N-(2,2-diphenylcyclopropyl)-urea was added 0.19 g. (ca. 0.0019 mole) of lithium ethoxide alcoholate. Nitrogen evolution began immediately and was essentially complete in 10 min. Stirring and cooling were continued for an additional 30 min. at which time the reaction mixture was filtered and the filtrate evaporated to give an oily residue that was analyzed by g.l.p.c.

Alternate Synthesis of 1,1-Diphenyl-4,5-tetramethylenespiropentane.—7,7-Dibromonorcarane[39] (14.0 g., 0.056 mole) and 10.0 g. (0.056 mole) of 1,1-diphenylethylene[40] were dissolved in 15 ml. of dry ether, and the mixture was cooled to 0°. Butyllithium in hexane (3.56 g., 0.056 mole) was added dropwise to the stirred and cooled mixture over a 45-min. period. After the addition was complete the reaction mixture was stirred for an additional 2 hr. at room temperature and filtered. The filtrate was washed with water and dried over magnesium sulfate. The dried solution was taken to near dryness and a small portion (0.25 ml.) was separated by gas chromatography to give about 10 mg. of the desired spiropentane. Recrystallization from ethyl acetate gave pure material, m.p. 82.0–82.5°; no depression on admixture with the material obtained from the reaction of the nitrosourea with lithium ethoxide in cyclohexane. The infrared spectra of the two materials were also identical.

Reaction of N-Nitroso-N-(2,2-diphenylcyclopropyl)-urea with Lithium Ethoxide in n-Heptane.—To a stirred mixture of the nitrosourea (1.00 g., 3.56 mmoles) in 25 ml. of reagent grade n-heptane at 0° was added lithium ethoxide alcoholate (0.35 g., ca. 3.6 mmoles). After 5 min. stirring, nitrogen evolution began and was 95% complete after 60 min. Stirring and cooling were continued for one additional hour after which the reaction mixture was filtered. The residue was washed thoroughly with reagent grade n-neptane and the filtrates combined. The filtrate was analyzed for 1,1-diphenylallene and found to contain 96% of that calculated.

The allene is a colorless oil when it is first formed or immediately after it is eluted from alumina (if it is kept cold). However, it apparently polymerizes rather rapidly when it is kept as the liquid at room temperature.[6] The structure of the allene was deduced from its infrared spectrum[41] and by partial reduction to

(39) W. von E. Doering and W. A. Henderson, Jr., J. Am. Chem. Soc., **80**, 5274 (1958).

(40) Prepared by the method of C. F. H. Allen and S. Converse, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1961, p. 226.

a product which was identical in every way with an authentic sample of 1,1-diphenyl-1-propene.

Reaction of N-Nitroso-N-(2,2-diphenylcyclopropyl)-urea with Lithium Ethoxide in Ethyl Ether.—To 2.00 g. (0.0071 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)-urea and 25 ml. of pure anhydrous ethyl ether stirred at 0° was added 0.70 g. (0.0071 mole) of lithium ethoxide alcoholate. Nitrogen evolution began immediately and continued for approximately 40 min. After a total of 2 hr. stirring and cooling the reaction mixture was filtered; the solid obtained was washed with anhydrous ethyl ether and the washing added to the filtrate. Evaporation of the filtrate gave a yellow oil which was chromatographed over alumina using pentane as the eluent. The oil obtained by this chromatography was shown by g.l.p.c. to be a complex mixture and at least three major components of this mixture are unique to the reaction in ethyl ether; they are not produced by this reaction when run in saturated hydrocarbon solvents. Attempted purification and isolation of the various components by preparative scale g.l.p.c. was not successful.

Decomposition of N-Nitroso-N-(2,2-diphenylcyclopropyl)-urea by Lithium Ethoxide in Diethyl Fumarate.—To 1.00 g. (0.00356 mole) of N-nitroso-N-(2,2-diphenylcyclopropyl)-urea in 20 ml. of diethyl fumarate (Eastman Organic Chemicals) at 0° was added 0.35 g. (0.0036 mole) of lithium ethoxide alcoholate. The mixture was stirred and cooled for 1 hr. at the end of which no nitrogen had evolved and a white solid had precipitated. Isolation of the solid by filtration was followed by thorough washing with pentane. (The filtrate was shown by g.l.p.c. to contain both benzophenone and a trace of 1,1-diphenylallene.) The isolated solid was then stirred with cold, dilute hydrochloric acid, filtered, washed with water, and dried. Recrystallization from methanol gave the pyrazoline in 47.5% yield, m.p. 147–149°, λ_{max} 320 mμ (ϵ 10,900); 3.00, 5.76, 5.99, 6.52 μ.

Anal. Calcd. for $C_{23}H_{24}N_2O_4$: C, 70.39; H, 6.16; N, 7.14. Found: C, 70.20; H, 6.30; N, 6.88.

