boxylic acids (**7**) was effected nearly quantitatively, and all the possible isomers were separable on TLC. The isomeric mixture of **7** was converted into the imidazolides[6e,f,14] and then into the benzenethiol esters, and subsequent oxidation with MnO_2[15] provided the protected thiol esters (**3**) of the tylonolide seco-acid. Treatment of **3** with mercury (II) methanesulfonate[6d] in the presence of Na_2HPO_4, followed by acetic acid hydrolysis, afforded an approximately 17% yield of the product, identical in every respect with **2**. A yield of this magnitude is very gratifying in that, in addition to complicated conformational problems (vide supra), the lactonization did indeed compete favorably with the β-lactone formation. The latter reaction which proceeds in the absence of other hydroxy compounds in the reaction medium was fortuitously found during the course of model studies and represents a means of synthesizing β-lactones from ketones and aldehydes conveniently and in excellent yields. A brief summary of the synthesis is given below.

The benzenethiol esters of β-hydroxycarboxylic acids (**8** and **9**), prepared from cyclohexanone (94%) and nonanal (80%) using the lithium salt of *S*-phenyl ethanethioate,[16] were reacted with 2 equiv of mercury. (II) methanesulfonate (0.07 M in acetonitrile) in the presence of 8 equiv of Na_2HPO_4 at 25 °C for 10 min to provide the corresponding β-lactones (**10** and **11**) in 86 and 90% yields, respectively. Although we have not examined other substrates, the generality of this reaction is obvious. Quantitative conversion of β-lactones to alkenes has been well-documented.[7,17,18]

Supplementary Material Available: A listing of spectral data (3 pages). Ordering information is given on any current masthead page.

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(13) When the C-3 hydroxy group was protected with the *tert*-butyldimethylsilyl group, the lactone opening required more drastic conditions and was accompanied by extensive dehydration to give α,β-unsaturated carboxylic acids.
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(17) Spectral data of all the compounds described in this note appear in the microfilm edition of this journal and experimental details will be available upon request.

(18) The authors thank Dr. P. E. Georghiou for his preliminary work on this project and the National Research Council of Canada for financial support.

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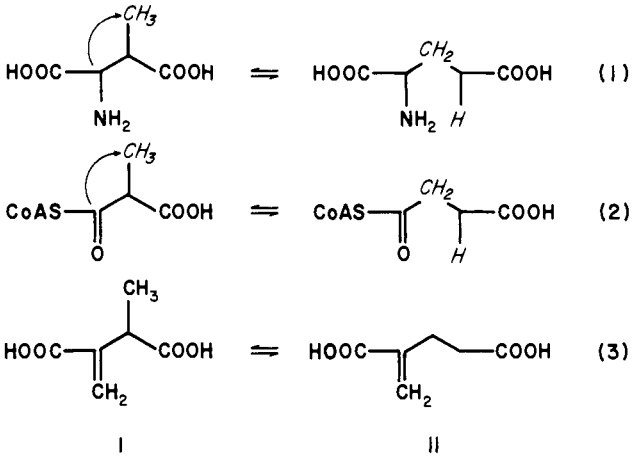
Vitamin B_{12} Model Studies. Migration of the Acrylate Fragment in the Carbon-Skeleton Rearrangement Leading to α-Methyleneglutaric Acid

Sir:

Coenzyme B_{12} is an essential cofactor in the three known enzyme-catalyzed carbon-skeleton rearrangements.[1] They are the reversible interconversions: β-methylaspartate $\rightleftarrows$ glutamate[2] (eq 1), methylmalonyl-SCoA $\rightleftarrows$ succinyl-SCoA[3] (eq 2), and methylitaconate $\rightleftarrows$ α-methyleneglutarate[4] (eq 3). It has been established by carbon labeling that the glycyl fragment migrates in the β-methylaspartate rearrangement[5] and that the carbonyl-SCoA group migrates in the methylmalonyl-SCoA rearrangement.[6] It has also been established that exchange with solvent water does not occur in the course of the rearrangements.[7] The latter observation was made understandable by the discovery[8] that the 5′-methylene of the deoxyadenosine of the coenzyme is the instrument of hydrogen transfer in all the coenzyme B_{12} dependent carbon-skeleton rearrangement reactions.

