.7.)[10]

The data reported below allow the calculation of $\Delta$p$K$ values for dissociation of the $CO_2H$ groups in the acid pairs $HXCH_2CO_2H$ *vs.* $^-XCH_2CO_2H$ (X = S, Se). Earlier estimates of p$K$ for the thiols exist, but no directly measured values for the selenols have been reported previously, presumably due to their instability and sensitivity to air.[11]

## Experimental Section

**Materials.**—Fisher Certified thioglycolic acid was distilled *in vacuo* (20 mm) and stored under $N_2$ at 4° until used. Potassium selenocyanoacetate, $NCSeCH_2CO_2K$, was prepared by the method of Hofmanns[12] and was converted into diselenodiacetic acid, $(SeCH_2CO_2H)_2$, according to the procedure of Behagel and Rollmann;[13] repeated recrystallization of this diacid from ethyl acetate–toluene gave pale yellow needles, mp 104.5–105.5° (corr) (*Anal.* Calcd for $C_4H_6O_4Se_2$: C, 17.39; H, 2.19. Found: C, 17.56; H, 2.34. Mol. wt. Calcd: 276.0. Found: 276.7) The corresponding dimethyl ester, $(SeCH_2CO_2CH_3)_2$, was prepared from the reaction of the diacid in solution in diethyl ether at −10° with a 20% excess of diazomethane in ether. The resulting yellow oil was chromatographed on Florisil using *n*-hexane–benzene as eluent and the middle fraction was subjected to short-path distillation at 0.05 mm. (*Anal.* Calcd for $C_6H_{10}O_4Se_2$: C, 23.68; H, 3.32. Found: C, 23.80; H, 3.28.) All other reagents were the best available commercial grade and were used without purification.

**Buffers.**—All buffers used in the spectrophotometric determinations of p$K$ had ionic strength $\leq 0.14$. Their pH values were measured at 25.0 ± 0.1° with a Beckman Model 1019 pH meter equipped with Fisher full-range glass and Beckman carborundum frit junction calomel electrodes which had been standardized against NBS borax and phthalate buffers. The stock solutions of selenols used in uv measurements contained significant amounts of strong base; the increase in the pH of each buffer which resulted from addition of an aliquot of one of those solutions was calculated, either from the known concentrations of the acidic and basic component of the buffer or from the value of the van Slyke $\beta$ for those buffers for which such values are tabulated.[14] These corrections were never greater than 0.04 pH unit.

**Uv Spectra.**—All uv spectra were obtained using a Cary 14 spectrophotometer equipped with a thermostated (25.0 ± 0.1° by measurement in the cell) cell holder. For each measurement, the cell was filled to within a few mm of the bottom of its stopper with a known volume of the buffer. The cell contents were deaerated by passing a rapid stream of Ar *via* a syringe needle through the solution for 15 min and then stoppering the cell. After scanning the "blank" spectrum of the buffer, an aliquot (10, 20, or 50 $\mu$l) of a stock solution of the acid being studied was added from a microsyringe and Ar bubbling was continued for 2 min to ensure mixing before the cell was restoppered and the spectrum recorded. The optical density (OD) values of solutions of selenols decreased with time; the spectra of such solutions were therefore scanned three times at appropriate time intervals and the OD at each wavelength of interest extrapolated back to the time of mixing. The decrease in OD was linear with time and the extrapolated value was never more than 5% higher than that observed in the first scan. Spectra of the thiols were not observed to be time dependent when oxygen was excluded by the described procedure.

Undissociated selenols and thiols show no strong absorption between 240 and 250 m$\mu$, while their conjugate bases have maxima in that region. The following absorptions were observed: $^-SeCH_2CO_2^-$, $\lambda_{max}$ 250 m$\mu$ ($\epsilon$ 6 × $10^3$); $^-SeCH_2CO_2CH_3$, $\lambda_{max}$ 241 m$\mu$ ($\epsilon$ 5 × $10^3$); $^-SCH_2CO_2^-$, $\lambda_{max}$ 244 m$\mu$ ($\epsilon$ 4.8 × $10^3$); $^-SCH_2CO_2CH_3$, no resolved maximum ($\epsilon_{244}$ = 3.8 × $10^3$). The $\epsilon$ values for the selenols are somewhat imprecise due to the loss by evaporation of an uncertain amount of solvent during nitrogen purging in the preparation of the stock solutions. The *OD* values used in calculating dissociation constants lay between 0.1 and 0.9.

