Barriers to Rotation in Methyl Formate by Dynamic NMR Spectroscopy and Barriers to 1,3 Oxygen-to-Oxygen Migration in Methyl Formate and Trifluoromethyl Formate by ab Initio Calculations

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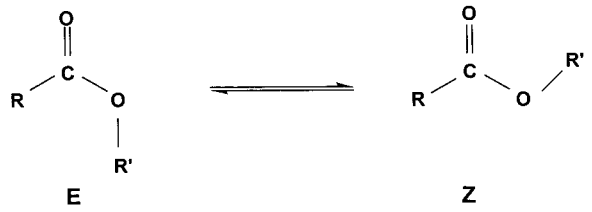
Free-energy barriers of 9.85 and 11.91 ± 0.15 kcal/mol at −70.8 °C were found by dynamic NMR spectroscopy for the *E*-to-*Z* and *Z*-to-*E* conversions, respectively, of methyl formate (**1**) enriched in ^{13}C to 99% for the carbonyl carbon [methyl formate ^{13}C (**2**)]. These barriers are higher than the literature values reported for −53 °C. The free-energy barrier to 1,3 oxygen-to-oxygen migration of the methyl group in methyl formate was determined by ab initio calculations at several levels. The value of 58.7 kcal/mol obtained at the MP2/6-311+G (df,pd) level was compared to a literature barrier for this process (MINDO/3) and to barriers for related compounds. A free-energy barrier of 63.0 kcal/mol for the oxygen − to − oxygen migration of the CF_3 group in trifluoromethyl formate (**3**) was calculated at the MP2/6-31+G* level.

The Z conformations of most esters are strongly favored[1,2] by both steric interactions and dipole−dipole interactions[3] over the *E* conformations. An *E* − *Z* energy difference for methyl acetate of 8.5 ± 1.0 kcal/mol was estimated[4] from matrix IR spectra. Most other esters will



have larger steric repulsions between R and R′ in the *E* isomers than exist for methyl acetate and, consequently, are expected to have even greater *E* − *Z* energy differences. By contrast, in formate esters, the steric repulsion in the *E* isomers between the formyl hydrogen and R′ will be smaller than the repulsion in the *Z* conformations between the carbonyl oxygen and R′, and the *E* isomers will be favored by steric effects, particularly when R′ is large. *E* − *Z* free-energy differences of 2.15, 1.67, 1.36, and 0.48 kcal/mol[5] were obtained by low-temperature NMR for solutions of methyl, ethyl, isopropyl, and *tert*-butyl formate in 50:50 DMF and acetone-d_6. Although steric effects favor the *E* isomers in these esters of formic acid, the *Z* isomers have larger populations due to other factors, including more favorable dipole−dipole interactions.[3]

The free-energy barriers for interconversion of *E* and *Z* conformations of the parent ester, methyl formate (**1**), are of interest for determining the accuracy of calculated values and for comparison with the barriers of other esters and carboxylic acids. Free-energy barriers of 7.97 kcal/mol (*E* to *Z*) and 9.93 kcal/mol (*Z* to *E*) were obtained[5] by NMR for methyl formate, but some evidence suggests that these barriers are too low. The free-energy barriers of *tert*-butyl thiolformate (8.9 and 9.4 kcal/mol)[6] were nearly the same as for *tert*-butyl formate (8.6 and 9.3 kcal/mol);[7] the free-energy barriers of 10.63 and 11.84 kcal/mol for methyl thiolformate[8] suggest that the barriers for **1** should be higher than the reported[5] values. Also, if the *E*-to-*Z* free-energy barrier of 7.97 kcal/mol[5] for **1** at −53.15 °C is assumed to be constant with temperature, then a rate constant between 2617 and 2686 s^{-1} is predicted[9] for the slow-exchange temperature of −83.15 °C. However, the rate constants are related to line widths at temperatures near slow exchange by the relationship $k = \pi W_{1/2}$,[10] and a rate constant of 2617−2686 s^{-1} would correspond to a line width of 833−855 Hz, which is not consistent with slow exchange. At the temperature used[5] to obtain rate constants and barriers, an averaged signal for the *E* and *Z* conformations was observed. In the present work, exchange broadening of the ^{13}C peak for the *E* isomer was studied at lower

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temperatures. The rate constant for the *E*-to-*Z* conversion was obtained from line shape matching of this peak for the minor conformation, and the rate constant for the reverse process was obtained from the *E*-to-*Z* rate constant and the populations, which could be measured directly by integration. For the experiment, methyl formate enriched to 99% ^{13}C in the carbonyl carbon (**2**) was used.

