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Use of Substituent Effects on Isotope Effects to Distinguish between Proton and Hydride Transfers. Part II. Mechanism of Decarboxylation of β-Keto Acids in Benzene[1-3]

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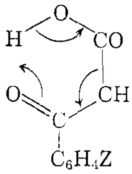
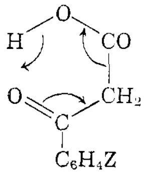
Isotope effects (k_{RCOOH}/k_{RCOOD}) in the decarboxylation of substituted benzoylacetic acids in benzene at 50° are 2.8 for *m*-nitro, 1.7 for *p*-chloro, 1.4 for unsubstituted, and 0.85 for *p*-methyl, although these substituents have a negligible effect on OH frequencies in the ground state. This large variation in isotope effect with substituents is inconsistent with a cyclic hydride transfer mechanism but in accord with a cyclic proton transfer mechanism.

Curved arrows are commonly used[4] for electronic bookkeeping in cyclic processes like the decarboxylation of β-keto acids, the Claisen rearrangement and the Cope rearrangement. However, it is commonly thought that one cannot know whether to write the arrows clockwise or counterclockwise.[5] The two possibilities for the decarboxylation of benzoylacetic acids are I (a proton transfer) and II (a hydride transfer).[6]



I



II

Substituent Effects on Isotope Effect.—The introduction of the previous paper[2] pointed out some physical differences between proton transfer and hydride transfer transition states and gave theoretical reasons for expecting the magnitude of substituent effects on the hydrogen isotope effect to be large for proton transfers but close to zero for hydride transfers. In brief, proton transfers have greater distances and more polarizable bonding between hydrogen-bonded atoms because antibonding orbitals are occupied. Use of this criterion to distinguish between proton and hydride transfers led to assignment of a reasonable (non-cyclic) mechanism for the oxidation of alcohols by bromine in acidic water solution. In this paper it is applied to cyclic decarboxylation since there is no apparent reason to limit this tool to non-cyclic processes. We cannot infer anything from such measurements about the motion of electrons or about any intermediate states between ground state and transition state or anything about the route between ground state and transition state. Nevertheless we can determine over-all changes from ground state to transition state and so hope to learn whether the electron distribution in the OHO group at the transition state corresponds to that expected for a proton transfer (which is all we mean to imply by I) or a hydride transfer (II).

Table I presents the results. The most electronegative substituent tested (*m*-nitro) gives the largest isotope effect (2.8). The other k_H/k_D values are 1.7 for *p*-chloro, 1.4 for unsubstituted, 1.2 for *p*-methoxy and 0.85 for *p*-methyl, in benzene solution at 50°. The abnormal position for *p*-methoxy may arise from a conflict between inductive and resonance effects. The hydrogen is much more loosely bonded in the transition state than in the ground state for the *m*-nitro compound (k_H/k_D = 2.8) but *more tightly bound in the transition state than in the ground state* for the *p*-methyl compound (0.85). This large variation in isotope effect (2.8–0.85) reflects a variation in transition states rather than in ground states, since ground state frequencies are very little affected by substituents (see Experimental section on "Infrared Spectra"). It is inconsistent with a hydride transfer (II) but in accord with a proton transfer (I).[2] The change in isotope effect is almost as large as the change in rate in this system.

TABLE I

RATES OF DECARBOXYLATION OF β-KETO ACIDS

Acid	Solvent	Temp., °C.	$k_H \times 10^4$, sec.$^{-1}$	$k_D \times 10^4$, sec.$^{-1}$
m-Nitrobenzoylacetic	Toluene	69.6	8.36 ± 0.06	2.36 ± 0.02
	Toluene	59.6	2.46	0.777 ± 0.008
	Toluene	50.2	0.74[a]	0.26[a]
p-Chlorobenzoylacetic	Benzene	50.2	1.03 ± 0.02	0.619 ± 0.012
Benzoylacetic	Benzene	50.2	2.56 ± 0.03	1.82 ± 0.04
	Benzene[b]	50.2	3.62	
	50% water[c]	50.2	22.7 ± 0.1	18.2 ± 0.1
p-Anisoylacetic	Benzene	50.2	5.76 ± .13	4.78 ± 0.13
p-Toluoylacetic	Benzene	50.2	3.88 ± .18	4.59 ± 0.24
	Water	50.2	9.4 ± .2	10.5 ± 0.0
Dimethylacetoacetic	Water	50.2	11.7 ± .1	
	Water	34.9	2.85 ± .07	3.56 ± 0.07
	Benzene	34.9	7.9 ± .2	5.9 ± 0.1

[a] Extrapolated from values at 69.6° and 59.6°. [b] Saturated with water. [c] 50% water–50% dioxane by volume before mixing.

