

one of the criteria for a mechanism-based inhibition of PFL by **1** have been fulfilled.¹¹

A proposal explaining these phenomena is outlined in Scheme I (path B). We suggest that **1** is recognized by PFL as a catalytically viable pyruvate analogue.¹² Homolysis of the C-P bond from the putative tetrahedral intermediate affords acetyl-PFL containing a quenched enzyme radical and the hypophosphoryl radical anion. This complex (**2**), essential equivalent to one generated by hypophosphite with active acetyl-PFL, can partition between inactivation involving the hypophosphoryl radical anion and regeneration of the enzyme-bound radical with concomitant formation of hypophosphite. Dissociation of hypophosphite leaves the enzyme in its active acetylated form which is protected against further inactivation by **1** until deacylation occurs. Dithiothreitol (DTT; 4 mM), present in the reaction mixture, causes a slow deacylation, accounting for the biphasic kinetics with **1** alone. Formate or CoA causes a rapid deacylation affording active PFL which is available for additional cycles of inactivation/protection by **1** until complete inactivation is achieved.

A key prediction of this hypothesis is the formation of pyruvate from **1** and formate during the cycling to inactivation. Preliminary studies with [¹⁴C]formate and unlabeled **1** have shown that inactivation is accompanied by the formation of 5 enzyme equivalents of [¹⁴C]pyruvate, suggesting ~5 turnovers per inactivation and verifying C-P bond cleavage. The inhibition of PFL by **1** differs significantly from its reversible, slow, tight-binding inhibition of pyruvate dehydrogenase.¹⁴ In this case, a dead-end complex between **1** and thiamine pyrophosphate is formed which cannot heterolytically dephosphinylate.

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Evidence of Vibrational Mode Coupling in 2-Fluoroethanol via High-Resolution Infrared Spectroscopy in a Molecular Beam

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The rotationally resolved spectrum of 2-fluoroethanol (2FE) has been measured to determine the extent of mode-selective vibrational coupling. The photoisomerization of 2FE in low-temperature matrices has been studied extensively.¹⁻¹⁰ By excitation of the OH or CH stretch in matrix-isolated 2FE it is possible to induce isomerization from the more stable Gg' to the Tt conformer. Controversial evidence from some experiments suggests that mode-selective vibrational coupling occurs between hydrogen stretching modes and modes that participate in the Gg'-to-Tt isomerization of 2FE.¹⁻⁴ The relative quantum efficiencies for isomerization in an Ar matrix show that excitation

of the OH stretch is 7 times more efficient in inducing isomerization than excitation of a CH stretch.⁴ Thus far, studies have failed to determine conclusively whether the discrepancy in isomerization efficiencies is caused by mode-selective coupling of the hydrogen stretches to the isomerization coordinate¹⁻⁴ or by matrix effects involving the surrounding media.⁸⁻¹⁰ By examining 2FE in a molecular beam we remove the ambiguity of the environmental effects, and the role of mode-selective coupling can be definitively and quantitatively evaluated.

High-resolution infrared spectroscopy in molecular beams measures the degree of vibrational coupling by identifying the molecular eigenstates directly. The molecular eigenstates in larger molecules are often superposition states of the zeroth-order vibrational states. The number and intensities of the transitions present in a rotationally resolved spectrum provide a direct measurement of the extent of mixing between different vibrational modes. de Souza, Kaun, and Perry first used high-resolution infrared spectroscopy to determine the molecular eigenstates in 1-butyne,^{11,12} and this study was later extended by McIlroy and Nesbitt.^{13,14} The spectra of McIlroy and Nesbitt clearly resolve transitions to many molecular eigenstates within the acetylenic stretch of 1-butyne. From analysis of the spectra it was determined that extensive coupling occurs between vibrational modes. Since 2FE is of a similar size and has a similar density of states, mode coupling should be spectrally apparent in 2FE as well. The extent of the coupling would be expected to correlate with the rate of the isomerization, if mode-selective coupling does in fact determine the rate of isomerization.

The rotationally resolved spectrum of the asymmetric CH stretch of the fluorinated carbon³ was measured covering the spectral region from 2978 to 2989 cm⁻¹ with a spectral resolution of 12 MHz. The experimental apparatus will be described in detail elsewhere¹⁵ but, briefly, consisted of a color-center laser pumped by a dye laser, which in turn was pumped by an argon ion laser. The laser was crossed with a skimmed molecular beam. The method of optothermal detection was used after the design of Miller and co-workers.¹⁶ Helium carrier gas at a pressure of 6 psig was passed over the liquid sample of 2FE and expanded through a nozzle of 50- μ m diameter.

To analyze the data, our experimental spectrum was compared to a calculated spectrum, using a rigid rotor model and exact diagonalization of the rotational Hamiltonian.¹⁷ The details of the data analysis, as well as a complete discussion of the results of this analysis, will be presented elsewhere.¹⁵ When the fit is optimized, there are more peaks in the experimental data than are calculated by using the rigid rotor model. The additional peaks are characteristic of vibrational mode coupling. Many, although not all, of the individual peaks in the calculated spectrum correspond to a small cluster of peaks in the experimental data. A cluster of peaks result when the intensity of a single peak from one vibrational mode is distributed over a number of vibrational modes. Thus, the presence of clusters of peaks is indicative of the presence of vibrational mode coupling between the asymmetric CH stretch and other vibrational modes in 2FE.