Another process of interest in methyl formate is the 1,3 oxygen-to-oxygen migration of the methyl group. Barriers of 80.7 and 60.2 kcal/mol were reported[11] for methyl migration in **1** and CF_3 migration in trifluoromethyl formate (**3**), respectively, from MINDO/3 calculations. In the present work, we have calculated barriers for these processes using ab initio calculations.

Experimental and Methods Section

Methyl formate enriched in ^{13}C to 99% in the carbonyl carbon (**2**) and solvents were purchased from Aldrich Chemical Co. and used as received. An adequate level of purity for the ester was established by the room-temperature ^{13}C NMR spectrum of the neat sample.

The compound was studied as a 20% solution in a 1:1 mixture of acetone-d_6 and undeuterated DMF, which was prepared in a 5 mm thin-walled NMR tube. A small amount of TMS was added to provide an internal reference for the spectra, which were recorded on a General Electric Model GN-300 wide-bore NMR spectrometer, operating at a frequency of 75.57 MHz for carbon and equipped with a 5 mm dual probe. A set of spectra was obtained at different temperatures with a sweep width, block size, and tip angle of ±19 841 Hz, 32 K, and 45°. Satisfactory spectra were obtained for the broad signals of the *E* isomer, but the digital resolution was insufficient for accurate determination of line widths for TMS. A second set of spectra was taken for several temperatures with a sweep width of ±10 500 Hz and 128K data points, and the TMS line widths measured from these spectra were used in calculation of matching line shapes for the first set of spectra, which had better signal-to-noise ratios. The delay times between pulses were 10.0 s at all temperatures. Spectra were processed without any line broadening.

Because of the difficulty in ejecting the sample at lower temperatures, temperature calibrations were performed separately, using a dummy sample tube. A Leeds-Northrup model 8690-2 millivolt potentiometer equipped with a copper−constantan thermocouple immersed in same solvents was used for this purpose, and the emf's were measured under conditions as nearly identical as possible. These calibrated temperatures were estimated to have an uncertainty of ±2 °C.

The *E*-to-*Z* rate constants were obtained at temperatures below coalescence by total line shape matching of the signals for the carbonyl carbon of the *E* isomer with spectra calculated[12] with an IBM-compatible PC. The corresponding *Z*-to-*E* rate constants were obtained by multiplying the *E*-to-*Z* rate constants by the ratio of populations (P_E/P_Z). Populations of *Z* and *E* conformations were obtained by the cut-and-weigh method, taking into account the different *Y* scales used in recording the peaks. Free-energy barriers were calculated from the Eyring equation with a program written by Newmark[9] and installed on an Apple computer.

For the computational studies, structures for the *Z* conformations and transition states for **1** and **3** were generated with Spartan 5.1 installed on a Silicon Graphics workstation. The geometries for the *Z* isomers of **1** and **3** were optimized with the Gaussian 94 series of programs[13] at different levels, starting from HF/STO-3G. This was followed by harmonic frequency calculations at the same levels using the analytical method. The initial transition state structure for **1** was created with the reported geometry (MINDO/3)[11] and optimized with the SYBYL[14] force field. The oxygen−methyl carbon bond length was adjusted from 4 to 1.6 Å. The input prepared in this way was subjected at different levels to full geometry optimization for transition states using the STQN method. A similar procedure was used for the transition state of **3**, with some of the initial structural parameters derived from the transition state structure of **1**. The optimized structures were tested by the presence of one imaginary frequency, and the vibrations were visualized using MOLDEN.