**Solutions of Selenols.**—The sodium salt of selenoglycolic acid, $NaSeCH_2CO_2Na$, was prepared in solution by reduction of 0.18 mmol of $(SeCH_2CO_2Na)_2$ dissolved in 10 ml of 0.10 *F* aqueous NaOH with 0.9 mmol of $NaBH_4$. The reaction was run under $N_2$ at room temperature and was stirred magnetically; aliquots of solution were removed through a serum cap with a microsyringe. After 24 hr, reduction was complete; the *OD* at 250 m$\mu$ of successive aliquots (injected into deaerated 0.10 *F* NaOH) had reached its maximum value and no longer changed with increasing reaction time, and the characteristic diselenide absorption was completely absent. The continued presence of excess borohydride at this stage was demonstrated by hydrogen evolution accompanying addition of aliquots to dilute acid.

The identity of the reduction product was established by extracting the free acid into $CHCl_3$ and observing its nmr spectrum. For those experiments, the reaction flask was fitted with a breakseal tube containing excess deaerated 6 *F* HCl and a Wilmad cylindrical micro nmr tube which was separated from the flask by a medium porosity glass filter disk. After reduction was complete, the colorless reaction mixture was degassed by successive freeze–thaw cycles *in vacuo* and all subsequent operations were carried out under vacuum. The breakseal was then opened, the water and excess HCl were removed by evaporation on the vacuum line at *ca.* 0°, and a 1-ml portion of $CHCl_3$ was distilled into the flask. The solid residue was pulverized with the magnetic stirring bar and the $CHCl_3$ extract was filtered through the sintered disk into the nmr tube which was then chilled in $CHCl_3$ slush (−63°) and sealed off. The nmr spectrum remained unchanged for at least 48 hr if the sample was kept cold. The observed nmr spectrum consisted of the sum of signals attributable to the selenol and signals due to a small amount of ethanol present in the $CHCl_3$. Resonances attributed to the selenol were $\delta$ 0.32 (triplet, $J$ = 7.5 Hz, 1.00 proton (defined)), 3.21 (doublet, $J$ = 7.5 Hz, 2.00 protons), *ca.* 9 (broad singlet, position varying with amount of ethanol present, 0.93 proton after correction for the contribution of the ethanol OH). No other resonances were detected with intensities greater than 0.05 protons.

Solutions of the sodium salt of the methyl ester of selenoglycolic acid were prepared in a similar fashion by reduction of $(SeCH_2CO_2CH_3)_2$ using 0.1 *F* $NaOCH_3$ in $CH_3OH$ as solvent. These solutions gave evidence of decomposition when kept at room temperature, but were stable (*i.e.*, successive aliquots gave identical uv spectra) when kept at −10°.

## Results

The identification of the reduction products from the diselenides as the corresponding selenols rests on their facile oxidation by air, the analogy between their uv spectra and those of the related thiols, and the nmr spectrum of the compound assumed to be selenoglycolic acid. For comparison, benzyl selenol has been reported[15] to have an nmr spectrum with $\delta$ −0.09 (triplet, $J$ = 7 Hz) and 3.49 (doublet, $J$ = 7 Hz), in good agreement with the selenol and methylene proton resonances reported above for selenoglycolic acid. Both the absence of extraneous peaks in that nmr spectrum and the close agreement between the form of the pH dependence of the uv absorptions of these compounds and those expected for pure compounds suggest that the reduction to the selenol is free from side reactions.

Hydrogen ion activities, $a_H$, were calculated from the

---

(10) J. L. Kurz, unpublished observation.

