Double Bond Stabilizing Abilities of Formyl, Carbo-*tert*-butoxy, and Carbomethoxy Substituents[1]

Jack Hine,* V. M. Kanagasabapathy, and Peter Ng

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received December 29, 1981

Equilibrium constants for reactions of the type *trans*-MeCH=CHCH$_2$COX ⇌ *trans*-EtCH=CHCOX, where X is H, OMe, and O-*t*-Bu, have been determined in *tert*-butyl alcohol solution at various temperatures by using basic catalysts. These equilibrium constants for formation of the conjugated isomer, extrapolated to 25 °C, are 24, 4.9, and 5.1 for the aldehyde, methyl ester, and *tert*-butyl ester, respectively. Possible explanations for the relative magnitudes of these equilibrium constants are discussed.

Equilibrium constants for isomerization of the type shown in eq 1 can be correlated by eq 2, in which D_X and

trans-XCH$_2$CH=CHY ⇌ *trans*-XCH=CHCH$_2$Y (1)

$$\Delta G_{XY}^{chem} = D_Y - D_X + \tau_v(\sigma_X\sigma_{CH_2Y} - \sigma_Y\sigma_{CH_2X}) \quad (2)$$

D_Y are the *double bond stabilizing parameters*, and the rest of the equation is a relatively small correction for polar interactions across the double bond.[2,3a] The σ constants used are Hammett para substituent constants; τ_v is a proportionality constant. In earlier work, D values were reported for acetyl[4] and carbomethoxy[2] groups. In order to understand the magnitude of these values better and to extend the scope of the correlation, we wished to study other groups of the type COX. The previously used study of the equilibration of the methyl esters of 2- and 3-pentenoic acid had been carried out at 117 °C.[5] We wished to obtain this equilibrium constant at a temperature nearer 25 °C, where most of the other data had been obtained. One new carbonyl substituent we studied was the formyl group, where the carbonyl group has an atom attached (hydrogen) that gives the minimum size and the minimum resonance interaction. The other was the carbo-*tert*-butoxy substituent, where resonance interactions between the carbonyl group and the alkoxy group may differ substantially from those found in esters of nontertiary alcohols. In order to have equilibria that are not too one-sided and correction terms in eq 2 that are not too large, we have evaluated these carbonyl substituents in comparison with the methyl group, whose D value is near those for the two carbonyl groups that have already been studied and whose σ value is not very large. Thus we determined equilibrium constants for reactions 3–5. In so doing we also learned something about the stabilities of the cis isomers, which will be designated as **1c–6c**.

trans-MeCH=CHCH$_2$CHO ⇌
1t

trans-MeCH$_2$CH=CHCHO (3)
2t

trans-MeCH=CHCH$_2$CO$_2$Bu-*t* ⇌
3t

trans-MeCH$_2$CH=CHCO$_2$Bu-*t* (4)
4t

trans-MeCH=CHCH$_2$CO$_2$Me ⇌
5t

trans-MeCH$_2$CH=CHCO$_2$Me (5)
6t

Experimental Section

***tert*-Butyl *trans*-2-Pentenoate (4t).** After 26.1 g of PCl_5 was added to 25.4 g of *trans*-2-pentenoic acid in 175 mL of dry ether, stirring was continued for 1 h, and the solvent was removed. The $POCl_3$ was removed by distillation at 55–65 °C (20–25 mm) and then by adding benzene and removing it in vacuo several times. The resulting acid chloride was added to 37 g of *t*-BuOH and 61 g of $PhNMe_2$ in 150 mL of dry ether with cooling. After 2.5 h of refluxing and 2 days of stirring, the mixture was poured into 250 mL of water and filtered through Celite. The ether layer combined with ether extracts of the water layer was washed several times with 2 N H_2SO_4 and then with ice-cold 10% Na_2CO_3 and dried over Na_2SO_4, and the ether was removed by distillation. Distillation of the residue at 0.6 mm gave, as the purest fraction, material boiling at 49–51 °C, found by VPC analysis[6a] to contain 0.3% **3**, 1.3% **4c**, and 98.4% **4t**: IR (neat) 2978 (s, CH), 2880 (s, CH), 1730 (s, C=O), 1600 cm^{-1} (m, conj C=C); NMR (60 MHz, $CDCl_3$) δ 6.9 (dt, 1, J = 15.5 Hz, J' = 6 Hz, CH_2CH=), 5.66 (dt, 1, J = 15.5 Hz, J' = 2 Hz, $CHCO_2$), 2.2 (m, 2, CH_2), 1.47 (s, 9, *t*-Bu), 1.04 (t, 3, J = 7 Hz, CH_3CH_2). Anal. Calcd for $C_9H_{16}O_2$: C, 69.14; H, 10.32. Found: C, 69.11; H, 10.32.

