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Nuclear Magnetic Resonance Study of Exchanging Systems. X.[1]
Rotational Barriers to *trans-cis* Isomerization in Esters

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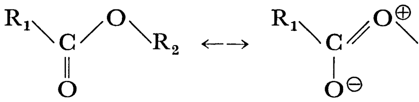
The ^{13}C NMR spectra of *t*-butyl formate (**1**), 1,1-diethylpropyl formate (**2**), and 2,6-dimethylphenyl formate (**3**) were measured at various temperatures. It was found that the signals of the *trans* and *cis* isomers in **1** and **2** are separated at very low temperatures, and that the signal of **3** only shows a slight line broadening. The complete line shape analyses of these temperature-dependent spectra were performed. The activation energies $E_a(t\text{-}c)$ of the isomerization from the *trans* isomer to the *cis* were determined to be 10.9 kcal/mol for **1** and 7.2 kcal/mol for **2**.

It is well known from a number of dynamic NMR spectroscopic studies[2] that the rotation about the amide C–N bond is sufficiently slow at room temperature, for the C–N bond has a partial double-bond character. In secondary amides, therefore, there is a possibility for two isomers (*trans* and *cis*) to exist. Indeed, in monosubstituted formamides, both *trans* and *cis* isomers exist in the solution state,[3] and the isomerization barrier between the two isomers in formanilide has been reported to be 20 kcal/mol.[4]

In contrast with the case of amides, however, the conformation of the ester, which is a compound structurally analogous to the amide, is reported to be *s-trans* only from the dipole moment and from NMR, IR, and microwave spectroscopic studies,[5] although it is also known[6] that the ester C–O bond has a partial double bond character due to the delocalization of electrons, as is shown below:



It has also been reported from ultrasonic absorption studies concerning various esters that the population of the *cis* isomer is small.[7–14]

However, in *t*-butyl formate (**1**) and other formates with a very bulky alcohol part, we previously found[15] from the results of studies using the dipole moment and the NMR, UV, and IR methods, that the *cis* isomer exists to a considerable extent. Similarly, the existence of the *cis* isomer was proved in several ester analogues (carbamates,[16] carbonates,[17] thiocarbonates,[18] and chloroformates[19]). Rotational barriers to the isomerization between the *trans* and the *cis* isomers have hardly been investigated at all except for the ultrasonic relaxation and IR investigation. The ΔH^* of the isomerization of methyl formate has been reported to be 7.8 kcal/mol from the ultrasonic relaxation analyses,[11,14,20] while Miyazawa supposed its potential barrier to be 13 kcal/mol in his analysis of the C–O out-of-plane vibrations of its infrared spectrum.[21] The discrepancy between these data is rather large, and so it is necessary to study in more detail the thermodynamic and kinetic parameters of the isomerization between the *trans* and *cis* conformers of the esters in other methods. In this connection, an NMR line-shape analysis is the most appropriate method.

In this paper, we will present the accurate isomerization parameters of formates, including both *trans* and *cis* isomers, on the basis of the complete line-shape analyses of their ^{13}C NMR spectra. In addition, we will discuss the influence of the bulkiness of the alkyl and aryl groups on the rotational barriers in the formates.

Experimental

Materials. *t*-Butyl formate (**1**), 1,1-diethylpropyl formate (**2**), and 2,6-dimethylphenyl formate (**3**) were prepared from the mixed anhydride of formic and acetic acids and the corresponding alcohols and phenol according to Stevens' method.[22] Methyl formate (**4**), ethyl formate (**5**), and isopropyl formate (**6**) were prepared from formic acid and the corresponding alcohols in the presence of a trace of sulfuric acid.

NMR Measurements. The ^{13}C NMR spectra of the esters were recorded on NEVA NV-14 (15.087 MHz) and Varian XL-100-15 (25.16 MHz) spectrometers. The pulsed FT method was made by a Varian 620/L computer (16k). Acetone-d_6 was used for the deuterium lock. The solvents and sample concentrations were as follows: 80 vol% in acetone and acetone-d_6 (5 vol%) for **1**, 30 vol% in dimethyl ether and acetone-d_6 (5 vol%) for **2**, and 10 vol% in dimethyl ether, carbon disulfide (25 vol%), acetone-d_6 (5 vol%) for **3**. The temperature was read by means of a calibrated copper-constantan thermocouple.

Spectral Calculations. The calculations of the theoretical spectra in the computer simulation were made by means of a FACOM 270/30 computer.