(11) An indirectly measured value of $K = 1.0 \times 10^{-7}$ for $HSeCH_2CO^-$ has been reported [B. Nygard, *Acta Chem. Scand.*, **15**, 1039 (1961)]. That value was derived from the pH dependence of the polarographic half-wave potential for reduction of $(SeCH_2CO_2^-)_2$. However, the effective value of the ionic strength at the surface of the charged mercury drop is not known, and the direct effect of the electrostatic potential at that surface on the apparent dissociation constant is uncertain; such values are therefore not sufficiently well established to be useful in this discussion.

(12) G. H. Hofmanns, *Justus Liebigs Ann. Chem.*, **250**, 294 (1888).

(13) O. Behagel and M. Rollmann, *Ber. Bunsenges. Phys. Chem.*, **62**, 2696 (1929).

(14) R. G. Bates, "Determination of pH; Theory and Practice," Wiley, New York, N. Y., 1954, pp 157, 160.

(15) A. Merijanian, R. A. Zingaro, L. S. Sagan, and K. J. Irgolic, *Spectrochim. Acta, Part A*, **25**, 1160 (1969).

observed pH values. Molar activity coefficients, $y$, were estimated from the Davies equation.[16] Since these approximations were used for both the thiols and the selenols, any error arising from their use should be present for both series of acids. The value of p$K$ found for thioglycolic acid is in good agreement with that (10.68 ±0.04) calculated by Irving, Nelander, and Wadsö[17] from measurements at much lower ionic strengths.

The ionizations of the thiols and of methyl selenoglycolate are not complicated by overlapping dissociations; the values of p$K$ for these acids were computed from eq 1, where $\mathrm{OD_{HA}}$ is the optical density of a solution of the undissociated acid (solutions in 0.1 $F$ HCl

$$\mathrm{p}K = \mathrm{pH} + \log\frac{\mathrm{OD_A} - \mathrm{OD}}{\mathrm{OD} - \mathrm{OD_{HA}}} + \log\frac{y_{\mathrm{HA}}}{y_{\mathrm{A}}} \qquad (1)$$

of the two methyl esters and a solution in pH 6 phosphate buffer of thioglycolic acid), $\mathrm{OD_A}$ is the optical density of a solution of the conjugate base (solutions in 0.1 $F$ NaOH of thioglycolic acid, in pH 11 phosphate buffer of methyl thioglycolate, and in pH 8 tris(hydroxymethyl)aminomethane buffer of methyl selenoglycolate), and OD is the optical density of a solution having the same total concentration, [HA] + [A], at the indicated pH. Corrections for small variations in the concentrations of different preparations of stock solutions of the acids were made by multiplying observed OD values by the factors which were required to bring all values of $\mathrm{OD_A}$ for the same acid into coincidence. Calculated p$K$ values were not changed if the wavelength at which OD values were measured was varied over a range of 20 m$\mu$. The results of these measurements are given in Table I. Average p$K$ values are $^-O_2CCH_2SH$, 10.58; $CH_3O_2CCH_2SH$, 8.08; $CH_3O_2CCH_2SeH$, 4.70.

TABLE I

OBSERVED DISSOCIATION CONSTANTS AT 25°

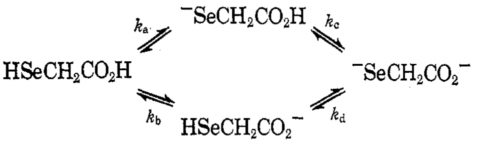
| Acid | pH | $I^a$ | p$K^b$ |
|---|---|---|---|
| $CH_3O_2CCH_2SH$ | 7.48[c] | 0.04 | 8.09 |
| | 7.72[c] | 0.04 | 8.08 |
| | 7.90[c] | 0.03 | 8.05 |
| | 8.06[c] | 0.03 | 8.09 |
| | 8.30[c] | 0.02 | 8.08 |
| | 8.53[c] | 0.02 | 8.12 |
| | 8.80[c] | 0.01 | 8.07 |
| $^-O_2CCH_2SH$ | 10.80[d] | 0.07 | 10.58 |
| | 10.60[d] | 0.06 | 10.60 |
| | 10.38[d] | 0.06 | 10.59 |
| | 10.21[d] | 0.05 | 10.56 |
| $CH_3O_2CCH_2SeH$ | 4.33[e] | 0.02 | 4.70 |
| | 4.42[e] | 0.03 | 4.66 |
| | 4.66[e] | 0.04 | 4.69 |
| | 4.87[e] | 0.05 | 4.75 |
| | 4.96[e] | 0.05 | 4.68 |