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[1] Supported in part by the National Science Foundation under Grant NSF-G464, the Atomic Energy Commission under Contract No. AT(30-1)-905, and the National Institutes of Health under Research Grant RG-3711 (C4).

[2] *Cf.* Part I, C. G. Swain, R. A. Wiles and R. F. W. Bader, *J. Am. Chem. Soc.*, **83**, 1945 (1961).

[3] For further details, *cf.* R. N. Griffin, Ph.D. Thesis in Organic Chemistry, M.I.T., October, 1957, pp. 6–27.

[4] P. D. Bartlett in H. Gilman, "Organic Chemistry," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 72, 106; J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, pp. 263, 290, 453–465; J. E. Leffler, "The Reactive Intermediates of Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, p. 234; E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry and Holt and Co., Inc., New York, N. Y., 1959, p. 347.

[5] For a clear statement of this point of view, *cf.* C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 596–597.

[6] Other mechanisms have been eliminated for decarboxylation in benzene solution by previous work summarized in several excellent recent reviews (P. D. Bartlett, ref. 4, p. 104; J. Hine, ref. 4, p. 284) and by experiments described below under "Solvent Effects on Rate."

Substituent Effects on Rate.—The effect of *m*- and *p*-substituents on the rate itself (rather than on the hydrogen isotope effect) gives information about the change in charge of the keto carbon from reactant to transition state. The fact that *m*-nitro retards the reaction means that this carbon is even more positive or electron-deficient in the transition state than in the ground state. This fact by itself is consistent with either I or II provided that the electron shift indicated by the ascending arrow is more complete than the one indicated by the descending arrow at the transition state. However, if we accept I from the evidence of substituent effects on the hydrogen isotope effect, then we can ascribe the low reactivity of the *m*-nitro compound to relatively low electron density on the keto oxygen which nucleophilically attacks the proton.

Solvent Effects on Rate.—Westheimer and Jones found only a 6% decrease in rate of decarboxylation of dimethylacetoacetic acid from water to 75% methanol–25% water.[7] A study of a wider range of β-keto acids and solvents[8] revealed that even changes from water to benzene or *n*-hexane have rather small effects on the rate (Table II). For example, the relative rates of decomposition of 2-ethyl-3-ketohexanoic acid in water, benzene and *n*-hexane are 6.3:1:0.7. The small spread between the benzene and *n*-hexane is strong evidence for a cyclic mechanism rather than a dipolar ion intermediate in benzene and *n*-hexane. In benzene the keto acid is predominantly in the un-ionized chelated form, as shown by the normal cryoscopic molecular weights reported in the Experimental section. Simple carboxylic acids, on the other hand, exist mainly as dimers under these conditions. The same should be true in *n*-hexane. Therefore in these solvents the reactant normally exists already in the reactive form for decarboxylation.

TABLE II

DECARBOXYLATION OF β-KETO ACIDS

Solvent	Init. concn., *M*	Temp., °C.	$k_1 \times 10^4$, sec.$^{-1}$
$CH_3(CH_2)_2COCH(C_2H_5)COOH$			
H_2O	0.0063	50.3	8.5
H_2O	.0093	45.2	4.5
H_2O	.027	45.2	5.3[a]
18% $(CH_3)_2CO$[b]	.0074	50.3	9.0
50% $(CH_3)_2CO$[b]	.0160	50.3	12.8
68% $(CH_3)_2CO$[b]	.0051	50.3	8.3
91% $(CH_3)_2CO$[b]	.0110	50.2	4.0
C_6H_6	.0067	50.3	1.35
C_6H_6	.0089	55.2	2.6
n-C_6H_{14}	.0084	50.3	0.95
n-C_6H_{14}	.0089	60.2	2.4
n-C_7H_{16}	.0069	50.3	0.92
$C_6H_5COCH_2COOH$			
H_2O	0.0068	50.3	7.8
H_2O	.0140	60.3	24.5
H_2O	.0044	50.3	9.3[a]
40% $(CH_3)_2CO$[b]	.0240	50.3	14.8
94% $(CH_3)_2CO$[b]	.0033	50.3	10.3
C_6H_6	.0066	50.1	2.35
C_6H_6	.0033	60.2	7.5
p-$CH_3OC_6H_4COCH_2COOH$			
H_2O	0.0310	50.3	6.0
50% $(CH_3)_2CO$[b]	.0220	50.3	27.0
$(CH_3)_2CO$	.0123	50.3	9.2

[a] Sulfuric acid (0.20 *M*) added. [b] % acetone by volume before mixing; residue is water.

