# *Intramolecular Hydrogen Bonding in α-Keto- and α-Alkoxy-carboxylic Acids. VI. Substituent Effects on the Energy of the Hydrogen Bonding in α-Alkoxy- and α-Aryloxyacetic Acids*[1]

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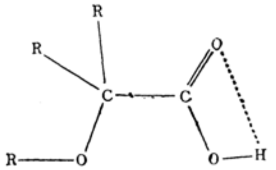
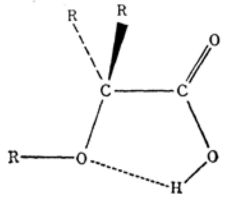
Infrared spectra of various carboxylic acids which are supposed to be capable of hydrogen bonding between the carboxyl group and a substituent at α-position have led to the conclusion that an intramolecular interaction exists between the O-H group and the C=O in a carboxyl group[1-3]. The conclusion is based on the following phenomena. (i) The cis structure I, otherwise less advantageous from the stand point of steric effect than the trans structure II, is exclusively realized when the carboxylic acid has no hydrogen accepting group at the α-position. (ii) The C=O stretching absorption attributed to the cis structure appears at 1760 $cm^{-1}$ region, which is ca. 30 $cm^{-1}$ lower than the C=O stretching frequency of the trans structure (1790 $cm^{-1}$) in carbon tetrachloride, the fact being reasonably explained from the effect of the increasing polarity of the C=O bond, and more contribution of the polar structure $C^+-O^-$ of less force constant value of the C=O bond. (iii) The intramolecular interaction IIIa of the O-H group with an aromatic nucleus or with a halogen atom at α-position was not observed in phenylacetic acid and chloroacetic acid.



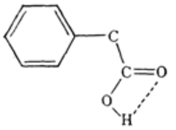
cis

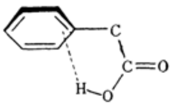
I



trans

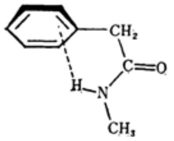
II





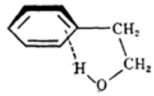
Phenylacetic acid

III IIIa



*N*-Methyl-phenylacetamide

IV



β-Phenylethanol

V

The absence of the interaction in phenylacetic acid would be contradictory with the results obtained with phenylacetamide IV[4] and β-phenylethyl alcohol V[5] which is in the similar steric condition with phenylacetic acid[6].

The temperature dependence of the intensity ratio of the two $\nu_{O-H}$ bands was measured in order to determine the energy difference of the cis and trans forms of these acids. This energy difference ($\Delta H$) may give the measure of the relative strength of the hydrogen bond between the carboxylic O-H group and the α-proton acceptor, because the energy of the cis form is thought to be almost unchanged throughout these series. Although the measurement, giving only the energy difference between the cis and the trans forms, cannot be related directly to the stability of the cis form, it may provide an important clue to the energy estimation when compared with the ordinary hydrogen bonding of O-H···O type. Thus the measurements were carried out with the carboxylic acids, ROCR'R''COOH, and the electronic and the steric effects of the substituents will be discussed in this paper in connection with the $\Delta H$ values.

## Experimental

**Preparation of Materials.**—Methoxyacetic, ethoxyacetic, isopropoxyacetic and *t*-butoxyacetic acids were prepared from the corresponding alkoxides (2 mol.) and chloroacetic acid (1 mol.) in the corresponding alcohols. This method has been described for ethoxyacetic acid in "Organic Syntheses"[7] and the authors followed this method.

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[1] Part V of this series: M. Ōki and M. Hirota, *Spectrochim. Acta*, **17**, 583 (1961); Presented at the 14th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1961.

[2] M. Ōki and M. Hirota, This Bulletin, **33**, 119 (1960).

[3] M. Ōki and M. Hirota, ibid., **34**, 374, 378 (1961).

[4] I. Suzuki, M. Tsuboi and T. Shimanouchi, *Spectrochim. Acta*, **16**, 469 (1960).

[5] M. Ōki and H. Iwamura, This Bulletin, **33**, 1135 (1959).

[6] M. Ōki and H. Iwamura, ibid., **35**, 283 (1962).

[7] R. C. Fuson and B. H. Wojcik, "Organic Syntheses", Col. Vol. II, 260 (1943).

Similarly, α-methoxypropionic and α-methoxyisobutyric acids were prepared from sodium methoxide and the corresponding α-bromo-acids. The analyses and physical constants are reported below with ether new or doubtful compounds.

Isopropoxyacetic acids, b. p. 108°C/25 mmHg. Found: C, 50.73; H, 8.50, Calcd.: C, 50.83; H, 8.53%.

α-Methoxypropionic acid, b. p. 98°C/18 mmHg. Found: C, 45.98; H, 7.91. Calcd.: C, 46.15; H, 7.75%.