[a] Ionic strength. [b] Calcd from eq 1. [c] Tris(hydroxymethyl)aminomethane buffer. [d] Carbonate buffer. [e] Acetate buffer.

In selenoglycolic acid, the p$K$ values of the SeH and $CO_2H$ groups are comparable, so that their dissociations overlap. If the extinction coefficients of $HO_2CCH_2Se^-$ and $^-O_2CCH_2Se^-$ were equal (and that of $^-O_2CCH_2SeH$ negligible), then the experimentally observed value of $\alpha$ (eq 2, $\mathrm{OD_{HA}}$ from a solution in 0.1 $F$

$$\alpha_{\mathrm{obs}} = \frac{\mathrm{OD} - \mathrm{OD_{HA}}}{\mathrm{OD_A} - \mathrm{OD_{HA}}} \qquad (2)$$

HCl, $\mathrm{OD_A}$ from a solution in 0.1 $F$ NaOH) would be equal to the fraction of the total selenoglycolic acid concentration which was present in those two forms. If they are not equal, then $\alpha_{\mathrm{obsd}}$ would give an approximation to that fraction which became more exact as the pH increased. If the four microscopic dissociation constants are defined according to the scheme shown in eq 3, and the extinction coefficients of the two $RSe^-$ species are assumed equal, then the predicted value of $\alpha$ is given by eq 4, where $a_{\mathrm{H}}$ is the hydrogen ion activity and $y_-$ and $y_{2-}$ are the molar activity coefficients of singly and doubly charged anions.



(3)

$$\alpha_{\mathrm{pred}} = \frac{a_{\mathrm{H}}y_{2-}k_{\mathrm{a}} + y_-k_{\mathrm{a}}k_{\mathrm{c}}}{a_{\mathrm{H}}y_{2-}k_{\mathrm{a}} + y_-k_{\mathrm{a}}k_{\mathrm{c}} + a_{\mathrm{H}}y_{2-}k_{\mathrm{b}} + a_{\mathrm{H}}^2y_-y_{2-}} \qquad (4)$$

The value of the microscopic constant, p$k_{\mathrm{a}}$, for dissociation of the SeH group in $HO_2CCH_2SeH$ was assumed to be equal to that measured for the p$K_{\mathrm{a}}$ of the corresponding methyl ester (4.7). Those values of p$k_{\mathrm{b}}$ and p$k_{\mathrm{c}}$ were then selected which gave the best agreement between the values of $\alpha_{\mathrm{obs}}$ and $\alpha_{\mathrm{pred}}$. In order to minimize any errors arising from inequality of the two extinction coefficients, only those eight values of $\alpha_{\mathrm{obs}}$ which were measured at pH ≥ 6.7 were used in fitting eq 4 to the data; in that region, $[^-SeCH_2CO_2^-]/[^-SeCH_2CO_2H] \geq 2$. The optimum values of the microscopic constants determined by this procedure are p$k_{\mathrm{b}}$ = 4.1, p$k_{\mathrm{c}}$ = 6.7, and p$k_{\mathrm{d}}$ (= p$k_{\mathrm{a}}$ + p$k_{\mathrm{c}}$ − p$k_{\mathrm{b}}$) = 7.3. Observed and predicted values of $\alpha$ are given in Table II.