Results and Discussion

Previously we found[15] in an ^{1}H NMR spectral study of *t*-butyl formate (**1**) in DMF, that the line width of the formyl proton signal, which is only a singlet at room temperature, becomes broader as the temperature is lowered, and finally two separate peaks, which were assigned to the *cis* and *trans* isomers, appear at −94.0 °C. It was also found that the two signals of the *trans* and *cis* formyl protons show very complex line shapes at such a conformationally frozen temperature as −99 °C. This occurs because they couple with the methyl protons of the *t*-butyl group through five chemical bonds, and the line shapes show that the long-range spin-spin coupling constant in the *trans* isomer ($^5J_{trans}$) is different from that in the *cis* isomer ($^5J_{cis}$). A complete line-shape analysis of these very complex ^{1}H NMR spectra of $AX_9 \rightleftarrows A'X'_9$ spin system must be made using the density matrix method.[23,24] The calculation for this multi-spin system is quite hard. Moreover, the population change in the isomers at different tempera-

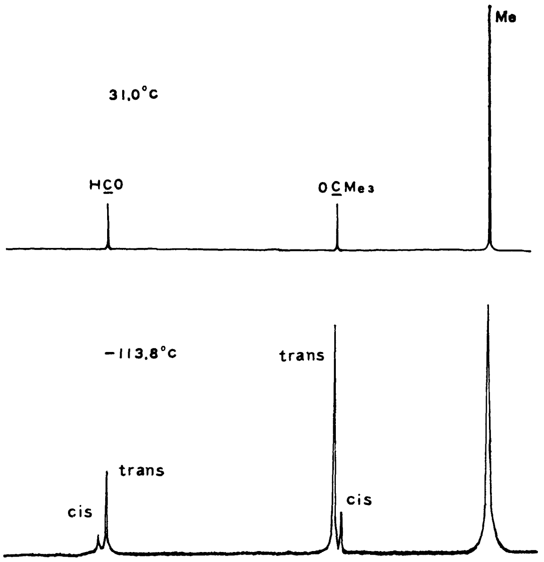


Fig. 1. ^{13}C NMR spectra of **1** at 31.0 and −113.8 °C.

tures makes the line-shape analysis very complex and difficult. Drakenberg *et al.* analyzed the ^1H NMR spectra of **1** using a rather approximate method.[25)]

On the other hand, it is known that an ^1H-decoupled ^{13}C NMR spectral pattern is much simper than that of the ^1H NMR spectrum. Therefore, the line-shape analysis can be made much easily in the ^{13}C NMR spectra.[26–28)]

Temperature-dependent ^{13}C NMR Line Shape. The ^{13}C NMR spectrum of **1** at an ambient temperature (Fig. 1) shows that the signals of the formyl, alkoxy ($O\mathbf{C}(CH_3)_3$), and methyl carbons are sharp singlets. This means that the rate of the isomerization between the *trans* and *cis* isomers is very rapid at that temperature. As the temperature is lowered, the line widths become broader. The signals of the formyl and alkoxy carbons begin to separate into two peaks at about −96 °C (see Fig. 2); the minor peaks were assigned to the *cis* isomer of the ester, because other spectroscopic data show that the population of the *cis* isomer is smaller than that of the *trans* in **1**.[15)] In contrast with this, the signal of the methyl groups is not divided into two peaks, even at temperature as low as −113.8 °C, although the line width becomes larger to some extent with the temperature decrease.* This may mean that the difference between the chemical shifts of the methyl groups in the two isomers is considerably smaller than those of the formyl and alkoxy carbon signals.

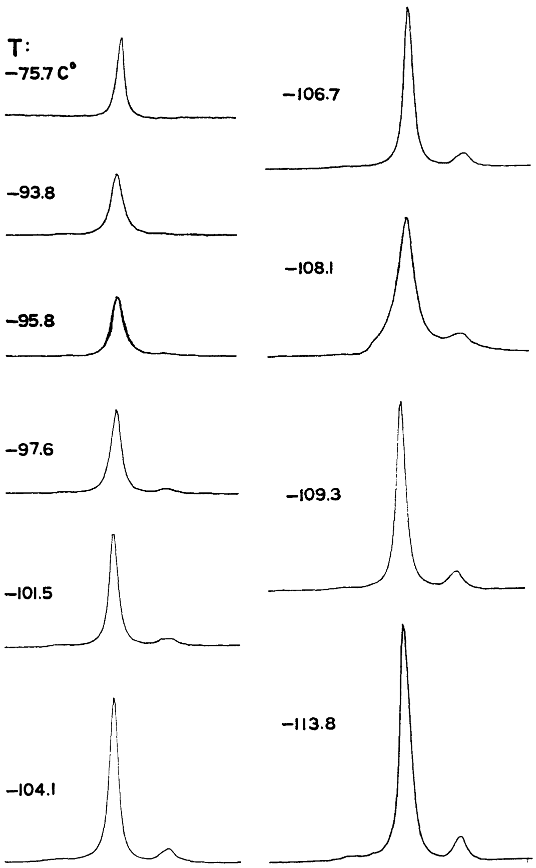
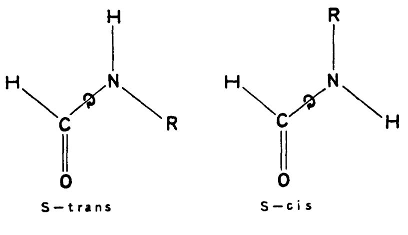
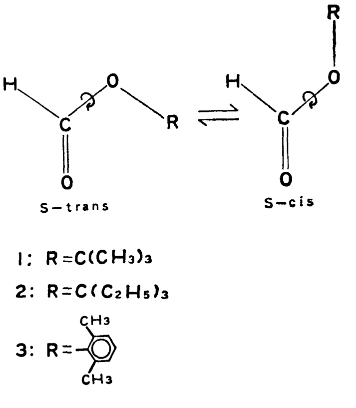