α-Methoxyisobutyric acid, b. p. 99.5°C/18 mmHg. Found: C, 51.08; H, 8.78. Calcd.: C, 50.83; H, 8.53%.

Preparation of aryloxyacetic acids and their homologs was already reported[1] in the preceding paper.

**Measurement of the Infrared Spectra and Calculation of the Energy Difference ($\Delta H$).**—Infrared spectra are determined with a Perkin-Elmer 112 G spectrophotometer as reported previously. The absorption intensities of the two O-H stretching bands attributed to the cis and the trans isomers ($\varepsilon_c$ and $\varepsilon_t$, respectively) are measured at various temperatures between 5°C and a temperature near the boiling point of carbon tetrachloride. The temperature of the solution was kept within the range of 1.5° during the measurement and the $T$ (°K) value was obtained as the mean of the temperatures of the solution at the beginning and at the end of the absorption measurement. From these infrared measurements, the intensity ratios ($\varepsilon_t/\varepsilon_c$) were calculated at various temperatures. Assuming that $\varepsilon$-values are proportional to the populations of the cis and the trans isomeric melecules and the linear relation (Eq. 5) is present between the log ($\varepsilon_t/\varepsilon_c$) and $1/T$ values, the energy difference ($\Delta H$) between the cis and the trans isomers are obtained from the gradient of log ($\varepsilon_t/\varepsilon_c$) versus $1/T$ line.

The gradient and the intercept of the line are calculated, by the least square method by the following formulae, where $n$ is the number of the measurement:

$$\sum[\log(\varepsilon_t/\varepsilon_c)]-n\cdot[\Delta S-\boldsymbol{R}\ln a]-[\sum(1/T)]\cdot[\Delta H]=0 \qquad (1)$$

$$\sum\{[\log(\varepsilon_t/\varepsilon_c)]\times[1/T]\}-[\sum(1/T)]\times[\Delta S-\boldsymbol{R}\ln a]-[\sum(1/T^2)]\cdot[\Delta H]=0 \qquad (2)$$

In these formulae, the values $\sum[\log(\varepsilon_t/\varepsilon_c)]$, $n$, $\sum(1/T)$, $\sum[\log(\varepsilon_t/\varepsilon_c)\cdot 1/T$ and $\sum(1/T^2)$ are known, and $\Delta H$ and ($\Delta S-\boldsymbol{R}.\ln a$) are obtained.

## Results and Discussion

Results of the measurement of the O-H stretching absorption intensity of the cis (I) and the trans (II) isomers at various temperatures are shown in Tables I—IX.

Assuming that the absorption intensity of the isomers are proportional to their concentration ($x_c$ and $x_t$, respectively), the energy difference ($\Delta H$) and the ($\Delta S/\boldsymbol{R}-\ln a$) term are calculated by applying the van't Hoff's equation (Eq.3).

TABLE I. METHOXYACETIC ACID

| $T$, °K | 1000/$T$ | Extinction coefficient $\varepsilon_c$ | Extinction coefficient $\varepsilon_t$ | Intensity ratio $\varepsilon_t/\varepsilon_c$ |
|---|---|---|---|---|
| 278.5 | 3.60 | 26.0 | 27.4 | 1.054 |
| 293.3 | 3.41 | 39.6 | 35.6 | 0.900 |
| 293.8 | 3.40 | 38.8 | 36.4 | 0.938 |
| 298.7 | 3.35 | 46.3 | 40.7 | 0.880 |
| 302.7 | 3.31 | 46.1 | 42.8 | 0.930 |
| 310.2 | 3.23 | 52.5 | 44.6 | 0.850 |
| 319.2 | 3.14 | 57.5 | 48.6 | 0.847 |
| 323.7 | 3.09 | 58.8 | 48.8 | 0.831 |
| 329.2 | 3.04 | 60.8 | 48.6 | 0.800 |
| 332.0 | 3.02 | 66.3 | 54.6 | 0.824 |
| 344.5 | 2.91 | 67.3 | 50.8 | 0.785 |

TABLE II. ETHOXYACETIC ACID

| $T$, °K | 1000/$T$ | Extinction coefficient $\varepsilon_c$ | Extinction coefficient $\varepsilon_t$ | Intensity ratio $\varepsilon_t/\varepsilon_c$ |
|---|---|---|---|---|
| 282.2 | 3.55 | 26.7 | 33.4 | 1.25 |
| 294.4 | 3.40 | 34.5 | 38.3 | 1.11 |
| 307.3 | 3.26 | 42.5 | 45.8 | 1.08 |
| 316.8 | 3.16 | 46.2 | 45.5 | 0.985 |
| 331.6 | 3.02 | 54.4 | 49.3 | 0.907 |
| 342.4 | 2.92 | 60.0 | 52.8 | 0.880 |
| 345.7 | 2.90 | 64.2 | 55.3 | 0.862 |