(41) T. L. Jacobs, R. Akawie, and R. G. Cooper, J. Am. Chem. Soc., **72**, 1272 (1950); J. H. Wotiz, ibid., **73**, 692, 5503 (1951); **74**, 1960 (1952); J. H. Wotiz and D. E. Mancuso, J. Org. Chem., **22**, 207 (1957).

Isotope Effects on Acidity of Deuterated Formic, Acetic, Pivalic, and Benzoic Acids[1]

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Conductivity measurements give the following results for $pK_D - pK_H$: DCOOH, 0.030 ± 0.004; CD₃COOH, 0.014 ± 0.002; C₆D₅COOH, 0.010 ± 0.002; 2,6-C₆H₃D₂COOH, 0.003 ± 0.001. The treatment of these isotope effects as "normal" inductive effects is discussed.

Introduction

During the past few years, many phenomena have been reported in which deuterium acts as an apparent electron-donating inductive substituent relative to hydrogen.[3] Examples include the nuclear quadrupole coupling constants of deuterated methyl halides in which deuterium is effectively more electropositive than hydrogen[4] and the n.m.r. chemical shifts in deuterated fluorocarbons.[5] These effects seem clearly to be due to the anharmonicity of C–H vibrations and the greater amplitude of C–H compared to C–D vibrations. Of especial importance in organic chemistry are the experimental findings that the magnitude of such isotope effects is sufficient to cause significant changes in equilibrium acidities. DCOOH,[6–8] CD₃COOH,[3,9,10] and

$C_6H_5CD_2COOH$[3,10,11] are reported to be 6–12% weaker acids than the corresponding protium acids.

In the normal treatment of isotope effects on equilibrium constants, changes in zero point energies on the vibrational partition functions are of primary importance. Bell and Crooks[12] have shown that the use of experimental values of all of the vibration frequencies of HCOOH, HCO₂⁻, DCOOH, and DCO₂⁻ gives a calculated isotope effect in such a treatment, $\Delta pK = 0.037$, which is close to Bell and Miller's carefully measured experimental value,[8] 0.035. The use of all of the experimental values automatically includes some anharmonicity influences and is clearly superior to methods which involve only a few of the molecular vibrations or

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(2) (a) Alfred P. Sloan Fellow, 1958–1962. (b) National Science Foundation Cooperative Graduate Fellow, 1959–1961; University of California Fellow, 1961–1962.

(3) For a complete summary, see E. A. Halevi in "Progress in Physical Organic Chemistry," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1963.

(4) J. W. Simmons and J. H. Goldstein, J. Chem. Phys., **20**, 1804 (1952).

(5) G. V. D. Tiers, J. Am. Chem. Soc., **79**, 5585 (1957).

(6) G. A. Ropp, ibid., **82**, 4252 (1960).

(7) R. P. Bell and M. B. Jensen, Proc. Chem. Soc., 307 (1960).

(8) R. P. Bell and W. B. T. Miller, Trans. Faraday Soc., in press.

(9) E. A. Halevi and M. Nussim, 16th Intl. Cong. Pure Appl. Chem., Paris, 1957.

(10) (a) E. A. Halevi, Intern. J. Appl. Radiation Isotopes, **7**, 192 (1960); (b) E. A. Halevi, M. Nussim, and A. Ron, J. Chem. Soc., 866 (1963).

(11) E. A. Halevi and M. Nussim, Bull. Research Council Israel, **5A**, 263 (1956).

(12) R. P. Bell and J. E. Crooks, Trans. Faraday Soc., **58**, 1407 (1962).

approximate relationships between vibration frequencies of isotopically substituted compounds.

It is fortunate that the use of the experimental frequencies is so successful in accounting for the isotope effects because a more explicit incorporation of anharmonicity would be extremely difficult even for simple molecules. Consequently, this demonstration for formic acid is important as an example of what can be done when all of the vibration frequencies for the conjugate acid and base and the deuterated acid and base are known; unfortunately, such complete information is available for but few organic acids and can be obtained in such detail only for comparatively simple structures. The extension of such a fundamental treatment to most organic acids is clearly impractical and a more empirical approach is called for. One such approach would entail experimental measurements of a series of acids and an attempt to discern regularities between them. We have adopted this philosophy in the present paper, and in our scrutiny of several deuterated acids, we have sought to find to what extent deuterium acts as a "normal" electron-donating inductive substituent.

