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Thermal Isomerizations of 1-^{13}C-2,2,3,3-d_4-Cyclopropane to Isotopically Labeled Trimethylene Diradicals, 1-Propylidenes, and Propenes

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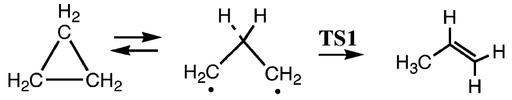
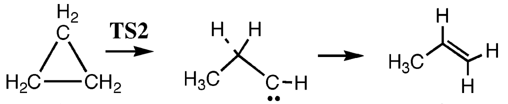
The unimolecular conversion of cyclopropane (**1**) to propene (**2**) has been known longer, and investigated in more detail, than any other thermal isomerization.[1,2] Detailed investigations of this reaction linking one C_3H_6 species to another have been unusually rewarding as they have led to fundamental understandings of reaction dynamics and mechanistic subtleties.[3] Experimental and theoretical studies have supported a mechanistic consensus: the overall reaction involves a reversible isomerization of **1** with the trimethylene diradical (**3**), which is transformed in the rate-determining step to **2** through a [1,2]-hydrogen shift.



1 **3** **2**

Another conceivable path, from **1** to singlet 1-propylidene (**4**) directly in the rate-determining step, followed by an extremely facile [1,2]-hydrogen shift to form **2**, has been considered but not supported experimentally.



1 **4** **2**

Theory-based consideration of the path through 1-propylidene has progressed in stages. An early 1974 theoretical assessment of the reaction path linking **1** with **4** located the transition structure (**TS2**) and placed it only 1.4 kcal/mol above the heat of formation of **4**.[4] The MINDO/2 calculations did not lend support to the proposition that mechanistic option **1** → **4** → **2** could be of kinetic significance. Better calculations by Doubleday in 1996 estimated the energy gap between **TS1** and **TS2** to be 5.46 kcal/mol.[5,6] Rate constant calculations suggested a kinetic advantage of 2 orders of magnitude for the **TS1**-mediated path relative to the **1** → **4** → **2** alternative.

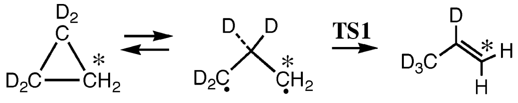
The most recent calculations at a still higher level of theory suggested that the **1** → **4** → **2** path might not be energetically incredible. Using ab initio coupled cluster methods the pathway through 1-propylidene was found to be only slightly higher in energy than the traditional path through the trimethylene diradical: $\Delta\Delta E_a = 2.4$ kcal/mol.[7] The propylidene-mediated path might be kinetically competitive and detectable experimentally. This possibility and the suitability of the several theoretical methods that have been used to examine the mechanistic question have been probed through an isotopic labeling experiment.

The labeled system selected for this study was 1-^{13}C-2,2,3,3-d_4-cyclopropane (**1**-^{13}C, d_4). It may be prepared easily. It does not present complications related to thermal stereomutations of the cyclopropane, for all possible one-center and two-center thermal epimerizations are cryptic. Finally, a clear analytical strategy for detecting distinct outcomes for the two possibly competitive reaction paths leading to labeled propenes in product mixtures could be discerned.

The labeled cyclopropane was prepared from diethyl malonate-2-^{13}C through reduction with $LiAlD_4$ followed by conversion of the labeled 1,3-propanediol to labeled 1,3-dibromopropane through reaction with 48% HBr and concd H_2SO_4.[8] The labeled 1,3-dibromopropane had a ^{1}H NMR spectrum with only two equal intensity absorptions, the two components of the doublet for $^{13}C(2)H_2$ at 2.548 and 2.115 ppm at 300 MHz ($J_{13C-H} = 130$ Hz). Proton absorption intensity at 3.54 ppm was ~1.5% of the $^{13}C(2)H_2$ intensity, indicative of a minor d_3-component. Finally treatment of the dibromide with zinc dust in aqueous ethanol gave the labeled cyclopropane, which was purified by preparative GC.[9] Its $^{13}C\{^1H\}$ NMR spectrum showed a single peak at −3.66 ppm; $^2J_{13C-D}$ coupling was not apparent.

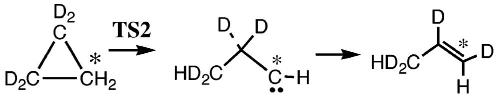
Three gas-phase thermal isomerizations of **1**-^{13}C, d_4 were run at 435 °C for 20, 21, and 42 h with total pressures of 94 to 133 Torr in a static reactor with cyclopentane as a bath gas. Reaction mixtures were collected, diluted with $CDCl_3$, sealed in NMR tubes, and analyzed by ^{13}C NMR at 151.2 MHz with inverse gated proton decoupling and 10 s pulse delays. Of particular interest was the region near 116 ppm for the $^{13}C(1)H_2$ or $^{13}C(1)HD$ absorptions from propene products.

For propene product formed through a trimethylene diradical intermediate and **TS1**, the $^{13}C(1)H_2$ NMR signal with proton decoupling can only be a singlet; the resonance would be expected[10] at about 0.13 ppm upfield from the chemical shift recorded for C(1) in unlabeled propene, 116 ppm.[11]



1-^{13}C, d_4 **3-^{13}C(1)-2,2,3,3-d_4** **2-^{13}C(1)-2,3,3,3-d_4**

For the path through a 1-propylidene intermediate, the $^{13}C(1)HD$ NMR signal for the propene product would be a 1:1:1 triplet, centered about 0.27 ppm upfield from the resonance seen for $CD_3CD{=}{*}CH_2$ and characterized by a $^1J_{13C-D}$ coupling constant of 24 Hz. The *E* and *Z* isomers of **2**-^{13}C(1)-1,2,3,3-d_4 would have nearly identical ^{13}C NMR spectra: the two C(1) $^1J_{13C-H}$ coupling constants in propene are 153.1 and 157 Hz,[11] corresponding to $^1J_{13C-D}$ values of 23.5 and 24.1 Hz, for the γ_H/γ_D ratio is 6.514.