TABLE III. ISOPROPOXYACETIC ACID

| $T$, °K | 1000/$T$ | Extinction coefficient $\varepsilon_c$ | Extinction coefficient $\varepsilon_t$ | Intensity ratio $\varepsilon_t/\varepsilon_c$ |
|---|---|---|---|---|
| 279.9 | 3.58 | 22.0 | 47.7 | 2.17 |
| 298.2 | 3.36 | 28.7 | 53.0 | 1.85 |
| 315.9 | 3.17 | 40.2 | 66.0 | 1.64 |
| 324.4 | 3.08 | 43.1 | 67.4 | 1.57 |
| 337.5 | 2.96 | 47.4 | 68.8 | 1.45 |
| 349.8 | 2.86 | 45.8 | 60.2 | 1.31 |

TABLE IV. α-METHOXYPROPIONIC ACID

| $T$, °K | 1000/$T$ | Extinction coefficient $\varepsilon_c$ | Extinction coefficient $\varepsilon_t$ | Intensity ratio $\varepsilon_t/\varepsilon_c$ |
|---|---|---|---|---|
| 280.5 | 3.57 | 21.9 | 22.4 | 1.02 |
| 293.1 | 3.42 | 34.9 | 32.1 | 0.920 |
| 302.5 | 3.31 | 39.2 | 33.0 | 0.843 |
| 315.9 | 3.17 | 46.3 | 38.7 | 0.804 |
| 329.5 | 3.04 | 54.8 | 40.8 | 0.744 |
| 339.7 | 2.95 | 59.7 | 42.0 | 0.704 |

TABLE V. α-METHOXYISOBUTYRIC ACID

| $T$, °K | 1000/$T$ | Extinction coefficient $\varepsilon_c$ | Extinction coefficient $\varepsilon_t$ | Intensity ratio $\varepsilon_t/\varepsilon_c$ |
|---|---|---|---|---|
| 280.3 | 3.57 | 24.1 | 35.3 | 1.46 |
| 292.5 | 3.42 | 32.2 | 42.4 | 1.32 |
| 306.4 | 3.27 | 34.8 | 42.7 | 1.23 |
| 314.0 | 3.19 | 44.6 | 50.5 | 1.13 |
| 332.2 | 3.01 | 47.8 | 48.4 | 1.03 |
| 341.3 | 2.93 | 51.1 | 59.1 | 0.961 |

TABLE VI. PHENOXYACETIC ACID

| $T$, °K | $1000/T$ | Extinction coefficient* |  | Intensity ratio |
|---|---|---|---|---|
|  |  | $\varepsilon_c$ | $\varepsilon_t$ | $\varepsilon_t/\varepsilon_c$ |
| 281.6 | 3.55 | 26.1 | 16.7 | 0.640 |
| 296.4 | 3.38 | 36.4 | 21.8 | 0.599 |
| 306.3 | 3.27 | 48.7 | 26.5 | 0.545 |
| 316.7 | 3.16 | 57.4 | 29.0 | 0.505 |
| 330.9 | 3.02 | 65.5 | 31.6 | 0.483 |
| 332.7 | 3.00 | 74.5 | 35.3 | 0.474 |
| 347.5 | 2.88 | 76.9 | 36.5 | 0.474 |

* Corrected by Eq. 7.

TAELE VII. $\alpha$-PHENOXYPROPIONIC ACID

| $T$, °K | $1000/T$ | Extinction coefficient* |  | Intensity ratio |
|---|---|---|---|---|
|  |  | $\varepsilon_c$ | $\varepsilon_t$ | $\varepsilon_t/\varepsilon_c$ |
| 281.6 | 3.56 | 25.7 | 10.8 | 0.421 |
| 297.3 | 3.37 | 38.7 | 14.8 | 0.383 |
| 305.2 | 3.28 | 63.4 | 22.9 | 0.361 |
| 310.0 | 3.23 | 48.9 | 17.1 | 0.350 |
| 320.6 | 3.12 | 57.3 | 19.3 | 0.337 |
| 341.9 | 2.93 | 98.8 | 31.0 | 0.314 |

* Corrected by Eq. 8.

TABLE VIII. $\alpha$-PHENOXYISOBUTYRIC ACID

| $T$, °K | $1000/T$ | Extinction coefficient |  | Intensity ratio |
|---|---|---|---|---|
|  |  | $\varepsilon_c$ | $\varepsilon_t$ | $\varepsilon_t/\varepsilon_c$ |
| 282.1 | 3.55 | 41.5 | 35.9 | 0.865 |
| 293.3 | 3.41 | 50.9 | 43.3 | 0.851 |
| 306.1 | 3.27 | 58.5 | 45.9 | 0.785 |
| 314.8 | 3.18 | 68.6 | 50.0 | 0.729 |
| 331.4 | 3.02 | 77.0 | 52.8 | 0.686 |
| 340.4 | 2.94 | 82.2 | 51.6 | 0.628 |