The extent of mode coupling was determined from the intensities and the spacing of peaks within a cluster of peaks. The number of peaks in the cluster depends on the density of states, as well as the degree of mixing between the optically active light state and the manifold of dark states. From the location and intensities of the individual transitions in a cluster of peaks, we can evaluate the magnitude of the matrix element which couples the light state to specific individual dark states. Note that the average separation

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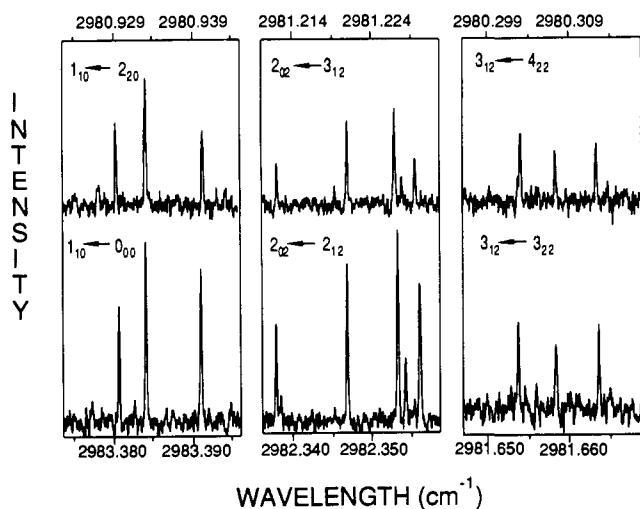


Figure 1. Each panel in the figure shows two sets of transitions to the same excited state. The transitions are labeled with the J , K_a , and K_c quantum numbers as J_{K_a, K_c} corresponding to the labels of the zeroth-order uncoupled states. The left panel shows two sets of transitions to the 1_{10} excited state. The middle and right panels are to the 2_{02} and 3_{12} excited states, respectively. In each case the similarity of the patterns of peak positions and intensities is apparent, demonstrating the presence of vibrational mode coupling.

between the peaks in these clusters is 0.004 cm^{-1} . Therefore, the magnitude of the matrix element need not be very large in order to have a significant effect in mixing states.

To verify that a cluster of peaks is, in fact, caused by mixing of states, one can compare two sets of transitions to the same excited state. The same pattern of peak spacing and intensities should appear for two different transitions to the same excited rotational state. Shown in Figure 1 are several spectral regions consisting of pairs of transitions to the same excited state. The similarity of the patterns is apparent, and we conclude that mode coupling is causing these clusters of peaks.

From a simple state-counting algorithm that treats the normal modes in 2FE as harmonic oscillators,¹⁸ with the exception that the C-C torsion and the O-H torsion are treated as hindered rotors,¹⁹ 2FE has 58 states/ cm^{-1} in the CH stretching region. With this density of states, virtually all modes must be coupled to the optically active mode. The fact that all modes appear to couple to the optically active mode is similar to the results of previous studies of terminal acetylenes.^{13,14} In contrast, however, the average matrix element that couples the asymmetric CH stretch to other modes is $0.0029 \pm 0.0011 \text{ cm}^{-1}$, which is a factor of 2-3 smaller than those calculated for the terminal acetylenes.¹⁹ The small magnitude of the matrix element in 2FE relative to butyne is particularly surprising given that the acetylenic CH stretch would be expected to couple poorly to the other modes in butyne, as the authors note. The small amount of coupling in 2FE is consistent with the slow rate of isomerization observed when this CH stretch was excited in a matrix. Further experiments are necessary to fully quantify the relationship between mode coupling and isomerization rates. In particular, the high-resolution infrared spectrum of the OH stretch is essential for comparison with the current high-resolution spectrum of the CH region. One might expect that the mode coupling would be more substantial in the OH stretch to account for the faster reaction rate upon excitation of this mode in matrices. Such experiments are currently underway in our laboratory. The results presented here demonstrate

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the power of high-resolution spectroscopy to resolve the controversy surrounding the role of mode-selective chemistry in the isomerization reaction of 2FE.

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Rhodium(II) Acetate Catalyzed Alkyne Insertion Reactions of α -Diazo Ketones: Mechanistic Inferences

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Readily prepared α -diazo ketones bearing tethered alkyne units have shown potential for the construction of polycyclic skeletons.^{2,3} Exposure of compounds like **1** (Scheme I) to a variety of transition-metal catalysts results in cycloisomerization of an initially formed α -keto carbene (**2**) to an intermediate in which carbene-like reactivity has been transferred to one of the alkyne carbons (cf. **3** and/or **5**). A second strategically disposed functional group G may then trap this monocyclic intermediate via known carbene chemistry⁴ to give various products. The specific role of certain metals throughout this type of transformation has been of interest to us. We report here the results of a study that addresses the fundamentally important mechanistic question of whether the metal moiety actually migrates to the alkyne carbon in the $\text{Rh}_2(\text{OAc})_4$ -catalyzed reactions of **1**.

Likely metal-containing intermediates lie within the continuum represented by **2-5**.⁵ We recognized that this manifold could also be entered from the vinylogous α -diazo ketones **6**. Presumably the distribution of products arising via **3**⁶ would be different from that via **5**. If metal migration were to occur in the conversion of **1**, then the reactions of isomeric **1** and **6** would both proceed via the common intermediate **5** and identical product distributions would result. Such is not the case; distinctly different product distributions arise. This strongly implies that migration of rhodium

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