In water, the keto acids would be associated with water to a considerable extent and would be less completely in the reactive chelated form. Therefore the rate constants for decarboxylation of the chelated form must be much greater in water to explain the generally higher rates observed. However, the change in rate from benzene to water is less with benzoylacetic acid than with 2-ethyl-3-ketohexanoic acid, and the rate is actually faster in benzene than in water with dimethylacetoacetic acid. Therefore it may be that even in water the mechanism is better described by cyclic mechanism than by one involving a dipolar ion intermediate. However, this is by no means as certain in water as in benzene. To be certain of the mechanism in water, measurements of the equilibrium between chelated and unchelated form and of isotope effects in light and heavy water would be needed.

All three β-keto acids in Table II show a rate in mixtures of acetone and water that is higher than in acetone or water alone. Wiig observed a similar result in the decarboxylation of acetone-α,α'-dicarboxylic acid in water–isopropyl alcohol mixtures at 40°.[9] This is consistent with an effect of the organic solvent favoring the chelated form coupled with a helpful effect of water in solvating partial charges in the transition state.

Two experiments in Table II with added sulfuric acid demonstrate that acid catalysis is very minor.

The Hammett reaction constant is approximately -1.0 for the normal acids and -1.5 for the deuterated acids. These are surprisingly large values for a reaction showing such a small effect of solvent.

Experimental

Solvents.—The benzene was Mallinckrodt thiophene-free, dried by azeotropic distillation and stored over sodium wire. Acetone was reagent grade, dried over Drierite. *n*-Hexane was Eastman Kodak Co. white label, shaken with sulfuric acid, with a neutral potassium permanganate solution, washed with water, and dried over sodium; b.p. 68.5–69.5°. Deuterium oxide was 99.5% pure as received from the Stuart Oxygen Co.

***m*-Nitrobenzoylacetic Acid.**—Ethyl *m*-nitrobenzoylacetate was made by the method of Boeseken and Jacobs[10] from 85.5 g. (0.46 mole) of *m*-nitrobenzoyl chloride, b.p. 153–154° (12 mm.), 59.8 g. (0.46 mole) of ethyl acetoacetate and 10.6 g. of sodium. The precipitate was shaken with ammonium hydroxide solution[11] for 20 min. The yield of ethyl *m*-nitrobenzoylacetate was 9.5 g. The ester was hydrolyzed in 85% sulfuric acid at 40° for 20 min. and the mixture poured over 150 g. of crushed ice. The precipitate was collected, dissolved in aqueous sodium bicarbonate, and reprecipitated with sulfuric acid.

***p*-Chlorobenzoylacetic Acid.**—Ethyl *p*-chlorobenzoylacetate was made by the method of Wallingford, Homeyer and Jones[12] from 80 g. (0.52 mole) of *p*-chloroacetophenone,

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(7) F. H. Westheimer and W. A. Jones, *J. Am. Chem. Soc.*, **63**, 3283 (1941).

(8) R. M. Esteve, Jr., Ph.D. Thesis in Organic Chemistry, M.I.T., December, 1950, pp. 34–126. Acetoacetic, 2-oxocyclopentanecarboxylic and 2-oxocyclohexanecarboxylic acids were also studied.

(9) E. O. Wiig, *J. Phys. Chem.*, **32**, 961 (1928).

(10) J. Böeseken and J. Jacobs, *Rec. trav. chim.*, **55**, 810 (1936)

(11) C. Bulow and E. Hailer, *Ber.*, **35**, 933 (1902).

11.9 g. (0.52 mole) of sodium and 500 ml. of diethyl carbonate, b.p. 60° (66 mm.). The ethyl *p*-chlorobenzoylacetate was distilled, b.p. 144–145° (3.7 mm.), and saponified for 48 hr. at room temperature in 10% potassium hydroxide solution. The acid precipitated on addition of 3 *M* sulfuric acid. It was filtered and dissolved in aqueous sodium bicarbonate, then filtered again and reprecipitated by addition of 3 *M* sulfuric acid. After drying under vacuum, it melted at 217–219° dec.; reported m.p. 232° dec.,[13] 215° dec.[8]

Benzoylacetic Acid.—Twenty-five grams of ethyl benzoylacetate was dissolved in 250 ml. of water containing 12.5 g. of potassium hydroxide. The solution remained at room temperature for 16 hr., then was cooled and acidified with 3 *M* sulfuric acid. Benzoylacetic acid precipitated; it was filtered and recrystallized from benzene; neut. equiv. 168, calcd. 164; m.p. 99.5–100° dec., reported[14] m.p. 103–104° dec.