TABLE IX. $\alpha$-ARYLOXYISOBUTYRIC ACIDS

A) $\alpha$-($p$-Methylphenoxy)isobutyric acid

| $T$, °K | $1000/T$ | Extinction coefficient |  | Intensity ratio |
|---|---|---|---|---|
|  |  | $\varepsilon_c$ | $\varepsilon_t$ | $\varepsilon_t/\varepsilon_c$ |
| 296.3 | 3.38 | 48.7 | 62.1 | 1.275 |
| 307.7 | 3.25 | 57.0 | 66.1 | 1.160 |
| 324.2 | 3.09 | 69.3 | 69.0 | 0.995 |
| 342.5 | 2.92 | 71.3 | 67.4 | 0.945 |

B) $\alpha$-($p$-Bromophenoxy)isobutyric acid

| $T$, °K | $1000/T$ | Extinction coefficient |  | Intensity ratio |
|---|---|---|---|---|
|  |  | $\varepsilon_c$ | $\varepsilon_t$ | $\varepsilon_t/\varepsilon_c$ |
| 297.1 | 3.37 | 64.0 | 30.2 | 0.472 |
| 313.7 | 3.19 | 81.7 | 35.6 | 0.436 |
| 329.3 | 3.04 | 95.2 | 39.4 | 0.414 |
| 345.4 | 2.90 | 107.2 | 40.9 | 0.381 |

$$-\boldsymbol{R}T\cdot\ln K=\varDelta F=\varDelta H-T\varDelta S \tag{3}$$

The equilibrium constant $K$ can be represented by multiplying the integrated intensity ratio by a constant which is a factor showing the ratio of intensity per molecule due to trans and cis forms and is assumed to be invariable throughout the temperature range in this investigation. Then, Eq. 4 is obtained.

$$K=x_t/x_c=a\,A_t/A_c=a\frac{\varepsilon_t\times(\varDelta\nu_{1/2})_t}{\varepsilon_c\times(\varDelta\nu_{1/2})_c} \tag{4}$$

Combining Eq. 3 and Eq. 4 gives

$$\log(\varepsilon_t/\varepsilon_c)=-\frac{\varDelta H}{2.30\,\boldsymbol{R}}\times\frac{1}{T}+\frac{1}{2.30}\left(\frac{\varDelta S}{\boldsymbol{R}}-\ln a\right)-\log\frac{(\varDelta\nu_{1/2})_t}{(\varDelta\nu_{1/2})_c} \tag{5}$$

The authors have found that the separation of two bands due to cis and trans forms are generally good and the half band widths are invariable in the spectra at various temperatures. It is then allowed to use the ratio of apparent molecular extinction coefficients instead of intensities to estimate the enthalpies. An example of these cases is shown with $\alpha$-methoxyacetic acid in Fig. 1. The absorption spectra of this compound shows two separate O–H stretching bands and the approximation of Eq. 6 holds good, the correction of $\log[(\varDelta\nu_{1/2})_t/(\varDelta\nu_{1/2})_c]$ being accounted to calculate the entropy term $(\varDelta S/\boldsymbol{R}-\ln a)$.

$$\varepsilon^a_{t_{max}}\doteqdot\varepsilon_{t_{max}},\quad \varepsilon^a_{c_{max}}\doteqdot\varepsilon_{c_{max}} \tag{6}$$

In Eq. 6, $\varepsilon^a_{c_{max}}$ and $\varepsilon^a_{t_{max}}$ are the apparent maximal extinction coefficients of the cis and the trans $\nu_{O-H}$ bands.

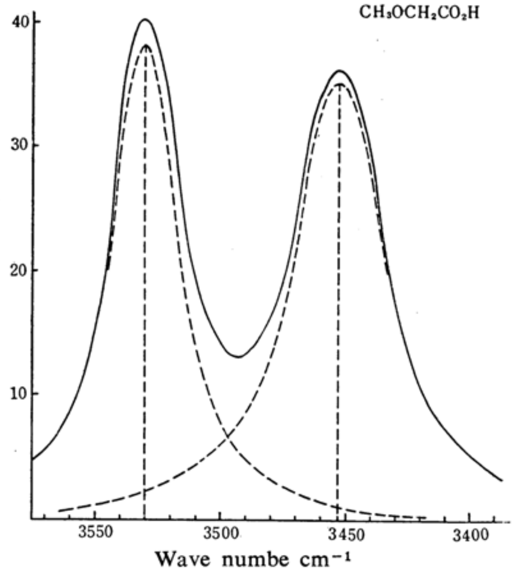

Fig. 1.

A considerable overlap of the two O–H stretching bands was observed in the spectra of phenoxyacetic and $\alpha$-phenoxypropionic acids and the following corrections (Eq. 7 for phenoxyacetic and Eq. 8 for $\alpha$-phenoxypropionic acids) were necessary. An example of this correction is shown in Fig. 2. Coefficients of the correcting terms were calculated from Eq. 9 by assuming the Lorentz envelopes for the two O–H stretching bands.