Results

Acetic Acid.—Acetic-d_3 acid-d, obtained from Merck and Co., Ltd., of Canada, was purified by distillation under vacuum at room temperature followed by fractional freezing. Undeuterated acetic acid was also purified by fractional freezing. Ordinary pH titrations showed only small differences in pK's for the two acids and more precise conductivity measurements were undertaken. The results are summarized as the first three items in Table I. The measurements of the resistances of aqueous solutions of deuterated and undeuterated acids were carried out as pairs at similar concen-

TABLE I

Conductivity Measurements of Deuterated and Undeuterated Carboxylic Acids

		Undeuterated acid		Deuterated acid		$100 \times \dfrac{K_H - K_D}{K_H}$
Run	Temp., °C.	R, ohms	Concn. $\times 10^3$	R, ohms	Concn. $\times 10^3$	
			CD$_3$COOH			
1[a]	24.60	4170	8.01	4225	8.07	3.4
2[a]	24.60	4159	8.04	4080	8.58	2.9
3[a]	25.00	1075	115.0	1133	107.0	3.2
4[a]	25.00	1075[b]	115.2	1313[c]	80.2	3.4
5[d]	25.00	3501.5	11.022	3468.2	11.606	3.4
6[d]	25.00	5718.5	4.294	5954.0	4.087	3.0
			C$_6$D$_5$COOH			
7	24.60	2299	7.99	2313	8.02	1.7
8	24.60	4665	2.1	4426	2.36	2.3
9	24.60	2460	6.97	2552	6.70	3.3
			2,6-C$_6$H$_3$D$_2$COOH			
10	25.00	1965.8	10.636	1973.5	10.588	0.5
11	25.00	3056.5	4.577	3236.0	4.144	0.9
			(CH$_3$)$_3$COOH			
12	25.00	12013	2.020	11642	2.231	4.0
13	25.00	6688.8	6.276	6789	6.328	3.8
14	25.00	6234	7.138	5972	8.138	4.7
15	25.00	4048	16.927	4449	14.633	4.4
			DCOOH			
16	25.00	461.0	56.5	510.5	50.05	8.0
17	25.00	691.4	26.2	775.2	22.6	7.5
18	25.00	573.6	37.59	568.0	40.7	6.3
19	25.00	1321.2	7.78	1207.5	9.7	6.1

[a] Acetic-d_3 acid-d obtained from Merck of Canada. [b] Acetic acid containing 1% malonic acid had $R = 1117$ ohms for $c = 0.094$. The R-value shown in the table is the result after refluxing for 3 days. [c] After refluxing for 3 days. [d] CD$_3$CO$_2$H prepared from CD$_3$MgBr and CO$_2$.

trations. From the usual relationship

$$K = \alpha^2 c / (1 - \alpha) \qquad (1)$$

in which K is the dissociation constant of an acid dissociated to the extent α ($= \Lambda_c/\Lambda_\infty$) at concentration, c, we derive

$$K = \frac{(\Lambda_c/\Lambda_\infty)^2 c}{1 - \Lambda_c/\Lambda_\infty} = \frac{10^6 k^2 c/R^2 \Lambda_\infty^2 c^2}{1 - 1000\, k/Rc\Lambda_\infty} \qquad (2)$$

k is the cell constant and R is the measured resistance. It follows that

$$\frac{K_H}{K_D} = \frac{R_D(R_D c_D - A)}{R_H(R_H c_H - A)} \qquad (3)$$

$$A \equiv 1000 k \Lambda_\infty$$

The same value of Λ_∞, 390.8, was taken for both the undeuterated and deuterated acetic acids. The error associated with this assumption is surely insignificant inasmuch as Λ_∞ for all carboxylic acids have similar values. By comparing deuterated and undeuterated acids at similar concentrations, activity coefficient effects tend to cancel. The A term in eq. 3 is small (1–3% of Rc) and was evaluated from a single measurement of the cell constant. This determination, together with the data in Table I, yields a value of 1.79 $\pm$ 0.01 $\times$ 10^{-5} for the apparent dissociation constant of acetic acid, uncorrected for activity effects. This value is close to the accepted value, $K_0 = 1.76 \times 10^{-5}$,[13] and shows that the techniques used are capable of yielding reasonable results.

The resulting isotope effect of 3.2% is much smaller than the 12% originally reported by Halevi[9,10] and is still significantly smaller than his revised result of 6%.[3,10b] In private correspondence, Halevi suggested that our low result may have been caused by the presence of small amounts of malonic acid, a presumed intermediate in the preparation of acetic-d_3 acid-d. We found that trace amounts of this stronger acid did, indeed, increase the conductivity of aqueous acetic acid and would give low values for K_H/K_D. When acetic acid containing 1% of malonic acid was refluxed for 3 days, its conductivity went down to the same value as pure acetic acid. These conditions clearly sufficed for complete decarboxylation of the malonic acid. The deuterated acetic acid was refluxed for 3 days, but the results were unchanged (run 4). We conclude that malonic acid is not a significant contaminant.

