Use of Gas-Phase ^{1}H NMR to Determine the Kinetics of Unimolecular Rearrangement of 2,2-Dichloro-1-methylenecyclopropane and the Bimolecular Dimerization of (Dichloromethylene)cyclopropane[†]

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Gas-phase ^{1}H NMR analysis has been applied to investigate the kinetics of the unimolecular rearrangement of 2,2-dichloro-1-methylenecyclopropane (**1**) to (dichloromethylene)cyclopropane (**2**) [$k_1 = 7.9 \times 10^{12} \exp(-34.4 \pm 0.6 \text{ kcal mol}^{-1}/RT)$], as well as for the subsequent second-order dimerization of **2** [$k_2 = 2.4 \times 10^6 \exp(-18.5 \pm 1.1 \text{ kcal mol}^{-1}/RT)$] to form 7,7,8,8-tetrachlorodispiro-[2.0.2.2]octane (**3**)

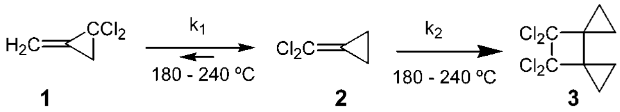
Introduction

Compared to the broad use of liquid-phase NMR as a tool for quantitative monitoring of chemical kinetics, the use of gas-phase NMR until recently was largely limited to studies of physical properties and conformational analysis, including spin relaxation, hydrogen bonding, hindered rotation, tautomerism, etc. As a result of our recent studies utilizing gas-phase ^{19}F NMR, it is now recognized that gas-phase NMR can be an exceptionally effective probe for kinetic studies. In our most recent publication,[1] second order cycloaddition reactions of chlorotrifluoroethylene, tetrafluoroethene, and difluoroallene were examined, with activation parameters of the former two correlating nicely with those reported earlier using classical kinetic techniques. The kinetic data reported for the [2 + 2] and [2 + 4] cycloadditions of difluoroallene with butadiene provided the first reported activation parameters for such allene reactions.

In this paper, we report the first example of the use of gas-phase ^{1}H NMR as a kinetic probe, in this case to examine the kinetics of a unimolecular, methylenecyclopropane rearrangement process, such process being coupled with a slower, bimolecular dimerization of the product of this rearrangement. The activation parameters obtained for the bimolecular process are, to our knowledge, the first such parameters to be reported for dimerization of a methylenecyclopropane compound.

In gas-phase NMR the nuclear spin relaxation, dominated by spin-rotation, plays a dramatic role, allowing one to significantly shorten the time of data acquisition. It also contributes to a broadening of the lines and a consequent lowering of the resolution.[2,3] Fortunately, with its small range of chemical shifts, relaxation times in proton NMR are longer (1−4 s) than those for ^{19}F NMR, which decreases the proton line widths compared to those of fluorine and increases their signal resolution. Thus, a line width of 0.7−1 Hz can routinely be obtained for TMS in the gas phase. In our ^{1}H NMR kinetic experiments, where there is no time for the adjustment of homogeneity of the field for each individual sample prior to its measurement, line widths of 3−6 Hz were usually observed.

Scheme 1



Results and Discussion

Unimolecular Rearrangement. In a reaction that is conveniently followed by gas-phase ^{1}H NMR, the thermal rearrangement of 2,2-dichloro-1-methylenecyclopropane (**1**)[4] leads to virtually complete conversion to (dichloromethylene)cyclopropane (**2**) (Scheme 1) after 15 min at 215 °C.

From data obtained over a range of 215−253 °C, the isomerization of **1** reaches an equilibrium with **2** that contains 93 ± 2.5% of **2** (Figure 1). By comparison, the analogous equilibration between 1,1-*difluoro*-1-methylenecyclopropane and (difluoromethylene)cyclopropane gave an 84:16 ratio of isomers at 236 °C.[5] Rate constants for rearrangement of **1** (k_1) were obtained by observing the disappearance of signals derived from the olefinic $=CH_2$ protons at 5.3 and 5.7 ppm. Although the isomerization rate at 253 °C was too fast for accurate measurement, rate constants for the conversion of **1** to **2** could be obtained at four temperatures. The plots of the data are shown in Figure 2, and the rate constants are given in Table 1.