***p*-Anisoylacetic Acid.**—Ethyl *p*-anisoylacetate was prepared according to Wallingford, Homeyer and Jones[12] from 50 g. (0.30 mole) of *p*-methyoxyacetophenone recrystallized from ethanol, m.p. 38–39°, 0.30 mole of sodium ethoxide and 500 ml. of diethyl carbonate, b.p. 126°. The ester was isolated as its enol copper salt by addition of saturated aqueous cupric acetate to an ethanol solution of the ester. The ester was contained in 100 ml. of ethanol and the cupric acetate solution added in 5-ml. portions until no more precipitate appeared on standing for several hours. The enol salt was decomposed in 1 *M* acetic acid and the ester extracted with ether. The ester was saponified with 10% sodium hydroxide solution and the acid precipitated by acidifying with concentrated hydrochloric acid and pouring over about 300 g. of crushed ice. The acid was dissolved in aqueous sodium bicarbonate, the solution filtered, and the acid reprecipitated by addition of hydrochloric acid. After drying under vacuum, the *p*-anisoylacetic acid had m.p. 80° dec., reported[8] m.p. 81–82° dec.

***p*-Toluoylacetic Acid.**—Ethyl acetoacetate (0.1 mole) was allowed to react with 1.1 equivalents of sodium.[15] *p*-Toluoyl chloride, b.p. 95–95.5° (10 mm.), was added slowly to the cooled sodium enolate. The mixture was warmed to room temperature and allowed to react for 6 hr. with stirring. After acidification with 1 *M* acetic acid, the diacyl compound was separated by filtration and hydrolyzed in ammonium hydroxide solution according to the method of Bulow and Hailer.[11] The ester was distilled, b.p. 110° (1 mm.). It was saponified for 48 hr. in 10% potassium hydroxide solution at room temperature, then precipitated by addition of 3 *M* sulfuric acid and filtered. *p*-Toluoylacetic acid was dissolved in aqueous sodium bicarbonate, filtered and reprecipitated with 3 *M* sulfuric acid. After drying under vacuum in an Abderhalden drying pistol, it melted at 82–84° dec. The second synthesis of *p*-toluoylacetic acid was by the method of Wallingford, Homeyer and Jones.[12] The acid was obtained from the ester as above. This product melted at 85–87° and showed no significant depression on mixture with a sample from the first synthesis.

Dimethylacetoacetic Acid.—Ethyl acetoacetate was distilled through a spinning band column, b.p. 102° (95 mm.), and a center cut used. One equivalent of sodium ethoxide in 500 ml. of toluene was allowed to react for 2 hr. under reflux with 0.392 mole of ethyl acetoacetate. The mixture was cooled and 82 g. of methyl iodide, b.p. 42.5°, added over a period of 2 hr. The reaction was allowed to proceed overnight with stirring. The ester (mostly ethyl α-methylacetoacetate) was distilled, b.p. 83.5–84° (22 mm.), yield 80%. Ethyl dimethylacetoacetate was made by the method of Folkers and Adkins[16] from 32 g. of ethyl α-methylacetoacetate. The crude product was purified by shaking for 1 hr. with a 25% solution of potassium hydroxide.[17] The ester was distilled, b.p. 82–83° (21 mm.), yield 18.5 g. It was then saponified in 145 ml. of 2.5% sodium hydroxide solution for 24 hr. at room temperature[18] followed by addition of saturated barium chloride solution, and the water partially evaporated under reduced pressure. The barium dimethylacetoacetate was removed by filtration. An aqueous solution of barium dimethylacetoacetate was acidified with 50% sulfuric acid in the cold. The solution was extracted with ether, the extracts collected and dried over sodium sulfate, and the ether evaporated under vacuum. The distillate was collected in a solid carbon dioxide trap. Almost no residue was left in the flask, but crystals of uncertain structure were found in the trap along with the ether. Filtration isolated white crystals which decomposed to liquid in about 15 sec. This corresponds to the description given by Ceresole[18] for α,α-dimethylacetic acid. However, these crystals (or the resultant liquid) showed no tendency to evolve carbon dioxide. The boiling point of the liquid was 100 ± 1° and no visible residue remained. It was concluded, therefore, that the crystals were ice from an incompletely dried ether solution. Further attempts to isolate dimethylacetoacetic acid were unsuccessful.