1-^{13}C, d_4 **4-^{13}C(1)-2,2,3,3-d_4** **2-^{13}C(1)-1,2,3,3-d_4**

The mixture of labeled propene isomerization products showed $^{13}C\{^1H\}$ NMR signals for **2**-^{13}C(3)-1,1,2,3-d_4, a product expected

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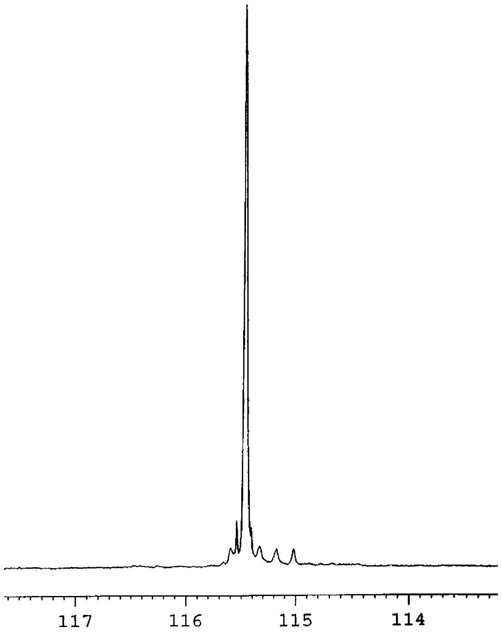

Figure 1. Proton-decoupled ^{13}C NMR spectrum of the methylene carbon signals from labeled propenes formed through thermal rearrangements of **1**-^{13}C, d_4. The singlet at 115.467 ppm is consistent with $*CH_2{=}CD{-}CD_3$. The 1:1:1 triplet ($^1J_{13C-D} = 24$ Hz) centered at 115.177 ppm is consistent with 1-^{13}C-1,2,3,3-d_4-propene. All three kinetic runs gave nearly identical spectra for product mixtures; unreacted **1**-^{13}C, d_4 was unscrambled.

from both paths. The 1:1:1 triplet was centered at 18.71 ppm with $^1J_{13C-D} = 19.5$ Hz. A very weak singlet at 18.98 ppm was ascribed to some $CD_2{=}CD{-}*CH_3$ derived from the trace of d_3-labeled starting material. No $CHD{=}CD{-}*CHD_2$ component was seen.

The ^{13}C(2)H resonance was observed at 133.66 ppm, just 0.34 ppm upfield from the chemical shift reported for propene,[11] consistent with the product being predominantly 1,1,3,3-d_4. The estimated deuterium isotope effect on the ^{13}C chemical shift for this isotopomer would be about 0.33 ppm.[10]

The proton-decoupled ^{13}C(1) NMR spectra for propene products showed both 2,3,3,3-d_4 and 1,2,3,3-d_4 isotopomers; the singlet expected for the first and the triplet uniquely characteristic of the second were both in evidence (Figure 1).

The singlet at 115.467 and the triplet centered at 115.177 ppm matched expectations; the difference, 0.29 ppm, compares well to a prediction based on deuterium isotope effects on ^{13}C chemical shifts in ethene-d, 0.274 ppm.[10] The intensity ratio recorded was 89:11. The $^1J_{13C-D}$ constant was 24 Hz, just as projected. The minor broad singlet at 115.596 seen in Figure 1 may be a trace amount of $*CH_2{=}CH{-}CD_3$ derived from d_3-labeled starting material. The difference in chemical shift downfield from the strong singlet, 0.129 ppm, is very close to the deuterium-induced chemical shift perturbation at C2 reported for ethene-d, 0.131 ppm.[10] The small sharp singlet at 115.542 is an artifact contributed by thermal decomposition of the bath gas; it varied in relative intensity from run to run, in parallel with initial ratios of cyclopentane to labeled cyclopropane.

Thus, the thermal isomerization of **1**-^{13}C, d_4 leads to isotopically labeled propene products consistent with both the commonly accepted mechanistic path involving trimethylene diradical intermediates and the theoretically predicted kinetically competitive and heretofore undemonstrated path through transient 1-propylidene intermediates. The $\mathbf{1} \rightarrow \mathbf{2}$ isomerization takes place through two distinct mechanistic paths, taking advantage of two reaction channels of similar free-energy requirements.

Attempts to uncover thermal isomerizations of deuterium-labeled 1,1-dimethylcyclopropane taking place through *tert*-butylcarbene or isobutylcarbene failed to provide any evidence implicating them as mechanistically significant intermediates.[12] The factors influencing possible cyclopropane-to-propylidene thermal transformations in substituted systems remain to be clarified through theory and experiments, and possibly related reactions of cyclopropene and silacyclopropanes merit reconsideration.[13]

In his 1882 paper reporting the first synthesis of cyclopropane, Freund explicitly considered 1-propylidene as a possible structure for his newly prepared C_3H_6 compound.[14] Cyclopropane and 1-propylidene have been closely associated from the beginning! That **1** rearranges thermally to **4** may be viewed with surprise, given the extended scrutiny the **1**-to-**2** isomerization has attracted over more than a century. The present experimental work supports the prediction based on coupled cluster methods in 1999[7] and re-emphasizes the ineluctable fact that the level of theory used needs to be appropriate to the issue being addressed if reliable predictions are to be attained.

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