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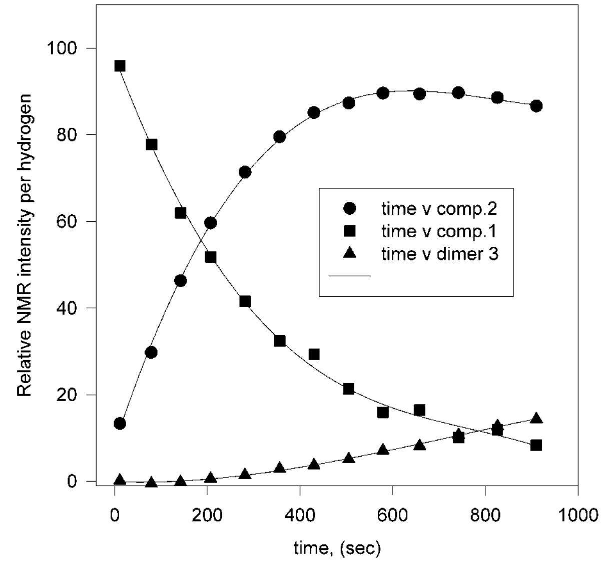

Figure 1. Rearrangement of **1** at 215.3 °C.

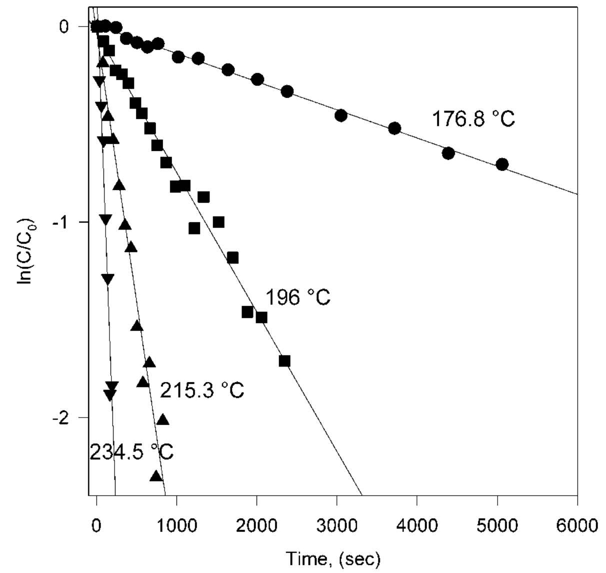

Figure 2. Kinetic plots ln(C/C_0) versus time for disappearance of **1**.

The rearrangement of **1** to **2** obviously proceeds via the intermediacy of trimethylenemethane (TMM) diradicals, as depicted in Scheme 2, [6] and it has been amply demonstrated that the activation parameters of such reactions are strongly influenced by substituents on the cyclopropane ring.[7,8] The rate constants in Table 1 yielded nonextraordinary activation parameters for the conversion of **1** → **2**: log $A = 12.9 \pm 0.3$, $E_a = 34.4 \pm 0.6$ kcal/mol,[9] ($\Delta H^{\ddagger} = 33.4 \pm 0.6$ kcal/mol and $\Delta S^{\ddagger} = -2.5 \pm 1.5$ cal/deg at 480 °K). The observed activation energy is lower than those of either the 2,2-difluoro- or 2,2-dimethyl-substituted analogues (Table 2).[8,10]

Table 1. Rate Constants of 2,2-Dichloro-1-methylenecyclopropane (1) Isomerization (k_1) and (Dichloromethylene)cyclopropane (2) Dimerization (k_2)

T, °C	$k_1 \times 10^4$, s^{-1}	$k_2{}^a \times 10^4$, M^{-1} s^{-1}
176.8	1.44 ± 0.027	50
196.0	7.14 ± 0.21	105
215.3	27.6 ± 1.7	220
234.5	110 ± 8.7	540

[a] k_2 is rate of (dichloromethylene)cyclopropane, **2**, disappearance, reported with average error ± 5%.