TABLE II

DISSOCIATION OF $HSeCH_2CO_2H$ AT 25°

| pH | $I^a$ | $\alpha_{\mathrm{obs}}{}^b$ | $\alpha_{\mathrm{pred}}{}^c$ |
|---|---|---|---|
| 3.09[d] | 0.02 | 0.007 | 0.025 |
| 3.61[d] | 0.05 | 0.045 | 0.066 |
| 3.77[e] | 0.03 | 0.045 | 0.082 |
| 3.98[d] | 0.07 | 0.060 | 0.108 |
| 4.07[e] | 0.05 | 0.090 | 0.118 |
| 4.37[e] | 0.07 | 0.136 | 0.150 |
| 5.19[e] | 0.20 | 0.196 | 0.202 |
| 6.70[f] | 0.09 | 0.424 | 0.430 |
| 6.93[f] | 0.10 | 0.500 | 0.532 |
| 7.01[g] | 0.05 | 0.590 | 0.535 |
| 7.17[f] | 0.12 | 0.621 | 0.647 |
| 7.38[f] | 0.13 | 0.727 | 0.741 |
| 7.39[g] | 0.04 | 0.757 | 0.703 |
| 7.62[f] | 0.14 | 0.848 | 0.828 |
| 7.83[f] | 0.14 | 0.878 | 0.885 |

[a] Ionic strength. [b] Equation 2. [c] Equation 4, using p$k_{\mathrm{a}}$ = 4.7, p$k_{\mathrm{b}}$ = 4.1, p$k_{\mathrm{c}}$ = 6.7. [d] Formate buffer. [e] Succinate buffer. [f] Phosphate buffer. [g] Tris(hydroxymethyl)aminomethane buffer.

The fit of eq 4 was significantly more sensitive to Δp$k$ (defined as p$k_{\mathrm{c}}$ − p$k_{\mathrm{b}}$) than to either p$k_{\mathrm{c}}$ or p$k_{\mathrm{b}}$ individually. For example, the root mean square (rms) differ-

---

[16] C. W. Davies, "Ion Association," Butterworths, London, 1962, p 41.

[17] F. R. Irving, L. Nelander, and I. Wadsö, *Acta Chem. Scand.*, **18**, 769 (1964).

ence between $\alpha_{obs}$ and $\alpha_{pred}$ which corresponds to the optimum p$k$ values is ±0.032;[18] decreasing both p$k_b$ and p$k_c$ by 0.1 unit (to 4.0 and 6.6) increases the rms deviation only to ±0.034, but decreasing only p$k_b$ by 0.1 unit (thus raising $\Delta$p$k$ from 2.6 to 2.7) increases the rms deviation to ±0.062. It is thus possible that the individual p$k$ values are in error by several tenths of a unit; however, the value of $\Delta$p$k$ (which is the parameter of greatest interest) very probably lies in the range 2.6 ± 0.1.

## Discussion

In a compound of the general structure $HXCH_2CO_2H$ the difference, $\Delta$p$K$($CO_2H$), between the p$K$ values of the $CO_2H$ moiety in $^-XCH_2CO_2H$ and in $HXCH_2CO_2H$ must be equal to the corresponding difference, $\Delta$p$K$(XH), between the p$K$ values of the XH moiety in $HXCH_2CO_2^-$ and ni $HXCH_2CO_2H$. It is convenient to discuss the mechanism of transmission of this substituent effect in terms of the latter difference, since the substituent change is then the same in all pairs of acids being compared. Table III lists p$K$ values which are relevant to such a discussion.