The conductivity measurements cover a concentration range of more than a factor of 10. Trace amounts of totally ionized salts in the deuterioacetic acid would also lead to low K_H/K_D values but would produce results changing with concentration. Nevertheless, because of the serious difference between our results and those of Halevi, we synthesized a second sample of CD$_3$COOH by carbonation of the Grignard reagent from CD$_3$Br. The results are shown as runs 5 and 6 in Table I and are identical with the earlier series. The average value of 1 $- K_D/K_H$ is 0.032 $\pm$ 0.002 corresponding to $\Delta pK = 0.014 \pm 0.001$. After this paper was prepared for publication the details of Halevi's procedure appeared[10b]; his results also demonstrate precision and reproducibility and the quantitative differences between the two investigations remain unresolved. Ropp's isotope effect of 6 $\pm$ 3%[14] obtained by pH titrations overlaps our results and those of Halevi. Fortunately, however, the qualitative arguments are not affected by these quantitative differences.

Benzoic Acid.—Benzene-d_6 was prepared by the gallium bromide-catalyzed exchange of benzene with

(13) Average value of best results summarized in G. Kortüm, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworths, London, 1961.

(14) G. A. Ropp, personal communication.

deuterium chloride. Density measurement and infrared spectrum indicated >95% deuteration. This material was brominated, converted to the Grignard reagent and carbonated to yield benzoic-d_5 acid. The conductivity measurements were carried out as in the acetic acid series on material sublimed immediately before use and are summarized in Table I. The value of Λ_∞ used for benzoic acid, 380, and the single measurement of the cell constant gives $K = 6.41 \pm 0.02 \times 10^{-5}$, in good agreement with the literature value of $K_0 = 6.32 \times 10^{-5}$.[13] The average value of $1 - K_D/K_H$, 0.024 ± 0.006, corresponds to $\Delta pK = 0.010 \pm 0.002$. Erlenmeyer and Epprecht[15] found no measurable difference in acidity between benzoic and benzoic-d_5 acids, but their measurements were not precise.

Bromobenzene-2,6-d_2 which was available from another study was converted to the Grignard reagent and carbonated to give benzoic-2,6-d_2 acid. The conductivity measurements with this material are summarized as runs 10 and 11 in Table I. The average value of $1 - K_D/K_H$, 0.007 ± 0.002, corresponds to $\Delta pK = 0.003 \pm 0.001$.

Pivalic Acid.—t-Butyl-d_9 chloride, obtained from Merck of Canada, was converted to Grignard reagent and carbonated to yield pivalic-d_9 acid. Ordinary pivalic acid was prepared by the same route from t-butyl chloride. Both acids were sublimed before the conductivity measurements summarized in Table I. Λ_∞ was taken as 381 and gave an average value of $9.07 \pm 0.05 \times 10^{-6}$ for the apparent K of pivalic acid; the literature value is 8.9–9.3×10^{-6}.[13] The average value of $1 - K_D/K_H$, 0.042 ± 0.003, corresponds to $\Delta pK = 0.018 \pm 0.001$. The less precise result of Ropp,[14] $6 \pm 2\%$, obtained by pH titrations overlaps our result.

Formic Acid.—Our conductivity runs were made with reagent grade formic acid and with DCOOH obtained from Merck of Canada, both fractionally crystallized several times. The results are summarized in Table I. The four runs for formic acid and $\Lambda_\infty = 404$ give an apparent K of $1.90 \pm 0.03 \times 10^{-4}$; the literature value is 1.77×10^{-4}.[13]

These measurements were completed before we learned of the more extensive experiments of Bell and Miller.[8] Our average value for $1 - K_D/K_H$, 0.070 ± 0.008, corresponds to $\Delta pK = 0.030 \pm 0.004$ and is somewhat lower than the value they report, $\Delta pK = 0.035 \pm 0.002$. Although the difference is within the combined experimental errors, our value may be less accurate because formic acid is a sufficiently strong acid that our comparisons of the experimental data with neglect of differential activity effects may cause significant error. Bell and Miller took explicit account of activity coefficients in their work. For these reasons, we treat our results simply as confirming the essential correctness of the magnitude of the isotope effect reported by Bell and Miller.

Discussion

In Table II are summarized values for the pK differences between the several carboxylic acids and their deuterated counterparts. For consistency we have used our values throughout except for formic acid. In every case, the deuterated acid is the less acidic.

There seems to be little question that inductive effects of normal substituents are largely the result of through space electrostatic interaction with bond dipoles; $e.g.$, field effects. The consideration of an isotope effect as a "normal" substituent effect poses several questions: Is the magnitude of the effect consistent with the bond dipole moment involved? Does the magnitude of the

(15) H. Erlenmeyer and A. Epprecht, $Helv.$ $Chim.$ $Acta$, **19**, 1056 (1936).