Comparing the activation parameters for rearrangement of the “unsubstituted” 2,2-dideuterio-1-methylenecyclopropane system (**4a**) with those for rearrangement of various 2,2-geminally substituted methylenecyclopropanes (2,2-dimethyl- (**4b**), 2,2-difluoro- (**4c**), and 2,2-dichloro- (**1**)), it can be seen that the geminal chlorine substituents facilitate this rearrangement best of those substituents studied. With respect to fluorine, this result is consistent with chlorine’s greater ability to stabilize radicals. For example, two fluorine and two chlorine substituents have been calculated to stabilize a methyl radical by 0.56 and 7.0 kcal/mol, respectively.[11] Interestingly, two methyl substituents (in substrate **4b**) do not appear to facilitate the methylenecyclopropane rearrangement to the extent that would be expected on the basis of their predicted 5.8 kcal/mol radical stabilization.[11] However, this apparent lack of influence has been demonstrated to derive from the relative stability of the two isomeric orthogonal TMM diradical intermediates that are involved in converting **4b** to **5b**, with the methylene group bearing the two methyl substituents having difficulty to become planar and preferring to play the role of the orthogonal, “pivot” carbon.[6] Indeed, when one looks at the activation parameters for the degenerate rearrangement of **4d** in which the two methyl substituents remain on the pivot carbon,[8] one can see that the methyls certainly do enhance homolysis to the TMM diradical as expected on the basis of their radical-stabilizing ability.

Dimerization Process. The rate of rearrangement of **1** increases faster with temperature than does the rate of dimerization of **2**. Therefore, it was possible to perform the controlled in situ conversion of **1** to **2** in NMR tubes at temperatures 215 °C or higher and then to distinctly observe the subsequent dimerization of **2**. Within the temperature range and under the specific concentration conditions that were used, the unimolecular rearrangement of **1** to **2** was always much faster than the bimolecular dimerization of **2** to **3** (Figure 1). For example, at the highest temperature used, where the two rates were most competitive, equilibration of **1** and **2** was essentially complete after 4 min, with only 6−8% of dimer **3** having been formed.

The kinetics of dimerization of **2** to form 7,7,8,8-tetrachlorodispiro[2.0.2.2]-octane, **3**, were determined by monitoring the disappearance of the four-proton (cyclopropane) signal of **2** at 1.22 ppm. The dimerization is quantitative, giving a 99% NMR yield of dimer **3**, and

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(6) Doering, W. v. E.; Roth, H. D. *Tetrahedron* **1970**, *26*, 2825.

(7) Creary, X.; Engel, P. S.; Kavaluskas, N.; Pan, L.; Wolf, A. *J. Org. Chem.* **1999**, *64*, 5634−5643.

(8) LeFevre, G. N.; Crawford, R. J. *J. Org. Chem.* **1986**, *51*, 747−749.

(9) Values were obtained from the Arrhenius plot by taking into account the weight of variance of each measured rate (see Table 1). Values for k_1 at the higher temperatures have larger error because fewer points were able to be obtained, and these rate constants are therefore less reliable. If each k_1 value were used with the same weight, the following activation parameters would be obtained: log $A = 12.6 \pm 0.2$ and $E_a = 33.8 \pm 0.5$.

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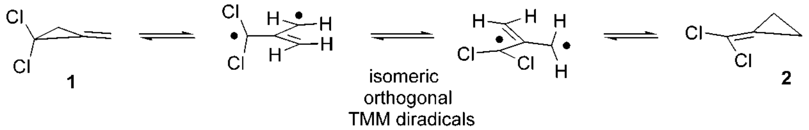
Scheme 2



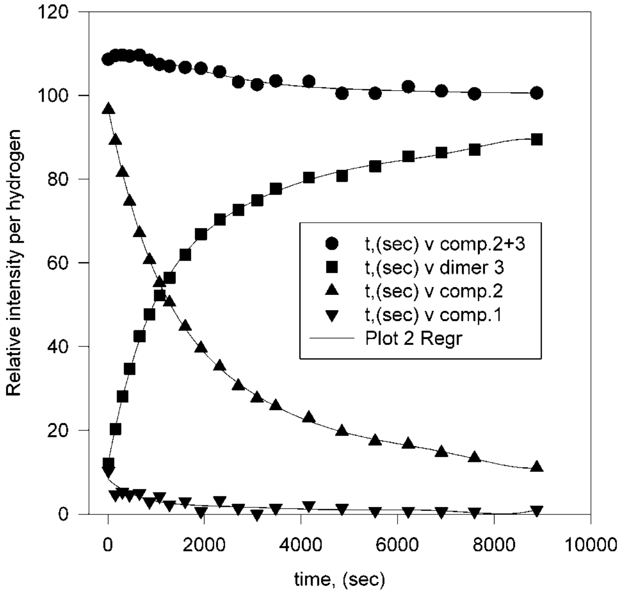


Figure 3. Dimerization of **2** at 234.5 °C.