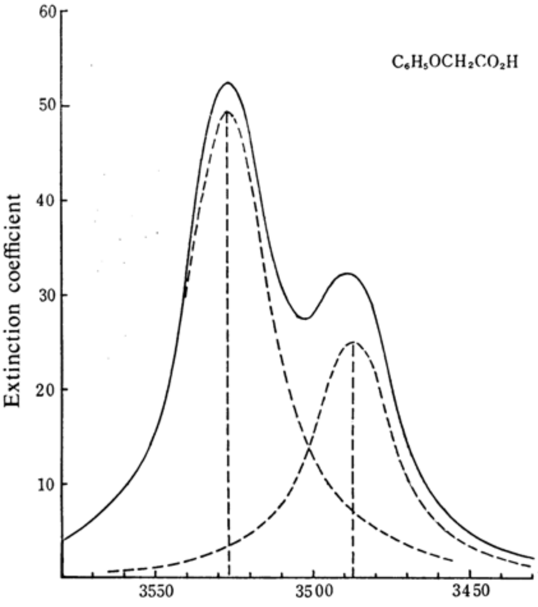

Fig. 2.

$$\left.\begin{aligned}\varepsilon_{c_{max}} &\doteqdot \varepsilon^{a}_{c_{max}} - (1/7.9)\,\varepsilon^{a}_{t_{max}}\\ \varepsilon_{t_{max}} &\doteqdot \varepsilon^{a}_{t_{max}} - (1/7.2)\,\varepsilon^{a}_{c_{max}}\end{aligned}\right\} \tag{7}$$

$$\left.\begin{aligned}\varepsilon_{c_{max}} &\doteqdot \varepsilon^{a}_{c_{max}} - (1/7.3)\,\varepsilon^{a}_{t_{max}}\\ \varepsilon_{t_{max}} &\doteqdot \varepsilon^{a}_{t_{max}} - (1/10.7)\,\varepsilon^{a}_{c_{max}}\end{aligned}\right\} \tag{8}$$

$$f(\nu) = a/[(\nu-\nu_{max})^2+b^2]^{8)} \tag{9}$$

where $\varepsilon_{max}=a/b^2$ and $\Delta\nu_{1/2}=b$.

The $(\varepsilon_t/\varepsilon_c)$ versus $1/T$ relationship is illustrated in Figs. 3, 4, 5 and 6.

In Table X are listed the calculated $\Delta H$ and $(\Delta S/\boldsymbol{R}-\ln a)$ values together with the exact band properties of the $\nu_{O-H}$ due to the cis and the trans isomers at the ordinary temperature (20~25°C). In Table XI are also summarized the relation between $\Delta H$ values and the frequency difference of the two absorption maxima $(\Delta\nu_{max})$. Though the general relationship could not be establishd, monotonous relation is found between the $\Delta H$ and $\Delta\nu_{max}$ values within each series of these acids and larger $\Delta\nu_{max}$ generally corresponds to larger $\Delta H$.

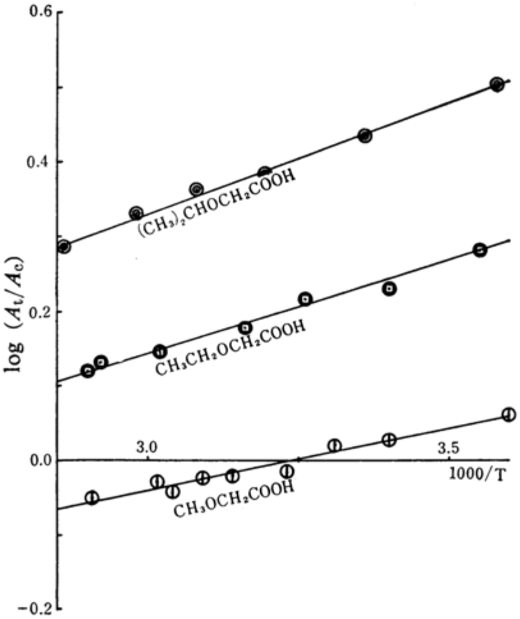

Fig. 3.

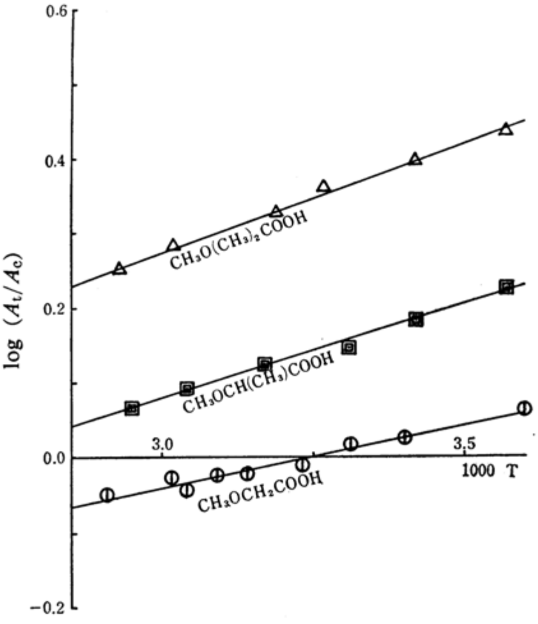

Fig. 4.