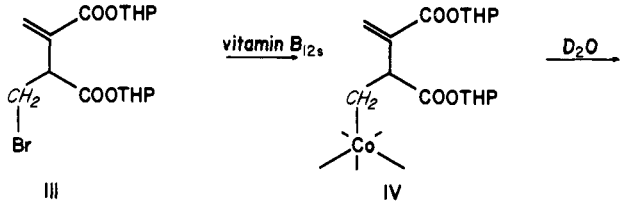


I II

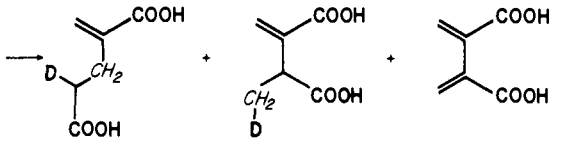
A nonenzymatic model intermediate (IV) for the methylitaconate $\rightleftarrows$ α-methyleneglutarate transformation (eq 3) has recently been introduced.[9] The model intermediate IV was synthesized by the reaction of vitamin B_{12s} with bis(tetrahydropyranyl) bromomethylitaconate (III). On standing in aqueous solution the model IV yields rearranged α-methyleneglutaric acid (II) together with unrearranged methylitaconic acid (I) and butadiene-2,3-dicarboxylic acid (VII).[9] Thus, I and II are the products of a reduction reaction. Since, the model reaction provides no role for deoxyadenosine, it was important to learn the source of the hydrogen introduced into the products I and II.

When the crude dry alkyl cobalamin IV was dissolved in D_2O and allowed to stand at 25 °C, in the dark, under nitrogen, for 200–300 h, at pH 5–9,[10] deuterium was incorporated into the products (V and VI).

The butadiene-2,3-dicarboxylic acid (VII) contained no deuterium as shown by its NMR and mass spectra. By con-



III IV

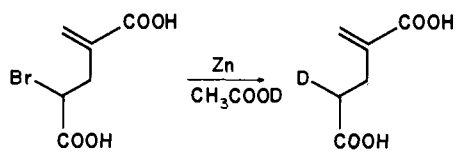


V VI VII

trast, the NMR spectrum (acetone-d_6) of methylitaconic acid (VI) showed two one-proton vinyl singlets at τ 3.70 and 4.22, a one-proton methine *triplet* at τ 6.41 (J = 6.5 Hz) and a *two*-proton methyl doublet (J = 6.5 Hz) at τ 8.63. The mass spectrum (70 eV) of VI showed molecular ion peaks at *m/e* 145 and 144 with intensities corresponding to 82% methylitaconic acid-d_1 (VI). The identity of VI was fully confirmed by comparison with an authentic sample synthesized by reduction of bromomethylitaconic acid III using zinc in acetic acid-*O*-*d*.

The presence of one atom of deuterium in the rearranged product, α-methyleneglutaric acid (V), was established by mass spectrometry. Although the molecular ion is extremely weak in both the 15 and 70 eV spectra of II and V, the extent of deuterium incorporation can be judged using the base peak which occurs at *m/e* 98 ($M^+ - H_2O - CO$; exact mass: calcd for $C_5H_6O_2$, 98.0368; found, 98.0352) in the undeuterated authentic sample V and at *m/e* 99 ($M^+ - H_2O - CO$; exact mass: calcd for $C_5H_6DO_2$, 99.043 06; found, 99.043 06) in the product V from reaction in D_2O. By this means it was estimated that the product contains 88% α-methyleneglutaric acid-d_1 (V). The NMR spectrum of V showed one-proton vinyl multiplets at τ 3.76 and 4.30 together with a *three*-proton aliphatic singlet at τ 7.44. In the 250-MHz NMR spectrum of V the apparent singlet at τ 7.44 is split into a multiplet, the high field portion of which is reduced in intensity by half in comparison with that of the undeuterated α-methyleneglutaric acid (II). It is thus established that the carbon–cobalt bond in the model series[9] is hydrolyzed by proton transfer from the solvent water.[11]

The most vital question to be answered is that of the position of the deuterium atom in the rearranged product V. In view of the almost negligible difference in chemical shift between the β- and γ-methylene protons in the α-methyleneglutarate II (0.1 ppm at 250 MHz), recourse was made to the carbon-13 NMR spectrum and to an authentic sample of α-methyleneglutaric acid-γ-d_1 (V). The latter was prepared by reduction of γ-bromo-α-methyleneglutaric acid (VIII)[12] using zinc in



VIII V

acetic acid-*O*-*d*. The product V is characterized by a carbon-13 NMR spectrum (D_2O, proton decoupled, Me_4Si reference) showing: carboxyl singlets at 180.23 and 173.28, quarternary vinyl at 141.14, vinyl methylene at 129.88, γ-methylene *triplet* (1:1:1, $J_{^{13}C-D}$ = 19.5 Hz) at 35.35, and β-methylene singlet at 29.17 ppm. The parent undeuterated compound II shows a sharp singlet at 35.35 ppm, equal in intensity to the peak at 29.17 ppm. It may be concluded that the γ-carbon is characterized by absorption at 35.35 ppm. This was confirmed by the carbon–hydrogen splitting pattern in the undecoupled carbon-13 NMR spectrum of the parent II, which showed the lower field methylene (35.35 ppm) as a clean triplet of triplets ($J_{^{13}C-H}$ = 132 Hz, $J_{^{13}C-C-H}$ = 6 Hz). The higher field methylene appears as a triplet ($J_{^{13}C-H}$ = 132 Hz), but each component of the latter is a complex multiplet by virtue of coupling to both the γ-hydrogens and the vinyl hydrogens.