TABLE II
SUMMARY OF ISOTOPE EFFECTS

	$pK_D - pK_H$
DCOOH	0.035 ± 0.002^a
CD$_3$COOH	$.014 \pm .001$
(CD$_3$)$_3$CCOOH	$.018 \pm .001$
C$_6$D$_5$COOH	$.010 \pm .002$
2,6-C$_6$H$_3$D$_2$COOH	$.003 \pm .001$

^{a} Bell and Miller's value, ref. 8.

effect carry over to other systems in the same way as other substituent effects?

With respect to the first question, the logic is clear-cut, and excellent pertinent data are available. It has long been known that there is a regular relationship between the bond dipole of a substituent, Y, as reflected, for example, in the dipole moment of CH$_3$Y, and the pK difference between CH$_3$COOH and YCH$_2$COOH.[16] The difference in dipole moments of t-butyl chloride $(2.13$ D.)[17] and isobutane $(0.13$ D.)[18] is 2.26 D.[19] The difference in pK's of trichloroacetic acid (0.63)[13] and acetic acid (4.75) is 4.12. A simple proportionality combined with the known $\Delta\mu$ between (CH$_3$)$_3$CD and (CH$_3$)$_3$CH, 0.0086 ± 0.0012 D.,[20] yields the ΔpK for CH$_3$COOH and CD$_3$COOH to be ascribed to a "normal" inductive effect

$$(0.0086)(4.12)/2.26 = 0.016$$

Considering the simplicity of the treatment, this result is in excellent agreement with our experimental difference of 0.014 pK unit.

The deuteriopivalic acid was measured specifically to evaluate the fall-off of the isotope effect with distance. The natural fall-off of the effect of an inductive substituent is usually taken as a factor of about 2.8 per carbon moved down the chain.[21] There are three times as many deuteriums in the pivalic acid; hence, the net effect expected if the isotope effect behaves in a "normal" inductive manner is

$$\Delta pK = (0.014)(3.0)/2.8 = 0.015$$

The result is also in excellent agreement with the experimental value of ΔpK, 0.018. A comparable fall-off between CD$_3$COOH and CD$_3$CH$_2$COOH has also been reported recently by Halevi.[10b]

These results testify that some of the effects of C–D substitution ($e.g.$, dipole moments and effect on acidity) are interrelated in the same manner as for normal inductive substituents in agreement with the conclusions of Halevi. There seems to be no need to include more specific nonbonded interactions of the sort proposed by Bartell.[22]

It is also convenient to discuss these effects in terms of Taft's σ^*-treatment.[23] An excellent correlation exists between the σ^*-value of a substituent and its effect on the acidity of acetic acid[23]; indeed, the correlation is so good that a simple and effective definition of

(16) W. A. Waters, $Phil.$ $Mag.$, [7] **8**, 436 (1929); W. S. Nathan and H. B. Watson, $J.$ $Chem.$ $Soc.$, 890 (1933); H. M. Smallwood, $J.$ $Am.$ $Chem.$ $Soc.$, **54**, 3048 (1932); A. Eucken, $Angew.$ $Chem.$, **45**, 203 (1932); F. H. Westheimer and M. W. Shookhoff, $J.$ $Am.$ $Chem.$ $Soc.$, **61**, 555 (1939).

(17) R. H. Wiswall, Jr., and C. P. Smyth, $J.$ $Chem.$ $Phys.$, **9**, 356 (1941).

(18) D. R. Lide, Jr., $ibid.$, **29**, 914 (1958).

(19) The direction of the dipole in isobutane is taken as away from the tertiary hydrogen and toward the tertiary carbon on the ground that replacing the hydrogen by deuterium increases the total dipole moment. This argument is weak and the conclusion may very well be wrong; however, because of the small magnitude of this dipole, the direction chosen is not critical to the argument. In t-butyl chloride, the direction of the dipole is clearly toward the chlorine.

(20) D. R. Lide, Jr., $J.$ $Chem.$ $Phys.$, **33**, 1519 (1960).

(21) G. E. K. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1941, Chapter VI.

(22) L. S. Bartell, $J.$ $Am.$ $Chem.$ $Soc.$, **83**, 3567 (1961).

(23) R. A. Taft in "Steric Effects in Organic Chemistry," ed. by M. S. Newman, J. Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13.

σ^*-values could have been based on these acidities alone.[21] The slope of this correlation, -1.72,[23] and the pK difference for CD_3COOH gives σ^* (CD_3-) $= -0.0081$ or σ^* (CH_2D-) $= -0.0027$.