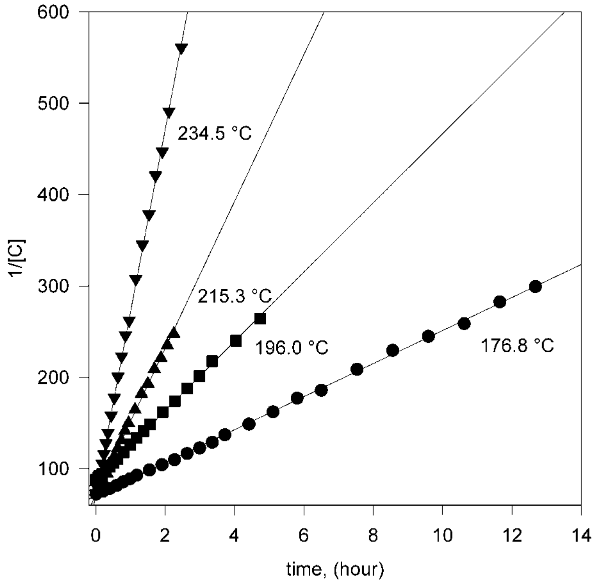
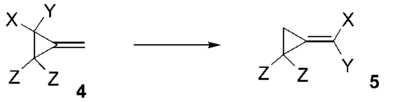


Figure 4. Kinetic plots 1/[*C*] versus time for disappearance of **2**.

Table 2. Comparison of Activation Parameters of 2,2-Disubstituted-1-methylenecyclopropanes



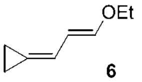
	log *A*	E_a[a]	$\Delta G^{\ddagger\,a,b}$	ref
4a: X = Y = D; Z = H	14.4	41.2	39.9	8
4b: X = Y = CH_3; Z = H	14.9	42.0	38.3	8
4a: X = Y = F; Z = H	13.2	38.3	37.7	10
1: X = Y = Cl; Z = H	13.3	34.4	34.5	this work
4d: X = Y = D; Z = CH_3	14.5	38.5	35.9	8

[a] Kcal/mol. [b] At 180 °C.

the ratio of **1**:**2** remained 7 ± 2.5% to 93 ± 2.5% throughout the dimerization kinetic runs. The presence of the small amount of **1** during dimerization was neglected in the kinetic analysis. Figure 3 shows the concentration **1**, **2**, and **3** versus time, Figure 4 shows the kinetic plots that were obtained from the data, and the rate constants are given in Table 1.

From the rate data in Table 1, the activation parameters for the dimerization of **2** were determined to be: log $A = 6.38 \pm 0.48$, $E_a = 18.5 \pm 1.1$ kcal/mol ($r^2 = 0.997$); $\Delta H_c^{\ddagger} = 17.5 \pm 1.1$ kcal/mol, $\Delta S_c^{\ddagger} = -34.3 \pm 2.2$ cal/deg.[12-14]

The log *A* and related entropy of activation values are in the range considered normal for [2 + 2] cycloadditions, whereas the observed activation energy appears to be unusually low. For example, tetrafluoroethylene and chlorotrifluoroethylene, which are generally considered to be relatively reactive [2 + 2] substrates, have identical activation energies for dimerization of 26.5 kcal/mol.[1] Among methylenecyclopropane substrates, the dichloromethylene compound (**1**), which dimerizes readily at temperatures as low as 100 °C, is much more reactive than the parent, methylenecyclopropane, which requires temperatures >245 °C to dimerize,[15] the monochloromethylene compound, which requires >185 °C,[16] or (difluoromethylene)cyclopropane, which requires temperatures >300 °C to dimerize.[17] Other methylenecyclopropane derivatives that dimerize under conditions similar to those required for **2** are compounds **6** and **7**, which dimerize to dispiro[2.0.2.2]octane products at 60 and 120 °C, respectively.