TABLE III

VALUES OF p$K$ AT 25° AND ZERO IONIC STRENGTH

| Acid | $r$,[a] Å | p$K$[b] |
|---|---|---|
| $HO_2CCH_2SeH$ | 4.1 | 4.7,$^{c,d}$(SeH) |
| $^-O_2CCH_2SeH$ | | 7.3$^{c}$ (SeH) |
| $HO_2CCH_2SH$ | 4.0 | 8.1$^{c,d}$ (SH) |
| $^-O_2CCH_2SH$ | | 10.6$^{c}$ (SH) |
| $HO_2CCH_2NH_3^+$ | 3.7 | 7.6$^{d,e}$ ($NH_3^+$) |
| $^-O_2CCH_2NH_3^+$ | | 9.8$^{e}$ ($NH_3^+$) |
| $HO_2CCOOH$ | 3.4 | 1.6$^{f,g}$ ($CO_2H$) |
| $^-O_2CCOOH$ | | 4.0$^{f,g}$ ($CO_2H$) |

[a] Intercharge distance in dianion assuming the charge on $X^-$ to lie at the nucleus and the charge on $CO_2^-$ to lie 1.45 Å (ref 2c) beyond the carboxyl carbon on the extension of the carbon–carbon bond. [b] Parenthetical expression indicates group to whose ionization p$K$ refers. [c] This work. [d] Assumed to be equal to p$K$ for the corresponding methyl ester. [e] Reference 10. [f] R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd ed, Butterworths, London, p 520. [g] Corrected for symmetry.

It is known[6] that a plot of log ($\Delta$p$K$) for dibasic acids in which the protons are bound to first-row elements against the interchange distance, $r$, in ångströms gives a straight line with a slope of −0.2. This slope corresponds to McGowan's[7] empirical rule that insertion of a methylene group (*i.e.*, $\Delta r = 1.5$) between a charged substituent and an acidic proton attenuates the substituent effect on p$K$ by a factor of 0.50 (*i.e.*, $\Delta$ log ($\Delta$p$K$) = −0.3).

This correlation would predict that $\Delta$p$K$(XH) should decrease from 2.2 for glycine (Table III) to 1.8 for $HSeCH_2CO_2H$ because of the increase in $r$ from 3.7 to 4.1 Å. Instead, $\Delta$p$K$(XH) increases to 2.6; $\Delta$p$K$ for selenoglycolic acid is thus 0.8 unit larger than is predicted from the corresponding value for glycine. Similarly, $\Delta$p$K$ for thioglycolic acid (2.5) is 0.6 unit larger than predicted, but p$K$ for oxalic acid (2.4) is approximately equal to its predicted value (2.5).

This increase in $\Delta$p$K$ which accompanies an increase in the atomic number of X could arise from either of two effects: (a) an increase in the efficiency of transmission of the effect of the charge on X (attributable to a decrease in $D_E$ produced by the increase in the radius of X), or (b) a decrease in the free energy of interaction between the XH dipole and the charge on $CO_2^-$ (attributable to the decrease in the XH bond moment). Each of these effects is discussed below.

**Variation in Effective Dielectric Constant.**—Tanford[3] has shown that the free energy of interaction between charges in the Kirkwood–Westheimer[2] cavity model of organic acids depends critically on the depth, $d$, within the cavity at which the charges are placed. He has demonstrated that the observed changes in acid dissociation constants which result from the interaction of charges located on nitrogen or oxygen atoms can be predicted if the charges in the model cavity are located with $d$ = 1.0 Å. The van der Waals radii of oxygen and nitrogen atoms are 1.4 and 1.5 Å, while those of sulfur and selenium are *ca.* 0.5 Å larger, 1.85 and 2.0 Å.[19] It would thus not be unreasonable if the correct value of $d$ describing the interaction between the charges in $^-SeCH_2CO_2^-$ were increased to a value between 1.0 and 1.5 Å. In fact, the observed values of $\Delta$p$K$ for glycine and selenoglycolic acid can be accounted for if $d$ for the latter acid is increased to 1.3 Å. Thus, using the distance parameters given in Table III, Tanford's ellipsoidal cavity model predicts for glycine ($R$ = 3.7 Å, $d$ = 1.0 Å) that $D_E$ = 30 and $\Delta$p$K$ = 2.2, and for selenoglycolic acid ($R$ = 4.1 Å, $d$ = 1.3 Å) that $D_E$ = 23 and $\Delta$p$K$ = 2.6.