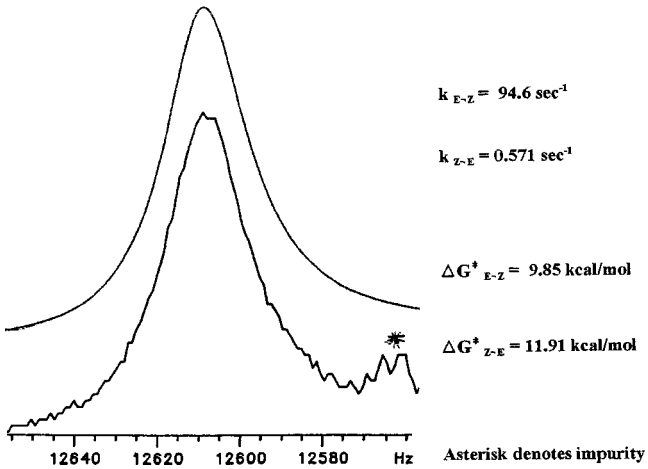

Figure 1. Experimental and simulated ^{13}C NMR spectra for the carbonyl carbon of the *E* isomer of ^{13}C-enriched methyl formate at −70.8 °C.

Results and Discussion

Experimental and simulated ^{13}C NMR spectra for the carbonyl carbon of the *E* isomer of **2** at −70.8 °C are shown in Figure 1. Chemical shifts for the *E* and *Z* conformations of δ 166.80 and 163.10, respectively, were found at this temperature and are close to the literature[5] chemical shifts for −83 °C. The population of the *E* isomer at − 70.8 °C was 0.006 ± 0.0015. The *E*-to-*Z* and *Z*-to-*E* rate constants of 94.6 and 0.571 s^{-1} corresponded to free-energy barriers of 9.85 and 11.91 ± 0.15 kcal/mol, respectively. Rate constants estimated at other temperatures gave similar barriers. The barriers are substantially larger than those reported[5] for methyl formate (7.97 and 9.93 kcal/mol). The *E*-to-*Z* free-energy barrier found in the present work is close to the reported[5] *Z*-to-*E* free-energy barrier.[15]

Estimates of line widths for ethyl formate and isopropyl formate were made by the procedure described in footnote 9 for methyl formate. The ranges of line widths, 222−227 Hz for ethyl at −83.15 °C and 135−139 Hz for isopropyl at −80.15 °C, are smaller than for methyl, but,

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Table 1. Relative Free Energies, Dipole Moments, and Low Frequencies of Methyl Formate, Calculated with the Gaussian 94 Program

	Z conformer			transition state for CH_3 migration		
method	dipole moment (D)	relative free energy[a] (kcal/mol)	low frequency (cm^{-1})	dipole moment (D)	relative free low energy[a] (kcal/mol)	low frequency (cm^{-1})
HF/STO-3G	0.82	0.00	162.3	0.64	100.23	1516.9 i
HF/6-31+G*	2.12	0.00	168.8	3.00	66.15	784.2 i
HF/6-311+G(df,pd)	2.09	0.00	164.5	2.97	67.5	789.4 i
MP2/6-31+G*	2.07	0.00	153.8	2.11	55.30	812.1 i
MP2/6-311+G(df,pd)	1.99	0.00	167.7	1.70	58.71	848.8 i

[a] At 25 °C.

Table 2. Relative Free Energies, Dipole Moments, and Low Frequencies of Trifluoromethyl Formate, Calculated with the Gaussian 94 Program

	Z conformer			transition state		
method	dipole moment (D)	relative free energy[a] (kcal/mol)	low frequency (cm^{-1})	dipole moment (D)	relative free energy[a] (kcal/mol)	low frequency (cm^{-1})
HF/3-21G*	2.69	0.00	74.5	1.91	89.80	748.0 i
HF/6-31+G*	2.49	0.00	102.0	0.15	89.34	687.1 i
HF/6-311+G(df,pd)	2.43	0.00	102.5	0.67	89.14	665.0 i
MP2/3-21G*	2.81	0.00	66.7	1.76	62.55	494.8 i
MP2/6-31+G*	2.71	0.00	102.5	1.46	62.98	496.3 i
MP2/6-311+G(df,pd)	2.56			1.18		

[a] At 25 °C.