2-Ethyl-3-ketohexanoic acid.—Ethyl 2-ethyl-3-ketohexanoate, b.p. 65–75° (1 mm.), n^{25}_{D} 1.4209, was prepared by the procedure of McElvain.[19] The acid was obtained by hydrolyzing the ester in a solution of 3 g. of potassium hydroxide in 140 ml. of water and 100 ml. of acetone. After 48 hours the solution was evaporated to 40 ml., cooled and acidified with 10 ml. of 2.5 *M* sulfuric acid. The acid was not isolated. The runs in water were made by diluting aliquots. For runs in benzene and hexane the aqueous solution was extracted with the solvent, and the extract dried with sodium sulfate and finally with Drierite.

Deuterated Acids.—A dry sample of the appropriate protium acid, about 0.5 g., was mixed with 5 ml. of deuterium oxide. Anhydrous sodium carbonate was added in small portions from the tip of a spatula, the solution being stirred until no more carbon dioxide was evolved before another portion of sodium carbonate was added. The solution was filtered under nitrogen and the deuterated acid precipitated by the dropwise addition of sirupy phosphoric acid-d_3 made by addition of deuterium oxide to phosphorus pentoxide.[20]

Infrared Spectra.—The spectroscopic examinations of the acids were made on Nujol and Perfluorolube (du Pont FCX-331) mulls by means of Baird model B and Perkin-Elmer model 21 double-beam recording spectrophotometers. The bands which were displaced significantly (more than 5 cm.$^{-1}$) by deuteration in the three acids studied are listed in Table III. Two bands were observed in each case for the OD stretch (near 2200 and 2000 cm.$^{-1}$. The OH stretch is strongly overlapped by the aromatic and aliphatic OH stretching vibrations and cannot be clearly separated from the intense CH absorption in this region. The OH stretching values listed in parentheses were calculated from the OD stretching frequencies using an isotopic frequency ratio of 1.36, the value observed for the OH and OD stretching frequencies in acetic acid.[21] In the case of the *m*-nitro acid, the spectrum for the H acid clearly showed that the principal OH absorption was now occurring slightly above 3000 cm.$^{-1}$. The bands displaced below 1500 cm.$^{-1}$ are in excellent agreement with the observations of previous investigators. Hadži and Sheppard[22] investigated the effects of deuteration on a large number of acids in the solid and liquid states. They found three bands to

TABLE III

FREQUENCIES OF THE CARBOXYL GROUP IN SUBSTITUTED BENZOYLACETIC ACIDS

p-Methoxy		*p*-Chloro		*m*-Nitro	
Acid	Acid-*d*	Acid	Acid-*d*	Acid	Acid-*d*
(2990)	2198	(2991)	2200	(3040)	2235
(2711)	1996	(2710)	1992	(2830)	2080
1460	1340	1425	1360	1427	1326
1318	1050	1325	1050	1305	1037
900	(644)	930	(665)	865	(618)

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[12] V. H. Wallingford, A. H. Homeyer and D. M. Jones, *J. Am. Chem. Soc.*, **63**, 2252 (1941).

[13] L. Thorp and E. Brunskill, *ibid.*, **37**, 1258 (1915).

[14] W. H. Perkin, *J. Chem. Soc.*, **45**, 177 (1884).

[15] H. Burton and C. K. Ingold, *ibid.*, 920 (1928).

[16] K. Folkers and H. Adkins, *J. Am. Chem. Soc.*, **53**, 1416 (1931).

[17] A. Michael, *Ber.*, **38**, 2083 (1905).

[18] M. Ceresole, *ibid.*, **15**, 1871 (1882).

[19] S. M. McElvain, *J. Am. Chem. Soc.*, **51**, 3124 (1929).

[20] G. Pannetier and H. Guenebaut, *Bull. soc. chim. France*, 636 (1955).

[21] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 165.

[22] D. Hadži and N. Sheppard, *Proc. Roy. Soc.* (*London*), **A216**, 247 (1953).

shift upon deuteration in each case, in the same regions as the bands noted in Table III for the hydrogen acids. The three new bands which appeared in their spectra for the deuterated acids also came at the same regions listed in Table III. They ascribed the 1420 and 1310 cm.$^{-1}$ bands to the CO stretching and COH in-plane bending modes. The 900 cm.$^{-1}$ band is due to the out-of-plane bending or torsion of the OH group. They investigated the spectra of the acids down to 500 cm.$^{-1}$ and found this latter band to shift by a factor of 1.40. The instrument employed in the present investigation was not capable of resolving clearly this low lying band in the deuterated acids. The values listed for the torsional motions of the deuterated acids were calculated from the values observed for the corresponding motions in the hydrogen acids (where they are very prominent) using the isotopic frequency ratio of 1.40. The calculations of the zero-point energy differences for the ground states of the molecules were based upon the higher values of the OH stretching vibrations and the three frequencies below 1500 cm.$^{-1}$.