**Variation in Charge–Dipole Interaction.**—When a charge is introduced into a molecule by adding or removing a proton, *two* contributions to changes in the electrostatic field of the molecule result: one arising from introduction of the charge, the other arising from creation or destruction of a dipolar bond between the proton and the basic atom to which it is bound. Although allusion has been made to the existence of this second term,[2a,20] no explicit estimation of the magnitude of its contribution is generally included in calculations of the electrostatic contribution to substituent effects on acid strength.

For the simplest case of a linear symmetric dibasic acid, HXH, the effect of the charge–dipole interaction in $HX^-$ will be to raise the free energy of that species, thus increasing p$K_1$, decreasing p$K_2$, and decreasing $\Delta$p$K$. Similarly the effect of the dipole–dipole interaction in HXH will be to increase $\Delta$p$K$. More generally, if the charge–dipole interaction is dominant, the net result of electrostatic interaction involving the X–H dipole in any[21] dibasic acid will be to decrease $\Delta$p$K$; the value of $\Delta$p$K$ calculated in the usual way from the charge–charge term is therefore an estimate of an upper limit on the total electrostatic contribution to $\Delta$p$K$.

That the contribution of the charge–dipole interaction may be large is suggested by the following argument. Consider two pairs of acids into which two

---

[18] The quoted rms differences are based on the eight values of $\alpha_{obsd}$ for which pH ≥ 6.7. The validity of the assumption of equality of the extinction coefficients is implied by the agreement observed between $\alpha_{obsd}$ and $\alpha_{pred}$ at lower pH values where $^-SeCH_2CO_2H$ is the predominant absorbing species. The rms difference based on all 15 values of $\alpha_{obsd}$ which correspond to the quoted optimum p$k$ values is ±0.030.

[19] L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 260.

[20] H. M. Peek and T. H. Hill, *J. Amer. Chem. Soc.*, **73**, 5304 (1951).

[21] It is assumed that the molecular geometry is the common one in which both charge–dipole and dipole–dipole interactions are repulsive.

bond dipoles with approximately the same orientation are introduced at the same distance: (1) H-$CH_2CH_2$-$CO_2H$ *vs.* Cl-$CH_2CH_2CO_2H$, for which $\Delta pK = 0.9$ and $\Delta\mu = \mu(CCl) - \mu(CH) \approx \mu(CH_3Cl) = 1.9$ D; (2) $NH_2CH_2CO_2H$ *vs.* H-$NH_2{}^+CH_2CO_2H$, for which $\Delta pK = 2.2$ and $\Delta\mu \approx 1.3$ D. If the value of $D_E$ govering the charge–dipole interaction were the same in both pairs, the value of $\Delta pK$ observed for (1) would require that the charge–dipole contribution to $\Delta pK$ for (2) be 0.6 p$K$ unit, which is 27% of the observed total $\Delta pK$. However, this direct comparison of HN and ClC dipoles disregards the large difference in size between Cl and H. The value of Tanford's $d$ which should be assigned to an NH dipole may be much less than the 1.5 Å which is required for halogen–carbon dipoles, and the estimate of 0.6 p$K$ unit must be considered as an upper limit on the contribution of the NH dipole to the value of $\Delta pK$ for glycine; the actual contribution may be very much less.

In the sequence NH, SH, SeH, the magnitude of the bond dipole decreases sharply. From the dipole moments[22] and molecular geometries[23] of $NH_3$, $H_2S$, and $H_2Se$, these bonds moments may be estimated to be 1.3, 0.7 and 0.3 D if the contributions of lone pair moments are assumed to be negligible. These estimated bond dipole moments contain errors due to the unknown magnitudes of the lone pair moments in $H_nX$; the effects of such errors on estimates of the dipolar contribution to $\Delta pK$ will tend to cancel with the effects on $\Delta pK$ of the corresponding lone pair moments in the substituted carboxylic acids. This cancellation will in general, however, not be complete.