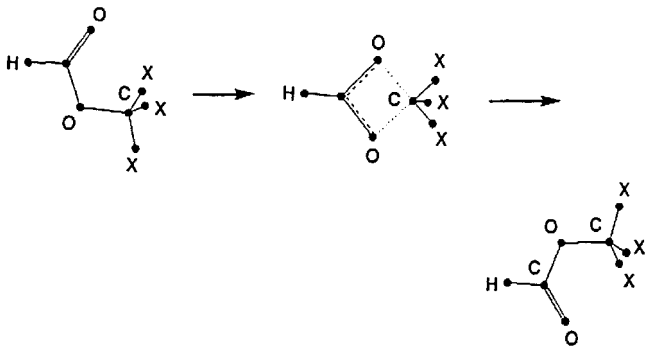
particularly for ethyl, suggest that the reported[5] free-energy barriers may be somewhat too low.

Relative free energies of 0.00, 12.41, and 1.66 kcal/mol were obtained[16] from ab initio calculations for the *Z* (0°), 90°, and *E* (180°) structures of methyl formate in acetonitrile solution ($\epsilon = 35.9$). If the conformation with the O=C−O−C torsional angle of 90° is taken to be an approximation of the transition state for rotation, then these values correspond to free-energy barriers of 10.75 and 12.41 kcal/mol for interconversion of *E* and *Z* conformations, in reasonable agreement with our experimental barriers for acetone-d_6/DMF. The experimental values provide a lower limit to the stabilization of the planar conformations by π bonding, as there is also a significant amount of π bonding in the transition state for rotation, as a consequence of having two lone pairs on oxygen.

E and *Z* populations for **2** could not be determined accurately enough to determine any trend with temperature. Calculated[16] *Z*/*E* ratios of **1** increased from 11.78 to 13.03 as the temperature increased from −50 to + 50 °C and the dielectric constant of the solvent decreased from 47.6 to 32.1 (acetonitrile). Populations of the *E* isomer of *tert*-butyl formate in DMF-d_7 were found experimentally by NMR[17] to be 0.17, 0.319, 0.264, 0.264, and 0.194 at temperatures of −100, −25, +24, +77, and +110 °C, respectively. The increase and then decrease in the population of the *E* isomer were suggested to result from the effect of the decrease in solvent polarity opposing the normal increase in population of the minor conformation with increasing temperature.

Populations, ^{13}C chemical shifts, and $^1J_{C-H}$ couplings were reported[18] for the *E* and *Z* conformations of methyl, ethyl, *n*-propyl, *tert*-butyl, *n*-butyl, isobutyl, and benzyl formate at room temperature and 125 MHz. However, it is actually not possible to see separate signals for *E* and *Z* conformations of alkyl formates under these conditions, and the study is invalid.

Calculated free-energy barriers for 1,3 oxygen-to-oxygen migration of the methyl group in **1** and the CF_3 group in **3** are summarized in Tables 1 and 2. In both



compounds, the barriers generally decrease at higher levels of calculation. Unexpectedly, the barrier for **1** is lower than for **3** (55.3 vs 63.0 kcal/mol at the MP2/6-31+G* level). A barrier of 58.7 kcal/mol for **1** was obtained at the MP2/6-311+G(df,pd) level, but the calculation could not be carried out for **3** at the same level. For silyl esters, electron-withdrawing groups on silicon facilitate the rearrangement,[19] and it is not known at the

(15) An error in temperature and/or rate constants could cause the calculated barriers for methyl formate to be too low. With the program described in footnote 9, we have estimated the range of rate constants that correspond to $\Delta G^{\ddagger} = 7.97$ kcal/mol at −53.15 °C (54 113 to 55 340 s^{-1}). The average of these numbers (54 726 s^{-1}) was used to calculate the temperature (−4 °C) that would give our *E*-to-*Z* free-energy barrier of 9.85 kcal/mol. This result indicates that the temperature in ref 5 would have had to be higher than estimated by about 49 °C in order for an error in temperature to account for the difference between the two barriers. If this same temperature error existed at −83 °C, then the actual temperature would have been about −34 °C, and at this temperature, separate signals for *E* and *Z* conformations could not have been observed. It is unlikely that an error in temperature could entirely account for the difference in free-energy barriers.

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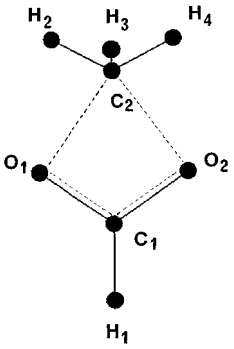

Figure 2. Geometry for the transition state for methyl migration in methyl formate, calculated at the MP2/6-311+G (df,pd) level.