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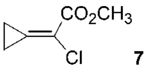

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The observed kinetic parameters for **2** are in agreement with its dimerization proceeding through the stepwise, diradical mechanism depicted in Scheme 3, such mechanism being consistent with orbital symmetry considerations as well as with most experimental data related to [2 + 2] cycloadditions.[18,19]

The low E_a for dimerization of **1** can be explained largely on the basis of the relief of strain (~10−12 kcal/

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(12) $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are calculated at 480 °K. The log *A* and $\Delta S^{\ddagger}$ values are derived from the rate of dimer formation: $k_{(\mathrm{formation})} = k_{(\mathrm{olefin\ disappearance})}/2$.

(13) According to ref 14, pp 8−11, 146. For 1 mol/L standard state $A_c = (k_BT/h)\,e^2 \exp(S_c^{\ddagger}/R)$ and $H_c^{\ddagger} = E_a - RT$.

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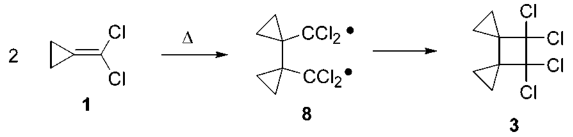
(18) Kienzle, F.; Stadlwieser, J. *Tetrahedron Lett.* **1991**, *32*, 551−552.

(19) Liese, T.; Teichmann, S.; de Meijere, A. *Synthesis* **1988**, 25−32.

Scheme 3



mol) that occurs during the rate-determining formation of diradical intermediate **8** (Scheme 3). Diradical **8** is considerably more stable than the alternative radical that would be formed by initial bond formation at the CCl_2 site.

Conclusion

Gas-phase ^{1}H NMR analysis was applied to study the unimolecular methylenecyclopropane rearrangement of 2,2-dichloro-1-methylenecyclopropane, as well as the bimolecular dimerization of (difluoromethylene)cyclopropane, the product of this isomerization. This kinetic technique therefore proved to be convenient for obtaining useful kinetic data from sequential kinetic processes.

Experimental Section

Materials. 2,2-Dichloro-1-methylenecyclopropane was prepared according to the earlier developed method. [4,20]

NMR Analysis. ^{1}H NMR spectra were measured using a GE 300-MHz instrument with a 10-mm high-temperature (up to 390 °C) probe using 10-mm ampules (approximately 5 cm in length and constant volume, ca. 3.8 mL) with a short coaxial 5-mm tube extension, as described earlier.[1,21] For acquiring one point in the ^{1}H NMR spectrum, 4−16 scans were accumulated with pulse delay of 1−3 s. Simple peak area integration was used to obtain the NMR signal intensity.

The sample loading procedure has been previously described.[1]

Kinetic Data Acquisition and Processing. The concentration of **1** was determined from the sum of integrals of the $=CH_2$ protons in ^{1}H NMR at δ 5.3 (1H) and 5.7 ppm (1H). To obtain the rate of rearrangement k_1, $\ln(A/A_0)$ was plotted versus time (Figure 2).

Dimerizations of (dichloromethylene)cyclopropane (**2**) were examined in separate kinetic runs that began after the equilibrations of **1** and **2** were essentially complete. The rate constants (k_2) for the disappearance of **2** were obtained following the disappearance of the four-proton cyclopropyl hydrogen singlet of **1** in its ^{1}H NMR spectrum at δ 1.22 ppm. The yields (92−97%) of dimer **3** were determined by measuring the growth of one of the four-proton triplet cyclopropyl signals of the product, δ 0.4 ppm. Dimerization rate constants that were obtained by monitoring such growth were only 1−8% lower than those reported in Table 1, and since the data at each temperature were similarly affected, activation parameters derived from such data did not deviate significantly from those reported. The second dimer four-proton cyclopropyl signal at 1.0 ppm (4H) was not baseline resolved, and it was therefore not used for integration. The rate constants (k_2) were obtained by plotting $1/C$ versus time according to the equation $1/C = k_2t + 1/C_0$ (Figure 4). Rates constants k_1 and k_2 are given in Table 1. The kinetic parameters for the dimerization ($\log A$ and $\Delta S^{\ddagger}$) were derived from the rates of dimer formation calculated.

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[20] The 2,2-dichloro-1-methylenecyclopropane that was used for the kinetic study contained 66% of ethyl methyl carbonate (peaks in ^{1}H NMR at δ 4.0, 3.5, and 1.05 ppm) and a water impurity that contributed to the signal at δ 1.75 ppm. It is significant that there was no detrimental impact on the kinetic study as a result of the presence of these impurities in the sample.

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