Unfortunately, there seems to be no simple way in which this value can be related to the isotope effect in DCOOH. Because of changes in hybridization and conjugation, inductive effects cannot normally be extended accurately to substituted formic acids. Nevertheless, the order of magnitude of the isotope effect in DCOOH is about what would be expected from an inductive effect. Moreover, such effects have been extended to benzoic acids, particularly with m-substitution; for example, it has long been known that the effects of m-substituents are also determined largely by the substituent bond dipole.[24] In terms of Taft's σ^*-treatment, the linear correlation that exists between σ_m (Y-) and σ^* (CH$_2$Y-) with a slope of 0.45 leads to a value of σ_m (D) of -0.0012 based on CD_3COOH; that is, treating the isotope effect on acidity of CD_3COOH as a normal inductive effect, we predict that one m-D should raise the pK of benzoic acid by 0.0012. We did not measure a simple m-deuterated benzoic acid; pentadeuteriobenzoic acid is less acidic than benzoic acid by 0.010 ± 0.002 pK unit. To determine whether the o-deuteriums were exerting an abnormal effect by their proximity to the carboxyl group, benzoic-2,6-d_2 acid was measured and was found to be less acidic than benzoic acid by Δp$K = 0.003 \pm 0.001$; hence, the effect of deuterium seems to be distributed roughly evenly about the ring and the predicted effect of 0.0024 for benzoic-3,5-d_2 acid is of about the right magnitude in comparison with the measurements made.

The generality of this inductive isotope effect is noteworthy. In a parallel study, we have examined the rates of solvolysis of various deuterated benzhydryl chlorides. The results will be discussed in subsequent papers in more detail, but one aspect is pertinent to the present discussion. In particular, of the results summarized in Table III, discussion of deuterium substitu-

TABLE III

SOLVOLYSIS OF DEUTERATED BENZHYDRYL CHLORIDES IN 80% AQUEOUS ACETONE AT 25°

Deuterium substitution	k_D/k_H	k_D/k_H per D
2,6,2',6'-d_4	1.070 ± 0.003	1.018 ± 0.001
3,5,3',5'-d_4	$1.057 \pm .002$	$1.014 \pm .001$
4,4'-d_2	$1.020 \pm .003$	$1.010 \pm .002$
2,4,6,2',4',6'-d_6	$1.094 \pm .004$	
2,3,4,5,6,2',3',4',5',6'-d_{10}	$1.160 \pm .001$	
α-d	$0.881 \pm .005$	

tion in the o- and p-positions is deferred pending the results of additional experiments now in progress—it appears that special effects may be operating in these positions because these positions are conjugated with the reacting center. The isotope effect in the m-position, however, is completely consistent with its consideration as an inductive effect. For solvolysis of benzhydryl chlorides in aqueous acetone, ρ is about -4;[25] hence, the predicted effect for a single m-D is $(-4)(-0.0012) = 0.0048 = \log k_D/k_H$. The predicted effect of $k_H/k_D = 1.011$ is in close agreement with the experimental value of 1.014 ± 0.001.

(24) G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, 17, 1183 (1934); F. H. Westheimer, *J. Am. Chem. Soc.*, 61, 1977 (1939); J. M. Sarmousakis, *J. Chem. Phys.*, 12, 277 (1944); M. Judson and M. Kilpatrick, *J. Am. Chem. Soc.*, 71, 3115 (1949); J. D. Roberts and W. T. Moreland, Jr., *ibid.*, 75, 2167 (1953).
(25) Y. Okamoto and H. C. Brown, *J. Org. Chem.*, 23, 420 (1958); V. J. Shiner and C. V. Verbanic, *J. Am. Chem. Soc.*, 79, 369 (1957).

Robertson, et al.,[26] have found k_D/k_H values ranging from 1.06–1.09 for aqueous solvolysis of propyl-3,3,3-d_3 halides and sulfonates. The number of atoms intervening between deuterium and the center of charge in the transition state of these solvolyses is the same as that in deuterioacetate ion; hence, the order of magnitude of the effect is such that a substantial portion may be due to a normal inductive isotope effect. A corollary of such a treatment is that deuterium in the β-position should stabilize a carbonium ion still more. The net destabilizing effect noted frequently[3,27] must, therefore, be the result of a second and overriding effect, usually attributed to hyperconjugation. The existence of the two effects operating in opposite directions was beautifully demonstrated by Shiner[28] who found a small rate acceleration in solvolysis of 2-chloro-2-methyl-5,6,7,8-dibenzobicyclo[3.3.3]octadiene-1,4-d_2 in which conjugation of the β-deuterium with the incipient carbonium ion is stereoelectronically inhibited. The magnitudes of the opposing effects may be roughly approximated: Acetolysis of secondary alkyl sulfonates and solvolysis of tertiary halides have ρ-values in a $\rho\sigma^*$ treatment of about 3–3.5[29]; our value of σ^* (CH_2D-) of -0.0027 implies that the replacement of CH_3- by CH_2D- in $CD_3CHOTsR$, for example, should cause an inductive rate acceleration in acetolysis of $\sim 2\%$. The net retardation actually observed is typically $\sim 20\%$; hence the hyperconjugative effect is an order of magnitude greater than the inductive effect in such systems.