The small variations observed in the zero-point energy differences for the ground states of the reactant molecules cannot begin to account for the large variation in observed isotope effect. The change in the value of the isotope effect when the substituent is changed from *p*-methoxy to *m*-nitro is equivalent to an increase of approximately 176 cm.$^{-1}$ in the zero-point energy differences. The ground state difference is only 9 cm.$^{-1}$. It is inconceivable that the change in substituent from *p*-methoxy to *m*-nitro could introduce a change in the ground state zero-point energy difference of the order of 176 cm.$^{-1}$. To increase the zero-point energy difference by 176 cm.$^{-1}$ over that observed for the *p*-methoxy acid would require the stretching frequency of the OH bond of the *m*-nitro acid be above 4000 cm.$^{-1}$. This is an impossibly high value and is not observed even for free, monomeric, non-hydrogen bonded acids. The observed OH stretching frequency for the *m*-nitro acid is actually 3040 cm.$^{-1}$ as compared to 2990 cm.$^{-1}$ for the *p*-methoxy acid. The variation in the isotope effect is therefore a direct measure of the variation in the strength of binding of the proton in the transition state. It is possible to calculate to a good approximation the zero-point energy differences for the binding of the protons in the transition state molecules. These values are 687, 595 and 506 cm.$^{-1}$ for the *p*-methoxy, *p*-chloro and *m*-nitro acids. It is evident that the binding of the proton is lessened considerably as the substituent is made more electronegative. It is not surprising that the substituent effect is much more pronounced in the zero-point energy differences of the proton in the transition state than in the ground state. In the transition state the proton is more directly coupled to the substituent through direct bonding with the keto oxygen atom, and the formation of partial charges and partial bonds enhances the effects exerted by the substituent. The calculated zero-point energy differences for the transition state molecules do in fact give a good straight line when plotted *vs.* the Hammett σ-values. (The zero-point energy differences are closely related to the differences in the free energies of the hydrogen and deuterium transition state molecules; the two quantities differ by only a small factor which is almost constant for all the molecules in the series.) If one assumes that the principal motions of the transition state molecules affected by the substitution of deuterium for hydrogen are approximated by the linear O—H—O system, then it is possible to calculate the bending frequencies for the hydrogen atom in the transition state molecules. Of the remaining two frequencies for this triatomic system, the antisymmetric mode is of course the reaction coördinate and the symmetric vibration will exhibit no isotopic shift in frequency if the transition state is close to symmetrical, which it most certainly is in this case. The values of the doubly degenerate bending frequencies are calculated to be 2440, 2110 and 1793 cm.$^{-1}$ for the *p*-methoxy, *p*-chloro and *m*-nitro acids, respectively. These values clearly illustrate the decrease in the strength of the binding of the proton as the electronegativity of the substituent is increased. It should be noted that these values for the bending frequencies represent upper limits in that we have ignored the contribution from the other frequencies such as the COH bending modes. The isotopic displacements in these frequencies will, however, be small in comparison to those for the OHO bending vibrations and their inclusion would not decrease the above values by any relatively large amount. One must conclude that the proton is indeed very tightly bonded in the transition state of this particular reaction.

Molecular Weights in Benzene.—Freezing point depressions in benzene obtained by the Beckmann method[23] indicated molecular weights of 170 and 165 *vs.* 164 calcd. for benzoylacetic acid, 191 and 200 *vs.* 194 calc. for *p*-anisoylacetic acid, and 200 and 185 *vs.* 198 calcd. for *p*-chlorobenzoylacetic acid. Thus they all appear to be monomeric.

Deuterium Analyses.—To determine whether the deuterated acids contained only deuterium on the carboxyl group, *p*-toluoylacetic acid-*d* was analyzed for deuterium content by the falling drop method using the equipment of Labes and McKnight.[24] The analysis showed 10.55 atom % deuterium rather than the expected 10.00%.

The benzylhydryl ester of *p*-toluoylacetic acid-*d* was made by reaction of the acid with diphenyldiazomethane. The ester was hydrolyzed and the benzhydrol analyzed for deuterium content. Results showed 1.00 deuterium atom per molecule on the carboxyl group.