Fig. 2. The temperature-dependent ^{13}C NMR spectra of ethereal carbons in the *trans* and *cis* isomers of **1**.

In a previous paper concerning the conformations of esters,[15)] it has been discussed that the steric bulkiness of the R group (HCO_2R) severely affects the stabilization of the *trans* and *cis* isomers. This reasonably leads us to consider that the barrier to the rotation about the ester C–O bond must also be influenced by the bulkiness of the R group. Thus, the ester **2** and **3**, whose R groups are bulkier than the *t*-butyl group, were prepared and their ^{13}C NMR spectra were measured at low temperatures. The change in the line shape of **2** with the temperature decrease was almost the same as that of **1**, although the temperature had to be lowered to about −130 °C in order to freeze the isomerization reaction in **2**. In the case of **3**, however, no peak sepa-





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* At temperatures below −110 °C, the broad line shape of the methyl carbon becomes unsymmetrical and a small shoulder signal appears at the lower field of the main peak, although it does not separate into peaks even at −120.3 °C.

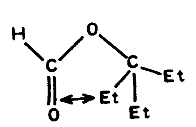
Table 1. ^{13}C chemical shifts and chemical-shift differences of the *cis* and *trans* isomers in **1**—**3** (ppm from TMS)

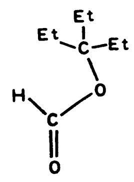
Signal	Isomer	**1**	**2**	**3**
H$\underline{C}$O	*cis*	169.4	168.2	162.6
	trans	166.7	165.8	
	Δδ	2.7	2.4	
O$\underline{C}$R$_3$	*cis*	84.8	90.8	151.2
	trans	86.0	93.5	
	Δδ	−1.2	−2.7	
$\underline{C}$H$_3$		32.6[a)]	12.1	20.0
$\underline{C}$H$_2$CH$_3$		—	30.9	—
ortho		—	—	133.8
meta		—	—	132.6
para		—	—	130.1
Temperature (°C)		−113.8	−130.1	−133.0

a) Probably δ of the signal of the *trans* isomer.

rations in the formyl, aryloxy, and methyl carbon signals were found even at temperatures as low as —133 °C, although the line-shape broadening in the formyl carbon signal is quite large.

*^{13}C NMR Chemical Shifts of **1**—**3**.* The chemical shifts and chemical-shift differences of the two isomers in **1**—**3** are given in Table 1. It is worthwhile pointing out that in the carbonyl region of **1** and **2**, the chemical shift of the *cis* isomer is at a lower field than that of the *trans*, while in the alkoxy carbon region, the reverse is the case. This interesting chemical-shift tendency in the carbonyl and alkoxy carbon regions of the *trans* and *cis* isomers in these esters was also found in a structually analogous compound, *N*-*t*-butylformamide (HCONH-^{t}Bu) (**7**).[29)] Table 1 shows that the chemical-shift difference (Δδ) of the carbonyl carbon signals of the two isomers in **1** is almost the same as that in **2**, while in the alkoxy-carbon region the difference, Δδ, in **2** is considerably larger than that in **1**. This result may be explained by considering that there is a very severe steric compression between the carbonyl and the 1,1-diethylpropyl groups in the *trans* isomer of **2**, and that the chemical shift moves to a lower field due to the steric compression effect,[30)] while in the *cis* isomer the compression can be expected to be greatly reduced because the counter group for the repulsion is the smallest formyl hydrogen atom.