From the constancy of the $\nu_{O-H}$ frequency of the cis isomer, the energy of the cis-isomer can be considered to be nearly constant in these substituted acetic acids. The $\Delta H$ value will, therefore, be a relative value of the energy of the intramolecular hydrogen bonding. The factors which affect the facility of the hydrogen bond formation are i) acidity (hydrogen donating power) of the carboxyl group, ii) basicity (hydrogen accepting power) of the ether oxygen of the alkoxyl or aryloxy group, and iii) steric effects of the alpha and other substituents. The factor i) may be neglected, because the inductive effect of the $\alpha$-methyl

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8) D. A. Ramsay, *J. Am. Chem. Soc.*, **74**, 72 (1952).

Table X. The O-H stretching absorptions and the energy difference values of the "cis" and "trans" forms of various carboxylic acids investigated

| Acid | $\nu_c$ cm$^{-1}$ | $\varepsilon_c$ | $(\Delta\nu_{1/2})_c$ | $A_b$ | $\nu_t$ cm$^{-1}$ | $\varepsilon_c$ | $(\Delta\nu_{1/2})_t$ | $A_t$ | $A_t/A_c$ | $\Delta\nu_{max}$ cm$^{-1}$ | $\Delta H$ kcal/mol. | $\Delta S/\boldsymbol{R}$ $-\ln a$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CH_3OCH_2COOH$ | 3534.0 | 38.2 | 31.2 | 4.30 | 3453.4 | 43.5 | 35.2 | 5.52 | 1.28 | 77.0 | 0.76 | −1.25 |
| $CH_3CH_2OCH_2COOH$ | 3531.0 | 46.7 | 32.0 | 5.37 | 3446.2 | 47.3 | 48.5 | 8.28 | 1.54 | 84.8 | 1.11 | −1.34 |
| $(CH_3)_2CHOCH_2COOH$ | 3531.9 | 29.9 | 33.9 | 3.66 | 3434.1 | 54.3 | 49.9 | 9.79 | 2.68 | 97.8 | 1.53 | −1.56 |
| $(CH_3)_3COCH_2COOH$ | 3528.0 | 39.1 | 28.2 | 3.98 | 3424.2 | 32.8 | 65.0 | 7.67 | 1.93 | 103.8 | — | — |
| $CH_3OCH_2COOH$ | 3534.0 | 38.2 | 31.2 | 4.30 | 3453.4 | 43.5 | 35.2 | 5.52 | 1.28 | 77.0 | 0.76 | −1.25 |
| $CH_3OCH(CH_3)COOH$ | 3528.5 | 41.9 | 32.3 | 4.87 | 3431.3 | 38.6 | 53.0 | 7.38 | 1.51 | 97.2 | 1.15 | −1.55 |
| $CH_3OC(CH_3)_2COOH$ | 3528.1 | 34.4 | 29.4 | 3.70 | 3408.8 | 45.2 | 54.7 | 8.91 | 2.40 | 119.3 | 1.28 | −1.30 |
| $C_6H_5OCH_2COOH$ | 3526.9 | 49.5 | 31.7 | 5.57 | 3487.5 | 25.1 | 29.7 | 2.69 | 0.484 | 39.4 | 0.98 | −2.27 |
| $C_6H_5OCH(CH_3)COOH$ | 3526.3 | 37.5 | 31.6 | 4.28 | 3475.1 | 14.9 | 41.0 | 2.20 | 0.516 | 51.2 | 0.94 | −2.29 |
| $C_6H_5OC(CH_3)_2COOH$ | 3526.2 | 50.3 | 32.0 | 6.80 | 3432.6 | 41.2 | 57.6 | 8.56 | 1.48 | 93.9 | 1.05 | −1.47 |
| $p$-$XC_6H_4OC(CH_3)_2COOH$ | | | | | | | | | | | | |
| X=$CH_3$ | 3526.2 | 49.4 | 32.0 | 5.70 | 3427.0 | 63.8 | 54.1 | 12.44 | 2.18 | 99.2 | 1.35 | — |
| H | 3526.5 | 50.3 | 32.0 | 6.80 | 3432.6 | 41.2 | 57.6 | 8.56 | 1.48 | 93.9 | 1.05 | −1.47 |
| Br | 3523.0 | 55.7 | 33.9 | 6.83 | 3443.5 | 25.8 | 52.4 | 4.88 | 0.715 | 79.5 | 0.88 | — |