The deuterated sample of α-methyleneglutaric acid (V) obtained from the vitamin B_{12} rearrangement reaction shows 250-MHz and carbon-13 NMR spectra identical with those of synthetic γ-deuterated acid V. If the reasonable assumption be made that the position of the deuterium is indicative of the position of the cobalt, prior to hydrolysis,[13,14] then the presence of deuterium exclusively at the γ-carbon requires that the acrylic acid moiety be the migrating group in the rearrangement reaction.

In both carbon-skeleton rearrangements for which the sense of rearrangement has been established[5,6] (eq 1 and 2), it is the more complex group which migrates. The migratory preference in the enzymic α-methyleneglutarate $\rightleftarrows$ methylitaconate rearrangement (eq 3) has yet to be established. The foregoing results lead one to expect that the acrylic acid group will be found to be the migrating group in that enzyme catalyzed rearrangement.

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(10) Reactions were run at pH 9, 8, 7, and 5.

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(12) Prepared by tin–copper couple reduction of α-bromomethyl-α,γ-dibromoglutaric acid; P. Dowd and L. K. Marwaha, *J. Org. Chem.*, in press.

(13) Reaction of vitamin B_{12s} with γ-bromo-α-methyleneglutaric acid (VIII) did not yield a stable alkyl cobalamin adduct analogous to IV. Only the reduction product, α-methyleneglutaric acid (II), was isolated (11%) from this reaction. When the reaction was carried out in D_2O, the deuterated acid V was isolated with 86% incorporation of deuterium exclusively in the γ-position.

(14) The possibility that the carboxylic acid group is the migratory group might be considered, as an alternative to the migration of the acrylic acid group. Then, the first-formed product would be that with cobalt attached to the β-carbon. It would now be required that migration be followed by elimination

of cobalt hydride and readdition in the opposite sense, or by some equivalent interchange of cobalt and γ-hydrogen. The final position of cobalt would be attachment to the γ-carbon resulting in deuterium incorporation at that position, following hydrolysis. This more complex scheme cannot be ruled out in the absence of a carbon labeling experiment (synthetic efforts directed toward that end are in progress). However, the absence of any detectable amount of deuterium attached to the β-carbon, the potential complexity of the elimination–addition sequence and the precedent provided by the enzyme catalyzed rearrangement reactions (eq 1 and 2) have led us to a preference for acrylate as the migratory group, as suggested in the body of the text.

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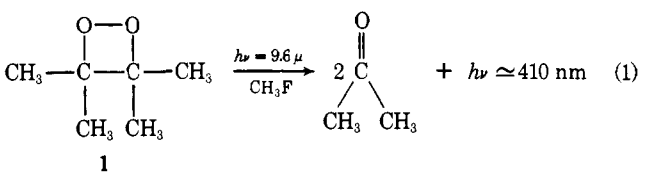
Time Resolved Infrared Laser Photochemistry and Spectroscopy: the Methyl Fluoride Sensitized Decomposition of Tetramethyl-1,2-dioxetane. An Example of Infrared Laser Induced Electronic Excitation

Sir:

The enhancement of chemical reactivity by infrared light absorption has been demonstrated in a variety of systems.[1] Efforts to date have fallen characteristically into one of two domains: (1) bimolecular reactions involving selectively excited small molecules (two, three atoms) in which the goal was to obtain detailed information on the dynamic course of the reaction,[2] (2) bulk reaction studies in which product identities and yields have been used to demonstrate the potential of IR laser excitation for production of unusual, or at least enhanced, chemical reactivity.[3] The competition between collisional energy transfer processes and chemical reaction, which plays a crucial role in determining the mechanism of a laser initiated chemical reaction, can be probed using pulsed infrared excitation followed by time resolved detection of the reaction and energy transfer coordinates. We report here initial studies on a system that is capable of yielding this type of information, the pulsed CO_2 laser-enhanced decomposition of gas phase tetramethyl-1,2-dioxetane (**1**) in a methyl fluoride bath. Methyl fluoride is a "sensitizer" for the CO_2 laser induced decomposition of tetramethyl-1,2-dioxetane (**1**) (eq 1). Some unique features of this system are: (1) the observed infrared photochemistry is extremely clean, acetone being formed quantitatively; (2) the IR laser induced decomposition of **1** is accompanied by the emission of blue light ($\lambda_{max} \simeq 410$ nm); (3) the thermochemistry of reaction 1 is well established and



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is such that acetone may be produced in an electronically *excited state*;[4] (4) the reaction dynamics can be probed after excitation by monitoring time-resolved visible emission from acetone, time-resolved spontaneous infrared emission from CH_3F, and time-resolved translational temperature changes (probed by the thermal lensing opto-acoustic technique);[5,6] (5) energy transfer processes in CH_3F are well understood[7,8] and serve as a benchmark for rate measurements in the mixture.