Populations of the Two Isomers. The populations of the *trans* and *cis* isomers change as the temperature is lowered. The determination of the populations was made using a computer simulation by the trial-and-error method in the conformationally frozen temperature range. This method was considered to be the most accurate for determining the populations, making it possible to dispense with the troublesome determination of the base line of the signals. This determination was made independently for the carbonyl and alkoxy carbon signals. The populations obtained in these two regions are in good agreement with each other. The population of the *cis* isomer in **1** is 9% at −113.8 °C, and that in **2** is 7% at −130.1 °C. The thermodynamic static parameters of the ester isomerization ($\Delta G°$, $\Delta H°$, and $\Delta S°$) were determined from these populations at different temperatures and their Arrhenius plots. The results are shown in Table 2.

Isomerization Barriers. The computer simulation of the temperature-dependent spectra of **1** and **2** was performed using the modified Bloch equation method in order to obtain the activation parameters of the isomerization. The computer program is EXNMR1.** The simulation in the line-shape analyses was made by

Table 2. Thermodynamic parameters of the isomerization between the *trans* and *cis* isomers in formates HCO$_2$R at −100.0 °C and 25.0 °C

The values in parentheses are those at 25.0 °C.

R Process	^{t}Bu		C(Et)$_3$	
	t→*c*	*c*→*t*	*t*→*c*	*c*→*t*
E_a (kcal/mol)	10.9±0.5 (10.9±0.5)	10.3±0.5 (10.3±0.5)	7.2±0.3 (7.2±0.3)	5.9±0.3 (5.9±0.3)
ΔG^* (kcal/mol)	9.3±0.02 (8.5±0.3)	8.6±0.02 (8.1±0.3)	8.4±0.03 (9.5±0.4)	7.6±0.09 (9.2±0.4)
ΔH^* (kcal/mol)	10.6±0.5 (10.3±0.5)	10.0±0.5 (9.7±0.5)	6.9±0.3 (6.6±0.3)	5.6±0.3 (5.3±0.3)
ΔS^* (e. u.)	4.4±1.7 (6.0±1.7)	4.7±1.7 (5.4±1.7)	−5.0±1.0 (−7.7±1.3)	−6.7±1.0 (−13.1±1.3)
$\Delta G°$ (kcal/mol)	0.69±0.05 (0.30±0.07)		0.74±0.08 (0.71±0.08)	
$\Delta H°$ (kcal/mol)	1.22±0.09 (1.22±0.09)		0.76±0.09 (0.76±0.09)	
$\Delta S°$ (e. u.)	1.8 ±0.3 (3.1 ±0.3)		0.1 ±0.3 (0.2 ±0.3)	

** A modified version of EXNMR0.[31)]

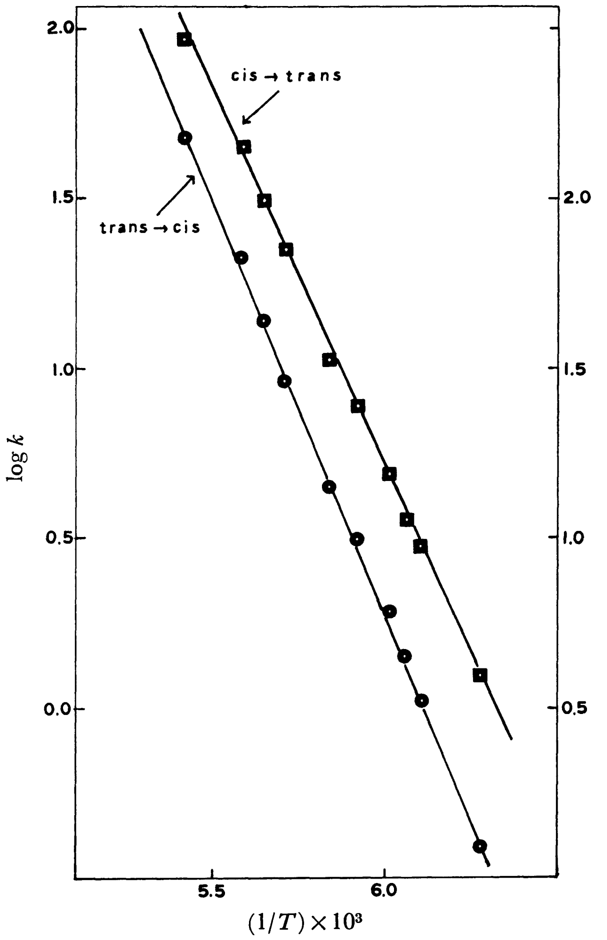
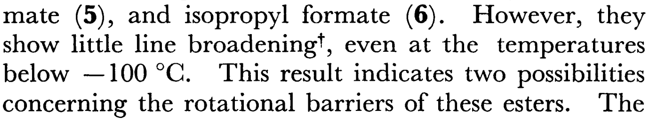