***tert*-Butyl *cis*-2-Pentenoate (4c).** Preparative VPC[6a] on a earlier fraction from the preceding preparation of the trans isomer gave the more rapidly eluted **4c**: NMR (60 MHz, $CDCl_3$) δ 6.12 (dt, 1, J = 11.5 Hz, J' = 6 Hz, CH_2CH=), 5.61 (dt, 1, J = 11.5 Hz, J' = 2 Hz, =CHCO), 2.60 (m, 2, CH_2), 1.49 (s, 9, *t*-Bu), 1.05 (t, 3, J = 7 Hz, CH_3CH_2), in addition to peaks from significant amounts of **4t**, which was also present.

***tert*-Butyl 3-Pentenoate (3).** The esterification procedure described for **4t** was applied to 3-pentenoic acid obtained by hydrolyzing 3-pentenenitrile.[7] The product [bp 27–28 °C (0.65 mm)] was more than 99.5% pure by VPC on using five different columns. This material showed the 360-MHz spectrum of **3t** ($CDCl_3$): δ 5.51 (dq, 1, J = 16 Hz, J' = 6.4 Hz, CH_3CH=), 5.35 (dt, 1, J = 16 Hz, J' = 7 Hz, CH_2CH=), 2.80 (dd, 2, J = 7 Hz, J' = 1 Hz, CH_2), 1.50 (dd, 3, J = 6.4 Hz, J' = 1.5 Hz, CH_3CH), 1.33 (s, 9, *t*-Bu). A singlet at δ 1.36 and multiplets at δ 2.72 and 1.53 were attributed to the *t*-Bu, CH_2, and CH_3CH= protons, respectively, of **3c**, and from their areas a **3c** content of 4–5% was calculated. The assignments shown were substantiated by decoupling measurements.

In order to obtain a sample containing more **3c**, we equilibrated some of the *t*-Bu ester (as described in a later paragraph). In the equilibrium mixture of **3** and **4**, all the **3c** peaks just described were seen. For the 95% **3t**–5% **3c** mixture: IR (neat) 2980 (s, CH), 1730 (s, C=O), 1155 (s, CO), 970 cm^{-1} (s, *trans*-CH=CH);

(1) (a) This research was supported in part by National Science Foundation Grants CHE 76 23337 and 79 26319. Part 24 in the series "Structural Effects on Rates and Equilibria". (b) For part 23 see: Hine, J.; Hahn, S. *J. Org. Chem.*, **1982**, *47*, 1738–41.

(2) Hine, J.; Flachskam, N. W. *J. Am. Chem. Soc.* **1973**, *95*, 1179–85.

(3) (a) Hine, J. "Structural Effects on Equilibria in Organic Chemistry"; Wiley-Interscience: New York, 1975; Section 8-3. (b) *Ibid.*, Section 1-2d.

(4) Hine, J.; Linden, S.-M., Wang, A.: Thiagarajan, V. *J. Org. Chem.* **1980**, *45*, 2821–5.

(5) Rhoads, S. J.; Chattopadhyay, J. K.; Waali, E. E. *J. Org. Chem.* **1970**, *35*, 3352–8.

(6) (a) 6 ft × 0.25 in. column with 10% Carbowax 20 M. (b) 6 ft × 0.25 in. column with 10% diisodecyl phthalate. (c) 20 ft × 0.38 in. column with 30% Apiezon L.

(7) Lane, J. F.; Fentress, J.; Sherwood, L. T. *J. Am. Chem. Soc.* **1944**, *66*, 545–8.