One might expect a greater electron-donating inductive effect for deuterium in the α-position of a carbonium ion, but the magnitude cannot be assessed more than qualitatively for the same reasons that the effect in DCOOH cannot be easily related to that in CD_3COOH. Nevertheless, it seems reasonable that the observed rate decrease of $\sim 15\%$ in acetolysis of R_2CDOTs,[3,30] for example, usually associated with coordination number or hybridization changes, would be still greater were it not for this superposed inductive effect. Similarly, part of the experimental rate decrease in the base-catalyzed deuterium–hydrogen exchange of toluene-α-d produced by additional α-deuteriums[31] is probably of inductive origin; however, the attempt to dissect the experimental effect into inductive and hybridization contributions[31] must be regarded as approximate for the reasons cited above. Finally, the inductive isotope effect is an additional effect that complicates the interpretation of the small magnitude of the isotope effects found in many aromatic substitutions.[3]

Our present purpose was to show that typical inductive constants based only on an isotope effect in acetic acid compare directly with independently measured quantities in other systems. The quantitative values so determined for σ^* (CH_2D-) and σ_m (D) may be modified somewhat by subsequent studies, but they demonstrate that these concepts may be applied in practice to isotope effects.

Experimental

Acetic Acids.—Brothers Chemical Co. reagent grade glacial acetic acid was purified by partial freezing and decanting the supernatant liquid. The process was repeated three times. Acetic-d_3 acid-d from Merck (Canada) was distilled under high vacuum at room temperature followed by fractional freezing. The n.m.r. spectrum showed >99.5% deuteration. Gas chro-

(26) K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *Chem. Ind.* (London), 588 (1960); *J. Am. Chem. Soc.*, 82, 6315 (1960).
(27) E. S. Lewis, *Tetrahedron*, 5, 143 (1959); V. J. Shiner, Jr., *ibid.*, 5, 243 (1959).
(28) V. J. Shiner, Jr., *J. Am. Chem. Soc.*, 82, 2655 (1960).
(29) A. Streitwieser, Jr., *ibid.*, 78, 4935 (1956).
(30) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 173.
(31) A. Streitwieser, Jr., and D. E. Van Sickle, *J. Am. Chem. Soc.*, 84, 254 (1962).

matography on a silicone column at 160° showed no detectable amount of impurities.[32]

The second sample of CD_3COOH was prepared by carbonation of the Grignard reagent prepared from 5 g. of CD_3Br (Merck, Canada; 99% deuterated) and 2.5 g. of crystalline magnesium in 45 ml. of dried ether. After hydrolysis with the minimum amount of 25% sulfuric acid, the ether solution was decanted and combined with subsequent ether washings of the magnesium salts. The ether was distilled and the acetic-d_3 acid was fractionated; a middle cut was used for the acidity measurements.

Pivalic-d_9 Acid.—Carbon dioxide was passed over a cooled and stirred solution of the Grignard reagent prepared from 5 g. of t-butyl-d_9 chloride (Merck of Canada) and 1.34 g. of crystalline magnesium. After hydrolysis with dilute sulfuric acid, the washed and dried ether solution was distilled giving 1.7 g. of pivalic-d_9 acid in two fractions, b.p. 160–165°. The second fraction was stored in a sublimer and a small amount was sublimed as required for the conductivity measurements.

$Anal.$[33] Calcd. for $C_5D_9HO_2$: D, 90 atom %. Found: D, 86 atom %.

Ordinary pivalic acid was prepared in the same manner from freshly distilled t-butyl chloride. It gave the same results as commercial pivalic acid.

Benzoic Acids.—Reagent grade benzoic acid was sublimed immediately before use in the conductivity measurements.

Deuterium chloride, prepared from D_2O and benzoyl chloride,[34]

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(32) Halevi (ref. 10b) reports that his sample of Merck CD_3COOD contained traces of several contaminants.

(33) Analysis of the Microanalytical Laboratory of the University of California. The deuterium analyses were by density measurement of the combustion water by a drop suspension method. At the time of this work, this method was not accurate for high deuterium content and tended to give low results. The analyses were used only as supplemental evidence for substantial deuterium content of our samples.

was passed through successive portions of a 1 mole % solution of sublimed gallium bromide in benzene until density measurements indicated an isotopic purity of >95%.[35] The highest value found for the density of our benzene-d_6 is d^{25}_{25} 0.9438, lit.[36] d^{25}_{25} 0.9461.

A sample having d^{25}_{25} 0.940 was brominated with bromine and iron yielding bromobenzene-d_5, b.p. 153–155°, $n^{25}D$ 1.5564.

$Anal.$[33] Calcd. for C_6D_5Br: D, 100 atom %. Found: D, 90 atom %.

The bromide was converted to the Grignard reagent and carbonated in the usual way. The product benzoic-d_5 acid, m.p. 122–123°, was crystallized from water and was sublimed immediately before use.