Since the excess deuterium must have been in the methylene group, and since exchange on the methylene group must have occurred *via* an enol form, studies were made on the amounts of enolization occurring under the conditions of synthesis and decarboxylation of the deuterated acids. Benzoylacetic acid (0.2011 g., 1.23 mmoles) was dissolved in water containing excess sodium carbonate (0.1430 g., 1.35 mmoles). These are harsher conditions than those used in the exchange reaction, but were necessary because of the expected liberation of hydrobromic acid. The solution was treated with bromine according to the procedure of Siggia.[25] The assumption was made that substitution of the second bromine was faster than the first as found in the bromination of ethyl acetoacetate.[26] When potassium iodide solution was added as soon as possible after the bromine, the bromine consumed was equivalent to 5.8% enolization. If the mixture remained at room temperature for 10 min. before addition of the potassium iodide solution, bromine equivalent to 10.6% enolization was consumed. By comparison, deuterated β-keto acids were subjected to basic conditions during their synthesis for a period of about 5 minutes.

When *m*-nitrobenzoylacetic acid was treated in the same manner for 10 minutes, bromine equivalent to 58.1% enolization was consumed. In excess sodium bicarbonate solution, sodium *m*-nitrobenzoylacetate consumed bromine equivalent to only 1.37% enolization.

Since it seemed likely that at least some of the deuterated acids contained significant amounts of deuterium on the methylene group, benzoylacetic-d_2 acid-*d* and benzoylacetic acid-*d* were synthesized. The former contained 2.77 deuterium atoms per molecule and the latter 1.05 deuterium atoms per molecule as determined by falling drop analysis. The rates of decarboxylation of the two acids were compared at 50.5° and found to differ by only 2%, which is within experimental error. The benzoylacetic acid-*d* used in this comparison was made by dissolving benzoylacetic acid in sodium deuterium carbonate solution, made by bubbling dry carbon dioxide through a deuterium oxide solution of sodium carbonate, and proceeding as described above under "Deuterated Acids." Benzoylacetic-d_2 acid-*d* was made by dissolving benzoylacetic acid in deuterium oxide containing about 1 *M* sodium deuteroxide, allowing the solution to remain overnight, and proceeding as above.

To determine whether enolization occurred under the conditions of decarboxylation, 0.0272 g. of benzoylacetic acid-*d* was dissolved in 50 ml. of benzene in the presence of 0.067 g. of bromine, and the mixture heated for 1 hr. at 50°. Bromine equivalent to 46% enolization was consumed. Since the half-life of the decarboxylation reaction

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(23) A. Findlay and J. A. Kitchener, "Practical Physical Chemistry," 8th ed., Longmans, Green and Co., New York, N. Y., 1954, p. 107; F. Daniels, J. H. Mathews, J. W. Williams, P. Bender and R. A. Alberty, "Experimental Physical Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 68.

(24) C. G. Swain and M. M. Labes, *J. Am. Chem. Soc.*, **79**, 1084 (1957); C. G. Swain, J. T. McKnight and V. P. Kreiter, *ibid.*, **79**, 1088 (1957).

(25) S. Siggia, "Quantitative Organic Analysis via Functional Groups," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 69–71.

(26) K. J. Pedersen, *Acta Chem. Scand.*, **2**, 252 (1948).

is 62 min., no enolization occurs under these conditions except that incidental to the decarboxylation.

Kinetic Procedure.—The apparatus used to follow the rate of decarboxylation of β-keto acids consisted of a 20-ml. glass-stoppered flask connected with small diameter Tygon tubing to an inverted 5- or 10-ml. buret. The buret was inverted over water saturated with carbon dioxide. The flask and stopper were kept completely submerged in a Nujol thermostat constant to ±0.05°.

The solvent (15 ml.) was introduced into the flask, saturated with carbon dioxide, and placed in the thermostat. The acid to be decarboxylated was introduced into the flask and the flask shaken until the acid dissolved. The initial concentration of acid was as near 0.02 *M* as possible. With *m*-nitrobenzoylacetic acid the limit of solubility appeared to be about 0.01 *M*. For each point, the flask was shaken for 30 seconds, and then 30 seconds later the buret reading and time were recorded. The first point was used as zero time.

First-order rate constants were calculated from the half-life ($k_1 = 0.693/t_{1/2}$), obtained by plotting fraction unreacted against time on semilogarithmic paper and fitting the best line to the data by eye. In general the plots were straight lines out to 95% reaction.[3,8]

Since dimethylacetoacetic acid could not be isolated, a slightly different procedure was followed in this case. The solvent was introduced along with an appropriate amount of barium dimethylacetoacetate and the mixture allowed to reach thermostat temperature. Less than one equivalent of sulfuric or phosphoric acid-d_3 was added, and the same procedure followed as above.