Fig. 3. The Arrhenius plots of log k *versus* $1/T$ in the two isomerization processes of **1**. The square dots ☐ are for the isomerization process from the *cis* to the *trans*, and the circular dots ○ are for that from the *trans* to the *cis*. The scale in the right hand is for the former process, and that the left hand is for the latter.

independently changing two parameters, the isomerization rate k_i and the populations p_i, at each temperature. The line-shape analyses were performed in the two regions. The activation parameters of the ester isomerization were obtained from the Arrhenius plots of the k's and from Eyring's equation (Fig. 3). The results are shown in Table 2.*** The activation energy of the isomerization in **1** is considerably larger than in **2**. This may be accounted for by the destabilization of the energy level of the *trans* isomer in **2** at the ground state in comparison with the case of **1** because of the severe steric repulsion between the carbonyl and 1,1-diethylpropyl groups. This steric interaction in the *trans* isomer of **2** is revealed in the steric-compression lower-field shift of the alkoxy carbon signal described before. The activation entropy (ΔS^*) of **2** is much smaller than that of **1**. The reason for the smaller $\Delta^* S$ of **2** is not clear at the present time, but it is certain that it causes the activation free energy (ΔG^*) of **2** to increase. Thus, the ΔG^* of **2** is quite near to the ΔG^* of **1** ($\Delta\Delta G^*$=0.9—1.0 kcal/mol), although the difference between the activation energies (E_a) of **1** and **2** is remarkably large (ΔE_a=3.7—4.4 kcal/mol).

In the case of **3**, the line broadening at low temperatures show the coexistence of the *trans* and *cis* isomers, which was also proved by the IR spectroscopic data.[15] However, we cannot determine the activation parameters of the isomerization in **3** because the signal of **3** does not separate into two peaks even at temperatures as low as −133 °C; therefore, we cannot know the chemical shifts and the populations of the two isomers. Assuming the chemical shift difference in the formyl carbon signals of the *trans* and *cis* isomers in **3** similar to those in **1** and **2**, however, it may be supposed that the activation energy in **3** is considerably smaller than those in **1** and **2**. The lower rotational barrier about the ester C–O bond in **3** may be explained by two factors: the destabilization of the *trans* isomer by the repulsion between the carbonyl and aryl groups, and the effect of the resonance between the ester and aryl groups. The latter effect may have a considerable influence, because, if the former factor is predominant, the activation energy in **3** must be larger than that in **2**, for the steric compression between the 2,6-xylyl and carbonyl groups in **3** is smaller than that between the 1,1-diethylpropyl and carbonyl groups in **2**. Concerning the latter factor, a full discussion cannot be made, but it is worthwhile pointing out that, if the resonance form, for example, **3c**, contributes to some extent, the single-bond character in the ester C–O bond may increase and the rotational barrier may be reduced.



3a **3b** **3c**

Therefore, as it was made clear that the steric bulkiness of the R group in HCO_2R strongly influences the rotational barrier about the ester C–O bond, we measured the ^{13}C spectra of methyl formate (**4**), ethyl formate (**5**), and isopropyl formate (**6**). However, they show little line broadening†, even at the temperatures below −100 °C. This result indicates two possibilities concerning the rotational barriers of these esters. The rotational barriers of these esters are so low that we cannot obtain information about them on the NMR time scale, even at these low temperatures. The second possibility is that, although the barriers of **4**—**6** are higher than those of **1** and **2**, the chemical-shift differences between the two isomers are so small, and/or the population of the *cis* (less stable) isomer is so small, that the line shapes hardly change with the temperature decrease. Since it has been reported[8] that the popu-

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*** The activation parameters obtained in this study are somewhat different from those obtained in an ^1H NMR investigation by Drakenberg *et al.*[25] For example, ΔH_{t-c} in **1** at −90 °C is reported to be 9.5 kcal/mol. This small discrepancy may be explained partly by the solvent or concentration effect on the activation parameters and partly by the systematic errors of their approximate method.

† The very slight line broadening is probably caused by the high viscosity effect at low temperature.

lation of the *cis* isomer in **5** is only a few percent at room temperature, it may be negligibly small for the NMR detection at such a low temperature as −100 °C. Thus, at present, unfortunately we cannot conclude which is the true case. Since the rotational barriers of **4** obtained from the ultrasonic relaxation and IR studies are considerably different from each other, as has been described before, more detailed investigation using other techniques should be made in the future.

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