0022-3263/82/1947-2745$01.25/0

^{13}C NMR (20 MHz, $CDCl_3$) δ 17 (q, CH_3CH), 26.5 (q, $(CH_3)_3C$), 37 (t, CH_2) 75.5 (s, $(CH_3)_3C$), 116 and 121 (m, CH=CH), 162 (s, C=O). Anal. Calcd for $C_9H_{16}O_2$: C, 69.14; H, 10.32. Found: C, 68.64; H, 10.21.

Methyl 3-Pentenoate (5). Preparation by the method of Goering and co-workers[8] gave ester that was 99.1% pure by VPC:[6b] bp 52.0–52.5 °C (34 mm); NMR (300 MHz, $CDCl_3$) δ 5.53–5.63 (m, 2, *cis*- and *trans*-CH=CH), 3.68 (s, 3, *trans*-OCH_3), 3.03 (m, 2, *trans*-CH_2), 1.70 (m, 3, *trans*-CH_3CH), 3.69 (s, *cis*-OCH_3), 3.10 (m, *cis*-CH_2), 1.64 (m, *cis*-CH_3CH=). From the relative areas of the OCH_3 peaks the mixture was found to contain 7% of the cis (**5c**) and 93% of the trans (**5t**) isomer. The assignments shown were substantiated by decoupling experiments, which also showed that for **5t**, $J_{2,3}$ = 5.5 Hz and $J_{4,5}$ = 4.8 Hz. In the equilibrium mixture of **5** and **6**, all the **5c** peaks just referred to were seen: IR (neat) 2950 (s, CH), 1730 (s, C=O), 1155 (s, CO), 965 cm^{-1} (s, *trans*-CH=CH).

Methyl 2-Pentenoate (6). The method of Buchta and Burger[9] gave ester containing, by VPC analysis,[6b] 1.7% **6c**, 3.0% **5**, and 95.3% **6t**: bp 50.5–51.0 °C (26 mm); NMR (60 MHz, $CDCl_3$) δ 7.04 (dt, 1, J = 15.5 Hz, J' = 6 Hz, CH_2CH=), 5.83 (dt, 1, J = 15.5 Hz, J' = 2.0 Hz, =CHCO), 3.76 (s, 3, OCH_3), 2.25 (m, 2, CH_2), 1.10 (t, 3, J = 7 Hz, CH_3CH_2).

Pentenals. Bromine was added to 1,3-pentadiene and the dibromide fraction of boiling point 80–98 °C (20 mm) used to make the diol by the method of Gouge.[10] The diol fraction of boiling point 107–16 °C (0.6 mm) was mainly 2-pentene-1,4-diol and was used to prepare the aldehyde mixture,[10] whose VPC[6c] analysis showed 41% **1**, 29% **2**, 24% ether, and 6% of an unknown material. Preparative VPC[6c] gave **2c,t** and **1**. **2c**: NMR (60 MHz, $CDCl_3$) δ 10.15 (d, 1, J = 8 Hz, CHO), 6.65 (dt, 1, J = 11 Hz, J' = 7 Hz, CH_2CH=), 5.95 (m, 1, =CHCO), 2.65 (m, 2, CH_2), 1.15 (t, 3, J = 7 Hz, CH_3). **2t**: NMR (60 MHz, $CDCl_3$) δ 9.55 (d, 1, J = 8 Hz, CHO), 6.95 (dt, 1, J = 16 Hz, J' = 6 Hz, CH_2CH), 6.05 (dd, 1, J = 15 Hz, J' = 8 Hz, $CHCHO$), 2.35 (m, 2, CH_2), 1.10 (t, 3, J = 7 Hz, CH_3); IR (neat) 2980 (s, aliphatic CH), 2820 and 2750 (w, aldehyde CH), 1690 (s, C=O), 985 cm^{-1} (s, *trans*-CH=CH). **1**: NMR (300 MHz, $CDCl_3$) δ 9.62 (t, 1, J = 2.0 Hz, CHO), 5.63 (m, 1, CH_3CH=), 5.51 (m, 1, CH_2CH=), 3.12 (m, 2, CH_2), 1.73 (m, 3, CH_3). Decoupling confirmed the preceding assignments for **1t** and showed $J_{2,3}$ = 6.5, $J_{2,4}$ = 1.2, $J_{3,4}$ = 16, $J_{3,5}$ = 1.5, and $J_{4,5}$ = 6 Hz. Also present were the following peaks attributed to about 3% of **1c**: δ 9.64 (CHO), 5.69 (CH_3CH=) 5.58 (CH_2CH=), 3.21 (CH_2), 1.65 (CH_3); IR (of neat mixture): 2930 (s, aliphatic CH), 2830 and 2740 (w, aldehyde CH), 1725 (unconjugated C=O), 975 cm^{-1} (*trans*-CH=CH).