Irradiation of mixtures of CH_3F (2–30 Torr) and **1** (vapor pressure $\simeq$ 1 Torr at 25 °C) with an unfocused CO_2 TEA laser (1 μs pulse duration; 300 mJ per pulse) operating on the P_{20} (9.6 μ) line is accompanied by blue luminescence from the reaction cell and results in a smooth conversion of **1** to acetone. Laser radiation at this frequency excites only CH_3F although the luminescence is observed only when both CH_3F and **1** are present in the cell. Thus, CH_3F is a true photosensitizer of reaction 1. The thermochemistry of this "up-conversion" of photon energy is displayed in Figure 1. Typical blue luminescence, detected broadbanded with a photomultiplier (RCA 31034) through a sapphire window (which completely blocks laser scatter) is displayed in Figure 1a. The signal decays back to the baseline on a millisecond timescale (not shown). Addition of several Torr of other bath gases, such as Kr, O_2, N_2, and $(CH_3)_2CO$ effectively quenches the luminescence. Attempts to generate luminescence using other CO_2 absorbers as sensitizing agents (SF_6, CO_2, OCS, COF_2) failed in every case except SF_6, which generates luminescence at least as effectively as CH_3F.

In two other experiments using different experimental configurations the 3 μ infrared emission emanating from the C–H stretches in CH_3F was monitored using the laser induced fluorescence technique,[9,10] and the translational temperature rise was monitored using the thermal lensing technique.[5,6] Typical results performed under conditions identical with those of the luminescence experiment are also displayed in Figures 1b and 1c, respectively. These results show clearly that reaction is initiated by IR absorption into CH_3F and that the visible light generated by decomposition of **1** is produced on an energy transfer timescale. The following mechanism serves as a model to explain these observations.

$$CH_3F + h\nu(\mathrm{IR}) \longrightarrow CH_3F^\dagger \quad \text{absorption of infrared light} \tag{2}$$

$$CH_3F^\dagger + 1 \rightleftharpoons CH_3F + 1^\dagger \quad \text{vibrational (V–V) energy transfer} \tag{3}$$

$$CH_3F^\dagger + 1 \longrightarrow 1(T') + CH_3F(T') \tag{4}$$

$$1^\dagger + CH_3F \rightleftharpoons 1(T') + CH_3F(T') \tag{5}$$

$$1^\dagger + 1 \rightleftharpoons 2\,1(T') \tag{6}$$

(4), (5), (6): vibration to translation (V–T) energy transfer

$$1^\dagger \text{ and/or } 1(T') \longrightarrow A^* + A \quad \text{chemielectronic excitations} \tag{7}$$

$$A^* \longrightarrow A + h\nu(\text{visible}) \quad \text{emission of visible light} \tag{8}$$

$$\text{heat diffusion} \tag{9}$$

In this mechanism, daggers refer to vibrationally hot, translationally cold molecules and asterisks refer to electronically excited acetone, while T′ refers to species whose translational temperature T′ is above the ambient equilibrium temperature of the gas mixture. The thermal decomposition of **1** is known to be chemiluminescent due to the efficient formation of A*. According to our mechanism, the blue luminescence should therefore correspond to electronic emission of acetone. Indeed, the blue emission produced in reaction 1 was shown to be experimentally identical with acetone *fluorescence*.[11]

The rapid rate of deactivation of vibrationally excited CH_3F (Figure 1b) is probably due to a combination of processes 3, 4, 5, and 6. Process 4 should not significantly contribute to the overall rate of decay based upon vibrational deactivation studies in CH_3F–rare gas mixtures[7b] and in pure CH_3F.[7a] In the latter case *the overall deactivation rate is two orders of magnitude slower than the rate observed here.* On the other hand, vibrational energy transfer processes like eq 3 are known to be rapid in many cases,[12] and eq 5 and 6 should also be efficient based upon the number and level spacing of states in **1.** In support of these assumptions we note that the rapid fall to the baseline in Figure 1b and the observation of greatly diminished 3 μ fluorescence intensity upon addition of **1** to pure CH_3F indicate negligible back-coupling in eq 3 implying eq 5 and 6 compete effectively with rapid V-V processes in pure CH_3F.[8]

Thermal lensing data in pure CH_3F[5] and CH_3F/O_2 mixtures[13] conclusively show that rapid V-V processes in pure CH_3F ($\simeq$2 μs at 5 Torr) are overall endothermic (translations cool), and that laser energy is stored in CH_3F vibrations on this V-V timescale. In contrast to this, the rapid rise in translational