The rate constants reported in Table I are usually averages of from two to six kinetic runs. The ± figures reported are average deviations.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WILLIAM M. RICE UNIVERSITY, HOUSTON, TEX.]

The Decomposition of Gaseous Chloroformates. I. The Rates of Simple Alkyl Compounds[1]

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The decompositions of some alkyl chloroformates near 250° in the gas phase are studied kinetically in a flow system First-order rate constants for the formation of alkyl chloride and of olefins are determined. Some serious discrepancies with the literature on ethyl chloroformate exist, and are attributed to a possible heterogeneous reaction. A rather polar S$_N$i mechanism is tentatively discussed.

Introduction

The thermal decomposition of alkyl chloroformates by reaction 1 has been considered to be an example of the S$_N$i mechanism.[2] The basis of this

$$\mathrm{ROCOCl} \longrightarrow \mathrm{RCl} + \mathrm{CO_2} \qquad (1)$$

assignment was that there was clean retention of configuration on reaction of the pure liquid[3] which is also observed in solution.[4]

The S$_N$i mechanism was defined as a one-step unimolecular mechanism passing through a cyclic transition state. Studies of the reactions of the apparently analogous chlorosulfites, ROSOCl, led to the conclusion that the S$_N$i picture was too simple, and that a carbonium ion or ion pair was intermediate. This satisfactorily explained a necessary solvent participation,[5] neighboring group participation,[6,7] secondary hydrogen isotope effects,[8] as well as several qualitative arguments based on substituent effects.[9] The analogy between chloroformates and chlorosulfites, originally based on the structural resemblance and the stereochemical course, is strengthened by the conclusion of Wiberg and Shryne[4] (based upon a large negative Hammett rho) that the decomposition of substituted α-phenylethyl chloroformates passed through a highly polar transition state.

The distinction between a highly polar transition state leading directly to neutral products and one leading to an ion pair is difficult. A clear distinction is possible if the ion pair is "solvent-separated"[10] by the simple technique of using a gas phase system, thus eliminating the solvent. Naturally, a solvent-free ion pair in the gas phase can be expected to differ markedly from even an "intimate"[10] ion pair in solution. Nevertheless, the non-chain gas phase pyrolyses of alkyl bromides show reactivities quite parallel to those in solvolytic reactions[11] and Ingold has gone to the extent of proposing ion pair intermediates for these reactions.[12]

The kinetics of the chloroformate reactions in the gas phase have been studied and a unimolecular reaction has been proposed. The rates and products reported in the literature are quite variable. The most thorough studies on ethyl chloroformate led to rate constants at 195°[13] larger than that reported at 267° for the isobutyl ester,[14] but comparable in rate to the isopropyl ester.[15] At far more elevated temperatures ethylene has been identified as a reaction product as well as ethyl chloride from ethyl chloroformate[16]; the suggestion that rates were measurable is difficult

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[1] From the Ph.D. Thesis of W. C. H., 1958, who thanks the National Science Foundation for a fellowship in 1954.

[2] W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1252 (1937); E. D. Hughes, C. K. Ingold and I. C. Whitfield, *Nature*, **147**, 206 (1941).

[3] A. H. J. Houssa and H. Phillips, *J. Chem. Soc.*, 108 (1932); 1232 (1932).

[4] K. B. Wiberg and T. M. Shryne, *J. Am. Chem. Soc.*, **77**, 2774 (1955).

[5] C. E. Boozer and E. S. Lewis, *ibid.*, **75**, 3182 (1953).

[6] D. J. Cram, *ibid.*, **75**, 332 (1953).

[7] H. J. Lucas and C. W. Gould, *ibid.*, **63**, 2541 (1941).

[8] C. E. Boozer and E. S. Lewis, *ibid.*, **76**, 794 (1954).

[9] E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959.

[10] S. Winstein and G. C. Robinson, *J. Am. Chem. Soc.*, **80**, 1690 (1958).

[11] A. Macoll and P. J. Thomas, *Nature*, **176**, 392 (1955).

[12] C. K. Ingold, *Proc. Chem. Soc.*, 279 (1957).

[13] A. R. Choppin, H. A. Frediani and G. F. Kirby, Jr., *J. Am. Chem. Soc.*, **61**, 3176 (1939).

[14] E. T. Lessig, *J. Phys. Chem.*, **36**, 2325 (1932).

[15] A. R. Choppin and E. L. Compere, *J. Am. Chem. Soc.*, **70**, 3797 (1948).

[16] L. E. Roberts, R. Lashbrook, M. J. Treat and W. Yates, *ibid.*, **74**, 5787 (1952).