Equilibration of *tert*-Butyl Pentenoates. In a typical run 0.5191 g of **4** was dissolved in 10 mL of 0.072 43 M *t*-BuOK in *t*-BuOH at 28 °C at zero time. The *t*-BuOK had been prepared under N_2 in a drybox, and the *t*-BuOH had been dried by using *t*-BuOK and $PhCO_2Bu$-*t* in a manner analogous to that described previously for drying *i*-PrOH.[11] If moisture is not excluded from the reaction mixture, it turns the basic catalyst into KOH, which is destroyed by reaction with the ester. At three different times, 2-mL samples were removed by pipet and added to 10 mL of 0.085 M aqueous $NaHCO_3$ at 0 °C. Two 7-mL ether extracts of the resulting mixture were combined, washed with 7 mL of ice–water, and dried over molecular sieves (Type 3A). The ether was removed at 15–20 mm pressure, fresh ether was added, the solution was dried again, and the ether was removed again. The residue was analyzed by VPC.[6a] The analyses after 19.9, 24, and 27.9 h were all within the experimental uncertainty of each other. At three other times, 1-mL samples were added to 4 mL of 0.2012 M HCl and back-titrated with 0.0502 M NaOH to the bromothymol blue end point, all at ~0 °C. The results showed that 68% of the original base was present after 2.4 h, 15% after 22.8 h, and 3% after 26.2 h. From other runs, in which VPC analyses were carried out at earlier times, it may be calculated that even the 19.9-h point was taken after more than 15 half-lives. Equilibrium was also approached by starting with **3**, and the same results were obtained. To test the analytical method, we dissolved synthetic mixtures of the *t*-Bu esters having compositions near that of the equilibrium mixture in *t*-BuOH without base, which were then quenched, extracted, dried, concentrated, and analyzed. No experimentally significant error in the analytical method was found. We also tested the possibility that in the basic equilibration mixtures, significant fractions of the *t*-Bu esters were present as carbanions, whose quenching gave a nonequilibrium ratio of esters. Starting *t*-BuOK concentrations up to 0.22 M were used, giving *t*-BuOK concentrations up to 0.16 M when ester equilibration had been attained; the same results were obtained.

At some of the higher temperatures used, *t*-BuOK is such an effective catalyst that equilibrium is established very rapidly. In some such cases the equilibration would be so fast that the position of equilibrium could shift substantially as the reaction mixture was being cooled from the intended equilibration temperature. For this reason DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) was used in all runs above 45 °C. At 45 °C both DBU and *t*-BuOK were used, and essentially the same results were obtained. A separate Teflon-valved pressure tube was used for each sample at temperatures of 45 °C and above, except for the *t*-BuOK run at 45 °C, where a separate glass-stoppered test tube was used for each sample to permit more rapid quenching of the sample.

The VPC analyses gave only the concentrations of **4c,t** and total **3**. However, an equilibration at 140 °C was carried out on 0.975 g of **3** and 1.119 g of DBU in enough *t*-BuOH to give 8 mL of solution, and after 9.7 h (shown by previous experiments to be more than enough time to give equilibration) the reaction mixture was quenched and extracted and the total ester fraction separated by preparative VPC. The 300-MHz ^1H NMR spectrum of this material was determined. From the CH_2 peaks at **3t**/**3c** ratio of 2.61 was calculated; the CH_3CH= peaks gave a ratio of 2.48; all the other peaks overlapped too much to be useful for quantitative analysis.