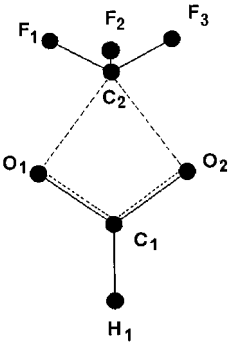

Figure 3. Geometry for the transition state for CF_3 migration in trifluoromethyl formate, calculated at the MP2/6-31+G* level.

present time whether the calculations are in error or whether the silyl esters respond differently to electron-withdrawing groups on the migrating atom. The barriers for **1** and **3** by MINDO/3 were 80.7 and 60.2 kcal/mol,[11] indicating a different order from that found in this work.

The trend toward lower barriers with higher levels observed in Table 1 suggests that the value of 58.7 kcal/mol at the highest level may be an upper limit for this process. Young and Robinson[20] observed by NMR that benzyl [^{13}C-*carboxy*, ^{18}O-*ether*] benzoate rearranges very slowly at 260 °C to the ^{18}O-carbonyl isotopomer and concluded that the calculated free-energy barrier of 45.5 kcal/mol was a lower limit for the intramolecular 1,3 migration of the benzyl group in this compound. These authors also obtained free-energy barriers for similarly labeled derivatives of trimethylsilyl benzoate (18.2 kcal/mol) and trimethylgermyl benzoate (14.2 kcal/mol). A study of dimethyl 2-butylsilylbenzoate indicated[20] that the silyl shift was occurring with retention of configuration, which was consistent with an internal nucleophilic displacement.

Barriers for the 1,3 hydrogen shift in formic acid were calculated[21] to decrease from 51.1 kcal/mol at the HF/6-311G** level to 36.7 kcal/mol at MP2/6-311++G** level, indicating a lower barrier for this process than for methyl migration in **1**.

Table 3. Structural Parameters for the Transition State for Methyl Migration in Methyl Formate, Calculated at the MP2/6-311+G(df,pd) Level and for the Trifluoromethyl Group Migration in Trifluoromethyl Formate, Calculated at the MP2/6-31+G* Level

	transition state	
parameter	methyl formate	trifluoromethyl formate
bond lengths (Å)		
H_1-C_1	1.094	1.085
C_1-O_1	1.250	1.291
C_1-O_2	1.250	1.291
O_1-C_2	1.987	2.019
O_2-C_2	1.987	2.018
C_2-H_2	1.083	
C_2-H_3	1.081	
C_2-H_4	1.083	
C_2-F_1		1.362
C_2-F_2		1.350
C_2-F_3		1.362
bond angles (deg.)		
$H_1-C_1-O_1$	120.32	121.14
$H_1-C_1-O_2$	120.32	121.14
$O_1-C_1-O_2$	119.36	117.73
$C_1-O_1-C_2$	87.43	87.86
$C_1-O_2-C_2$	87.43	87.86
$O_1-C_2-O_2$	65.75	66.51
$H_2-C_2-H_3$	113.57	
$H_2-C_2-H_4$	111.83	
$H_3-C_2-H_4$	113.57	
$F_1-C_2-F_2$		111.05
$F_1-C_2-F_3$		104.11
$F_2-C_2-F_3$		111.05
dihedral angles (deg.)		
$C_1-O_2-C_2-H_3$	93.96	
$C_1-O_2-C_2-F_2$		94.09

Structures for the transition states for **1** and **3** are shown in Figures 2 and 3, and the bond lengths and bond angles are listed in Table 3. The preferred conformations of *Z*-**1** and *Z*-**3** have a C(formyl)OCH or C(formyl)OCF dihedral angle of 180°, but the transition states have a corresponding angle of 94°. Rotation of the CH_3 or CF_3 group occurs during the migration.

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Supporting Information Available: The Cartesian coordinates and total computed energies for the *Z*-conformations and transition states of methyl formate and trifluoromethyl formate for all levels indicated in Tables 1 and 2 are provided. Five low-temperature ^{13}C NMR spectra for methyl formate are also provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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