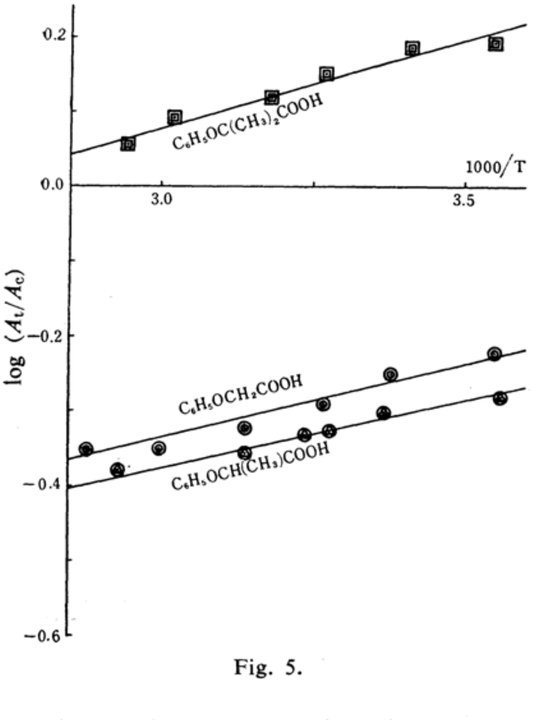

Fig. 5.

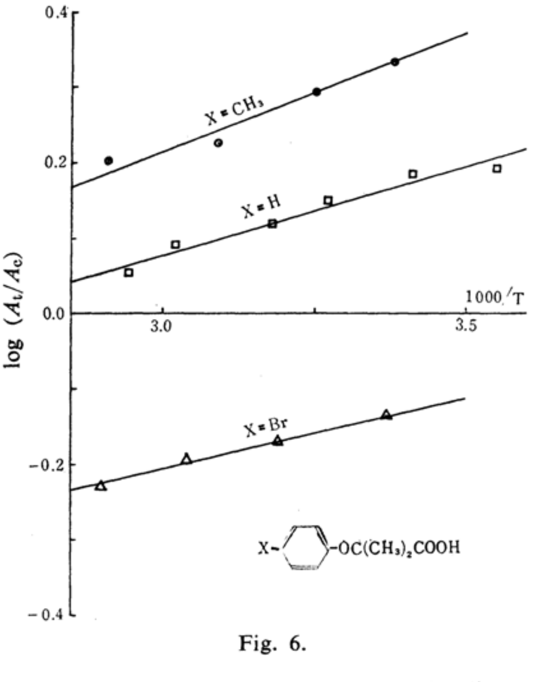

Fig. 6.

substituent does not greatly affect the p$K_a$ values of acetic acids (p$K_a$ values of acetic, propionic and isobutyric acids are known to be 4.76, 4.88 and 4.86[9], respectively), nor the O-H stretching absorption frequencies[10], and the hydrogen donating powers of the acids in the present discussion seem to be nearly the same.

The $\Delta H$ value is largely affected by the $O$-substituent and to the lesser extent by the $\alpha$-substituent, though the $\Delta\nu_{max}$ value is affected by both factors in almost the same way. Extreme is the case of phenoxy-acids, in which the $\Delta H$ value is nearly equal while the acid changes from phenoxyacetic to phenoxyisobutyric acid. The results may be attributed to the fact that the O-H···O hydrogen bond formation occurs between the carboxylic O-H group and the lone pair electrons of the ether oxygen which conjugates with the aromatic $\pi$-electrons. The effects of nuclear substitution on the $\Delta H$ value also support this hypothesis and the electron-repelling substituent gives higher $\Delta H$ value than the electron-attracting substituent.

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[9] J. F. J. Dippy, *Chem. Revs.*, 25, 151 (1939).

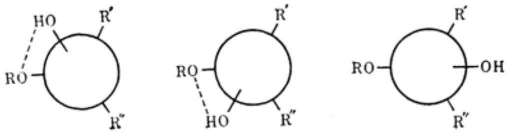
[10] Effects of the acidity on the O-H stretching frequency has been investigated widely by Goulden (J. D. S. Goulden, *Spectrochim. Acta*, 6, 129 (1954)).

The substituents on oxygen gives the stronger effect than the methyl groups at α-position as shown in Table XI. It is clear that both the steric and the electronic (inductive) effects should be considered to discuss the effect of the α-substituent on the hydrogen bonding.