Equilibration of the Methyl Pentenoates. The equilibration of the methyl pentenoates with DBU as a catalyst in *t*-BuOH solution was carried out at 59, 91, and 140 °C essentially as described for the *t*-Bu esters. Equilibrium was approached from both sides. Attempts to equilibrate at 30 °C with KOMe as the catalyst led to the disappearance of all the pentenoate esters at a rate faster than the isomerization. Polymerization via a Michael reaction may have occurred; very little of the *t*-Bu esters were formed. The DBU-catalyzed reaction at 30 °C was too slow to be useful. The total amount of ester present at higher temperatures did not decrease significantly as the equilibration proceeded; polymerization was negligible under these conditions. The analytical method was tested by using synthetic mixtures. Material that had been equilibrated at 140 °C was analyzed by 300-MHz ^1H NMR measurements, just as had been done with the *t*-Bu esters. The CH_2 peaks gave a **5t**/**5c** ratio of 2.09; the CH_3CH= peaks gave a ratio of 2.45.

Equilibration of the Pentenals. Starting from **1** and from **2**, each at a concentration around 0.1 M, equilibrium in *t*-BuOH was established at 80 °C. Both 0.11 M Et_3N and various concentrations of DBU–DBU·HCl buffers were used as catalysts in different runs. At significantly lower temperatures formation of higher molecular weight products prevented us from obtaining reliable equilibrium constants. At 122 and 160 °C *N*-methylmorpholine was used as the catalyst. The reaction mixtures were quenched with dilute perchloric acid and extracted with toluene but treated like the *t*-Bu esters otherwise, except that toluene was not removed before VPC analysis. This procedure and the VPC analysis[6c] were found, by use of synthetic mixtures, to increase the **2t**/**1** ratio by a factor of 1.89 (standard deviation 0.43) and the **2t**/**2c** ratio by a factor of 1.26 (standard deviation 0.33).

Early points on *N*-methylmorpholine-catalyzed reactions showed that the isomerization of **1** gave a much larger ratio of **2c** to **2t** than that present at equilibrium. At 119 °C, for example, when an initial **1** content of almost 100% had dropped to 26.8%, 19.6% **2c** and 53.6% **2t** were present. This was not seen in the isomerization of **1** by Et_3N or DBU or in the DBU-catalyzed isomerization of **3** or **5**, although early points were also analyzed in these reactions.

Kinetic Measurements. In the process of learning what conditions were necessary to achieve equilibrium, we acquired

(8) Goering, H. L.; Cristol, S. J.; Dittmer, K. *J. Am. Chem. Soc.* **1948**, *70*, 3314–6.
(9) Buchta, V. E.; Burger, K. *Justus Liebigs Ann. Chem.* **1952**, *576*, 155–68.
(10) Gouge, M. *Ann. Chim. (Paris)* **1951**, *6*, 648–704.
(11) Hine, J.; Tanabe, K. *J. Phys. Chem.* **1958**, *62*, 1463–4.

Table I. Composition of Equilibrium Mixtures[a]

compd[b]	temp, °C	no. of readings[c]	% reactant[d] cis	% reactant[d] trans	% product[d] cis	% product[d] trans
3, 4	28 ± 0.2	6	4.3 (0.7)[e]	15.4 (0.9)[e]	1.7 (0.2)	78.7 (0.9)
	45 ± 0.2	5	5.5 (0.9)[e]	18.6 (1.2)[e]	2.8 (0.8)	73.1 (0.9)
	88 ± 3	2	8.2 (1.3)[e]	24.0 (1.4)[e]	2.8 (0.4)	65.0 (0.8)
	140 ± 3	3	10.8 (0.4)	27.5 (0.9)	3.2 (0.9)	58.5 (1.2)
5, 6	59 ± 0.1	3	6.7 (1.0)[e]	18.7 (1.1)[e]	2.9 (0.6)	71.6 (1.0)
	91 ± 1	4	8.5 (1.3)[e]	21.6 (1.4)[e]	2.7 (0.3)	67.2 (0.8)
	140 ± 2	10	10.9 (0.9)	24.6 (1.3)	2.9 (0.5)	61.6 (1.7)
1, 2	80 ± 1	11	1.7 (0.7)[e]	4.4 (1.6)[e]	1.6 (0.9)	92.3 (2.4)
	122 ± 2	2	2.2 (0.7)[e]	5.2 (1.6)[e]	3.4 (1.6)	89.2 (2.7)
	160 ± 2	5	2.3 (0.8)[e]	5.1 (1.6)[e]	2.4 (1.0)	90.2 (2.4)