$Anal.$[33] Calcd. for $C_7D_5HO_2$: D, 83 atom %. Found: D, 75 atom %.

Benzoic-2,6-d_2 acid was prepared in a similar manner from bromobenzene-2,6-d_2.[37] The product was also crystallized from water and sublimed; m.p. 122.0–122.6°.

$Anal.$[33] Calcd. for $C_7D_2H_4O_2$: D, 33 atom %. Found: D, 30 atom %.

Conductivity Measurements.—Solutions were made up using distilled water which had been passed through a Penfield mixed-bed demineralizer, model M-8, and aliquots were titrated with standardized sodium hydroxide. Conductivity measurements were made in a cell of conventional design in a thermostat controlled to ±0.01°. Resistance measurements were taken on an Electro-Measurements Inc., impedance bridge, model 250-DA.

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(34) H. C. Brown and C. Groot, $J. Am. Chem. Soc.$, **64**, 2223 (1942).

(35) We are indebted to Professor F. R. Jensen for suggesting this method and providing apparatus and details.

(36) L. H. P. Weldon and C. L. Wilson, $J. Chem. Soc.$, 237 (1946).

(37) The preparation of this and other deuterated bromobenzenes will be described in a later paper.

The Protonation of Pyrroles

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Formation of stable α-protonated salts of pyrrole and methylpyrroles in aqueous sulfuric acid is demonstrated by their proton magnetic resonance spectra. The observed rates of deuterium exchange in N-methylpyrrole require, however, that β-protonation of the base occur at the faster rate in concentrated H_2SO_4 solutions. The basicity constant of pyrrole is redetermined as $pK_a = -3.8$, considerably below the currently accepted value, and the variation of the ratio of protonated to unprotonated base with sulfuric acid concentrations, while self-consistent within the methylpyrrole series, differs from previously defined class acidity functions. The basicity constants vary with methyl substitution in a semi-empirically predictable manner.

The basicity of pyrrole, which is of theoretical interest in connection with aromaticity in heterocyclic systems and of practical importance to many aspects of its chemistry, has been variously estimated to be in the range -1.7 to $+0.3$ on the pK_a scale.[1] It is commonly felt that side reactions, particularly trimerization,[2] render the base unamenable to conventional measurements by indicator methods, although results have been obtained for a number of its methyl derivatives.[3,4] Also, the position of protonation in pyrrole itself has not been clearly established.

Since the trimerization of pyrrole is very likely controlled by a second-order process involving attack by the conjugate acid on the free base,[2] one would infer that solutions of the salt are stable provided the medium is sufficiently acidic to ensure complete protonation. The failure of earlier workers[3] to obtain stable solutions of pyrrole in acid, if due to this cause, would imply that it is a weaker base than expected. One might also argue from what is known about the rate and mechanism of the trimerization[2] that very dilute solutions ($\sim 10^{-4}$ M) of pyrrole would

react slowly enough to make ultraviolet indicator measurements of the protonation ratio feasible. The fact that the very pronounced change that occurs in the spectra of methylpyrroles[3,4] was not observed in the most recent measurement of pyrrole[1] is explicable only on the basis that C-protonation was never effected, so that the reported pK_a, at least for C-protonation, would be much too high. Finally, a pK_a of -2.3 was recently reported for the β-protonation of indole.[5] One intuitively expects pyrrole to be a weaker base than indole for the same reasons that benzene is a weaker base than naphthalene, or that cyclopentadiene is a stronger acid than indene,[6] although the issue is clouded by the presence of a heteroatom and the availability of several different protonation sites.

1. Structure of Methylpyrrole Salts in Solution.—The proton magnetic resonance spectra of pyrrole, N-methylpyrrole, and N-phenylpyrrole in 16 M sulfuric acid all show a characteristic pattern of four main envelopes due to protons on the ring carbon atoms, and the intensity ratios of $1:1:1:2$ require

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(1) M. Navqui and Q. Fernando, $J. Org. Chem.$, **25**, 551 (1960).

(2) H. A. Potts and G. F. Smith, $J. Chem. Soc.$, 4018 (1957).

(3) R. J. Abraham, E. Bullock, and S. S. Mitra, $Can. J. Chem.$, **37**, 1859 (1959).

(4) E. B. Whipple, Y. Chiang, and R. L. Hinman, $J. Am. Chem. Soc.$, **85**, 26 (1963).

(5) R. L. Hinman and J. Lang, Abstracts, 141st National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1961, p. 98Q. The authors are grateful to Dr. Hinman for advanced communication of his detailed results, which are to be published.

(6) R. E. Dessy, Y. Okuzumi, and A. Chen, $J. Am. Chem. Soc.$, **84**, 2899 (1962). See also the discussion in A. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., p. 347.