TABLE XI. THE $\Delta H$ AND $\Delta\nu_{\max}$ INCREASE BY THE SUBSTITUTION OF ONE ADDITIONAL METHYL GROUP

| Acid | $\Delta H$ Increase | $\Delta\nu_{\max}$ Increase |
|---|---|---|
| Methoxyacetic | 0.35 | 7.8 |
| Ethoxyacetic | 0.42 | 13.0 |
| Isopropoxyacetic | | |
| Methoxyacetic | 0.39 | 20.2 |
| α-Methoxypropionic | 0.13 | 22.1 |
| α-Methoxyisobutyric | | |
| Phenoxyacetic | −0.04 | 11.8 |
| α-Phenoxypropionic | 0.11 | 42.7 |
| α-Phenoxyisobutyric | | |

The carboxylic acid may include three rotational isomers with respect to the axis between the carboxylic carbon and the alpha carbon ($C_{C=O}-C_{\alpha}$), being represented by VII, VIII and IX. The oxo-groups are omitted in the formulae VII—IX for the sake of simplicity. As is clear from the Newman projections, the methyl group at the α-position increases the steric interaction with the hydroxyl group in the isomer IX in which the hydrogen-bonded structure is impossible, and consequently, the relative stability of the rotational isomers VII and VIII, which have the possibility of existing as hydrogen-bonded structure II, may rise.



Rotamers of alkoxyacetic acid

VII VIII IX

Therefore, formation of hydrogen-bonding in α-alkoxyisobutyric acid is favored over that in α-alkoxyacetic acid, as far as the steric influence is concerned.

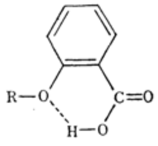
As to the electronic effect of the methyl groups at α-position of the carboxyl group, they will strengthen the basicity of the ether oxygen through the inductive effect, leaving the acidity of the carboxyl group intact as mentioned above. However, the extent of the effects cannot be estimated separately at the present stage. Thus both steric and electronic effects of the methyl groups favor the formation of hydrogen-bonding.

The effect of methyl group substituting methoxyl moiety of methoxyacetic acid seems to be of inductive nature, since the basicity of the corresponding alcohols are in the order; methanol < ethanol < isopropyl alcohol (< t-butyl alcohol), and this is the same order as the $\Delta H$ and $\Delta\nu_{\max}$ values increase, although the $\Delta H$ measurement has not been complete with *t*-butoxyacetic acid. The result is in accordance with the fact that no serious steric hindrance is expected from the Fischer's molecular scale models between the alkyl group and *trans*-O–H group.

The order of $A_t/A_c$ ratio (Table X) is not the same as the order of the basicity of oxygen atom. Namely abrupt decrease of $A_t/A_c$ ratio is observed with *t*-butoxyacetic acid in spite of increasing $\Delta\nu_{\max}$. The fact may be attributed to the steric effect of bulky *t*-butyl group hindering appoach of the hydroxyl group to ether oxygen, but, even in this compound no serious steric effect was foreseen from the model. Therefore, this phenomenon remains unexplained.

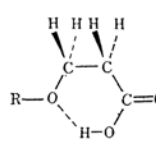
This intramolecular hydrogen bonding forms a five-membered ring and the maximal energy difference ($\Delta H$) is 1.53 kcal./mol. This $\Delta H$ value is much smaller than the case of a six-membered intramolecularly hydrogen-bonded system of the same type. The $\Delta H$ values for *o*-methoxybenzoic and *o*-phenoxybenzoic acids are 3.3 kcal./mol.[11] and 1.89 kcal./mol.[12], respectively.

In spite of the greater energy, the hydrogen bonding of six-membered ring X has been found only in benzoic acid derivatives which carries an oxygen atom at ortho-position to the carboxyl group and neither β-alkoxy- nor β-aryloxy-propionic acid shows[13] the hydrogen bonding of this type XI.



*o*-Alkoxybenzoic acid

X



β-Alkoxypropionic acid

XI

These facts may be attributed to the following reasons: i) the six-membered hydrogen-bond system of *o*-alkoxybenzoic acids is a conjugate system, and ii) β-alkoxypropionic acids are enforced to assume the sterically unfavorable

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[11] M. Davies, "Hydrogen Bonding"—Papers presented at the Symposium on Hydrogen Bonding held at Ljubljana, 29, July 3, August, 1957. (Pergamon Press)

[12] M. Ōki and M. Hirota, This Bulletin, 35, 1948 (1962).

[13] M. Ōki and M. Hirota, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **81**, 855 (1960).

cis-rotational form (as illustrated by XI) to make a planar six-membered hydrogen-bond system.

Temperature dependence study of the intensities of two $\nu_{O-H}$ bands at 3630 cm$^{-1}$ and 3280 cm$^{-1}$ in a ternary system of acetic acid, dibutyl ether and carbon tetrachloride indicates the enthalpy of hydrogen bond be 4.56±0.3 kcal./mol. Provided that this value is applicable for the internal hydrogen bond as in methoxyacetic acid, then it is concluded that the cis form of the carboxyl group is stabilized by 3∼4 kcal./mol. over the trans form.

The entropy term has an ambiguity of $(-\ln a)$ and no quantitative relation with other physical properties can be fonud, although it increases with the increase of $\Delta H$ value.

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