[a] In *t*-BuOH solution. [b] Although equilibrium was approached from both sides, in reporting the results the first compound listed is defined as the reactant. [c] In almost all runs, two to four readings were made. [d] The parenthesized figures are estimated standard deviations. [e] The total percent reactant was obtained by VPC analysis. The separation into cis and trans was based on the assumptions described in the Treatment of Data section.

some rate data from points taken substantially before equilibrium was reached. These were obtained as first-order rate constants for approach to equilibrium. Such a rate constant is the sum of the rate constants for the forward and reverse reactions. The first-order rate constant for equilibration of **3** at 45 °C in the presence of 0.46 M DBU is about 8×10^{-7} s^{-1}. The value for **5** at 59 °C in the presence of 0.66 M DBU is 3×10^{-5} s^{-1}. For equilibration of **1** the first-order rate constants were assumed to be proportional to the concentrations of amine catalysts. Thus, first-order rate constants were divided by the catalyst concentrations to obtain k_2 values of 0.1, 9×10^{-3}, and 7×10^{-4} M^{-1} s^{-1} for DBU, Et_3N, and *N*-methylmorpholine, respectively, all at 80 °C. For *N*-methylmorpholine, k_2 values of 1.7×10^{-3} and 6×10^{-3} M^{-1} s^{-1} were obtained at 119 and 160 °C, respectively. From the *N*-methylmorpholine data at three temperatures, an Arrhenius activation energy of 8.1 kcal/mol was calculated.

Treatment of Data. Since the VPC analyses used did not separate the cis and trans isomers of **1**, **3**, and **5**, analysis by NMR was attempted at one of the higher temperatures, where the cis β,γ-unsaturated compound (the minor geometric isomer of the minor double bond isomer) was present in the largest amounts. This was not successful with the **1–2** equilibrium mixture because so little **1** was present. It did give **3c–3t** and **5c–5t** analyses at 140 °C, as already described. To estimate the equilibrium constants for **1** and for **3** and **5** at other temperatures, we relied on the fact that for species of the type $CH_3CH{=}CHCH_2X$, the thermodynamics of cis–trans isomerization are not greatly dependent on the nature of X. For example, 2-heptene is about 27% cis at equilibrium at 149 °C,[12] and **3** and **5** are about 28% and 31% cis, respectively, at 140 °C. We have therefore assumed that the entropies of geometric isomerizations of **1**, **3**, and **5**, like that of 2-heptene,[12] are essentially zero. For **3** and **5**, enthalpies of cis to trans isomerization (767 and 673 cal/mol, respectively) were calculated from the results obtained at 140 °C. The value for **1** was assumed to be the same as that for **5**. Equilibrium constants calculated in this way were assumed to have a 20% standard deviation. The resulting variance was added to the variances from other sources to obtain the variance of the final equilibrium constant.

Results and Discussion

The composition of the equilibrium mixtures obtained are shown in Table I. The equilibrium constants for reactions 3–5 are plotted logarithmically against $10^3/T$ in Figure 1. In Table II are the resulting enthalpies and entropies of reaction and the *K* values extrapolated to 25 °C (except for reaction 4, where the experimental *K* value at 28 °C is used as the 25 °C value). The formyl group is seen to be much better at stabilizing double bonds than any of the other carbonyl-containing groups. This fact itself suggests that the near identity of *K* for the other three groups is a coincidence, resulting from the approximate cancelation of factors working in opposite directions. When the COX group is formyl, there is minimal interaction between the carbonyl group and X. Correlation of thermodynamic properties in terms of bond contributions plus pairwise and trio interactions[3b] shows an 11.45-kcal/mol[13] stabilizing interaction between a carbonyl group and an sp^3 carbon atom as in a ketone and a 34.50-kcal/mol[13] stabilizing interaction between a carbonyl group and an alkoxy group, as in an ester. Thus, relative to the conjugation present in α,β-unsaturated aldehydes, the conjugation present in α,β-unsaturated ketones and esters should provide less stabilization because it is cross conjugation. The decrease in stabilization would be expected