Although the magnitude of the variation in $\Delta pK$ which should result from changes in the XH bond moment (or from changes in the mean orientation of the XH dipole) cannot be quantitatively estimated, it is clear that a difference of *ca.* 1 D between the effective NH and SeH moments is probable; if the effect on $\Delta pK$ from this source had a magnitude about equal to its estimated maximum possible value, it could account for the observed total variation in $\Delta pK$. Since that variation, however, lies well within the range which could be accounted for by changes in the value of $D_E$ for charge–charge interactions, at least a major part of it very probably arises from an increase in the efficiency of transmission of the effect of a charge as the atom which bears that charge increases in size.

**Registry No.**—Selenoglycolic acid, 25244-47-7; selenoglycolic methyl ester, 25244-48-8.

**Acknowledgment.**—This work was supported in part by grants (GP-7488 and GP-13513) from the National Science Foundation.

[22] A. L. McClellan, "Tables of Experimental Dipole Moments," W. H. Freeman, San Francisco, Calif., 1963.

[23] "Table of Interatomic Distances," Special Publications No. 11 and 18, The Chemical Society, London, 1958 and 1963.

---

# Free-Radical Bromination of Methyl Abietate by N-Bromosuccinimide and Solvolysis of the Products

J. C. SIRCAR[1a] AND G. S. FISHER

*Naval Stores Laboratory,*[1b] *Olustee, Florida 32072*

*Received October 14, 1969*

The major product from the solvolysis of the methyl bromoabietate formed by the NBS–methyl abietate reaction was methyl 12α-methoxyabietate. The structure was proved by independent synthesis from 12α-hydroxyabietic acid. Methyl 18-methoxyabietate was also formed. The three possible methyl methoxydehydroabietates were obtained as secondary reaction products from the methyl dehydroabietate formed during the NBS–abietate reaction. They have also been prepared by the solvolysis of NBS–methyl dehydroabietate reaction products. The structures of the intermediate bromo compounds have been assigned by analogy to the ethers.

As one approach to the identification of a methyl methoxyabietate obtained by photolysis of methyl neoabietate in methanol,[2] preparation of similar compounds from methyl abietate (**1**) by free-radical bromination followed by methanolysis of the bromides was investigated. Bromination with N-bromosuccinimide (NBS) followed by dehydrobromination[3] has been used to make dehydroabietic acid from abietic acid. In the present investigation methyl dehydroabietate (**10**) was still the major product, but a fair yield of ethers was also obtained.

On the basis of the identity of its uv spectrum with that of methyl abietate and the splitting pattern of the $C_{12}$ proton[4] in its nmr spectrum,[5] it should be **2a**. This structure was confirmed by comparison with an authentic sample prepared from methyl 12α-hydroxyabietate[6] (**2b**). Of the minor products, only one exhibited the uv absorption characteristic of an abietate structure. Its gas chromatographic behavior was identical with that of the ether obtained by photolysis and subsequently identified as methyl 18-methoxyabietate[2] (**6a**).

The other products had uv and ir spectra which were consistent with aromatic structures, indicating that **10**

---

[1] (a) National Research Council Resident Postdoctoral Research Associate, 1967–1969. (b) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

[2] J. C. Sircar and G. S. Fisher, *Chem. Ind.* (*London*), 26 (1970).

[3] O. Jeger, O. Durst, and G. Buchi, *Helv. Chim. Acta*, **30**, 1853 (1947).

[4] (a) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 77. (b) J. C. Sircar and G. S. Fisher, *J. Org. Chem.*, **34**, 404 (1969).

[5] Nmr spectra were run in deuteriochloroform on a Varian A-60 spectrometer unless otherwise specified. Frequencies are given in cps with tetramethylsilane as internal standard. s = singlet, d = doublet, t = triplet, m = multiplet. The mention of firm names of trademarks does not imply that they are endorsed or recommended by the Department of Agriculture over others not mentioned.

[6] W. Herz, H. J. Wahlborg, W. D. Lloyd, W. H. Schuller, and G. W. Hedrick, *J. Org. Chem.*, **30**, 3190 (1965).