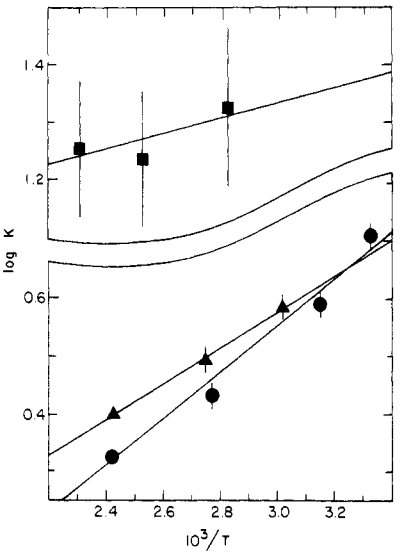


Figure 1. van't Hoff plots of equilibrium constants for isomerization of *trans*-$MeCH{=}CHCH_2COX$ to $EtCH{=}CHCOX$, where X is: ■, H; ▲, OMe; ●, OBu-*t*.

Table II. Equilibria of the Type $MeCH{=}CHCH_2COX \rightleftharpoons EtCH{=}CHCOX$[a]

COX	K	ΔH, kcal/mol	ΔS, eu
CHO	24 (13)	−0.6 (1.6)	4 (4)
CO_2Me	4.9 (0.3)	−1.4 (0.2)	−1.6 (0.6)
CO_2Bu-*t*	5.1 (0.3)	−1.8 (0.2)	−3.0 (0.5)
COMe	4.8 (0.5)[b]		

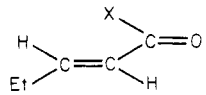
[a] In *t*-BuOH at 25 °C. The parenthesized figures are the estimated standard deviations. [b] Reference 4.

(12) Egger, K. W. *J. Am. Chem. Soc.* **1967**, *89*, 504–9.

(13) These are the values of $\Gamma_{CC_dO_d}$ and $\Gamma_{OC_dO_d}$, respectively.[3b] By definition $\Gamma_{HC_dO_d}$ is zero.

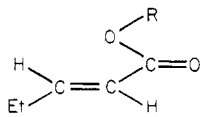
to be larger with the esters than with the ketones.

A second factor that explains the greater double bond stabilizing ability of the formyl group is steric. Electronic factors should favor the coplanar transoid conformation of **2t**, **4t**, **6t**, and *trans*-3-hexen-2-one shown in **7**, which



7

is analogous to the preferred conformations of acrolein, 1,3-butadiene, and glyoxal.[14] When X is hydrogen there will be the least steric hindrance to coplanarity. When X is methyl more hindrance is expected than when X is methoxyl, because of the preference of esters for eclipsing the carbon–oxygen double bond with the carbon–oxygen single bond,[15,16] as in **8**. Perhaps there is greater steric



8

strain in the α,β-unsaturated ester. Observations on *tert*-butyl formate show that although detectable fractions of this species are in other conformations, most of the material is in a conformation in which the carbonyl group is eclipsed by the O–Bu bond.[17,18] Steric repulsions are estimated to have expanded the C–O–C angle in this conformer to greater than 120°.[18,19] Our ester **4t** probably exists largely in a similar conformation, but the expanded C–O–C angle and possible presence of small amounts of a second conformer have not made the equilibrium constants for eq 4 much different from those for eq 5 at a given temperature.

However, there do appear to be significant differences in rates of isomerization between the two esters. On the assumption that at 59 °C **3** is twice as reactive as at 45 °C and **1** is half as reactive as at 80 °C, the relative rates of DBU-catalyzed equilibration at 59 °C are 1:13:14 000 for **3**, **5**, and **1**, respectively.

To calculate D values, Skoglund[20] has added the equilibrium constants reported here plus all the additional values that would be found in the literature to the compilation reported earlier.[2] In the least-squares treatment, the carbomethoxy, carbo-*tert*-butoxy, and all other CO_2R groups were treated as a single substituent. Values of 0.43 and 0.05 were used for $\sigma_{p\text{-}CO_2R}$ and $\sigma_{p\text{-}CH_2CO_2R}$, respectively. For $\sigma_{p\text{-}CHO}$ and $\sigma_{p\text{-}CH_2CHO}$, the values used were 0.44[21] and 0.05, respectively. D_{CO_2R} was found to be 3.14 kcal/mol and D_{CHO} to be 4.32 kcal/mol.

In the conjugated isomers there should be inhibited rotation around the bond between the carbonyl group and the α-carbon atom. This will tend to make the entropy of reaction negative. The ΔS value obtained for the pentenals is positive, but the experimental uncertainty is so large that we are not sure that this fact is significant. It is not obvious to us why ΔS should be more positive for the pentenals than for the esters. Both esters have negative ΔS values, as expected. The more negative value for the *tert*-butyl esters suggests that the bulky *tert*-butyl group gives increased interference with rotations around single bonds in the conjugated isomer. It is also possible that there is significance in the curvature of the van't Hoff plot for the *tert*-butyl ester that is seen in Figure 1.

Registry No. **1c**, 53448-06-9; **1t**, 58838-14-5; **2c**, 1576-86-9; **2t**, 1576-87-0; **3c**, 81643-00-7; **3t**, 81643-01-8; **4c**, 81643-02-9; **4t**, 81643-03-0; **5c**, 36781-66-5; **5t**, 20515-19-9; **6c**, 15790-87-1; **6t**, 15790-88-2; *trans*-2-pentenoic acid, 13991-37-2; *trans*-2-pentenoyl chloride, 33698-85-0; 3-pentenoic acid, 5204-64-8.

(14) Kuchitsu, K.; Fukuyama, T.; Morino, Y. *J. Mol. Struct.* **1968**, *1*, 463–79.
(15) Jones, G. I. L.; Owen, N. L. *J. Mol. Struct.* **1973**, *18*, 1–32.
(16) Ruschin, S.; Bauer, S. H. *J. Phys. Chem.* **1980**, *84*, 3061–5.
(17) Drakenberg, T.; Forsén, S. *J. Phys. Chem.* **1972**, *76*, 3582–6.
(18) Omura, Y.; Corset, J.; Moravie, R. M. *J. Mol. Struct.* **1979**, *52*, 175–94.
(19) True, N. S.; Bohn, R. K. *J. Phys. Chem.* **1978**, *82*, 478–9.
(20) Skoglund, M. J. Ph.D. Dissertation, The Ohio State University, Columbus, OH, 1981.
(21) Humffray, A. A.; Ryan, J. J.; Warren, J. P.; Yung, Y. H. *Chem. Commun.* **1965**, 610–1.

^{1}H NMR Evidence for High Barriers to Amino Group Rotation in 4-Aminopyrimidines, Including Thiamin, at Low pH in Water[1]

Frank Jordan

Department of Chemistry, Rutgers, The State University of New Jersey, Newark, New Jersey 07102

Received September 1, 1981

The ^{1}H NMR spectrum of thiamin (**1**), 4-aminopyrimidine (**2**), 4-amino-5-(methoxymethyl)-2-methylpyrimidine (**3**), and thiothiamin (**4**) was recorded at a variety of concentrations, temperatures, and pH's in 80:20 (v/v) H_2O–^2H_2O employing correlation spectroscopy and Redfield 2–1–4 sequences at 360 and 500 MHz. At pH's 1.5 to 3.0 units below the pK for N1 protonation, two amino hydrogen resonances were observed to persist at temperatures below about 10 °C for **1**, 26 °C for **2**, 40 °C for **3**, and 15 °C for **4**, indicative of hindered amino group rotation under these conditions. The concentration and temperature dependence of the behavior of the two NH resonances at low pH suggest that the increased barrier is not due to intermolecular interactions but simply to the favorable resonance interaction between the amino group nitrogen lone pair and the pyrimidine ring once the latter is N1 protonated. The barrier to amino group rotation in N1′-protonated thiamin was estimated to be 14.6 kcal/mol at pH 1.56, 12 °C, in 1 M KCl solution.

The possibility that the aminopyrimidine portion of thiamin (**1**) diphosphate (the vitamin B_1 coenzyme) has a catalytic function was raised by Schellenberger,[3] whose studies demonstrated that the coenzyme devoid of the

0022-3263/82/1947-2748$01.25/0