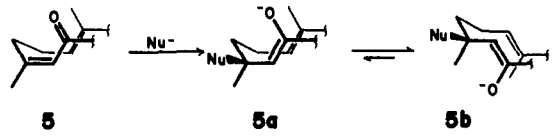
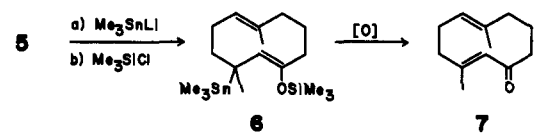
cyclodecadienes and the chemical reactivity of organotin compounds might merge to provide a simple solution to the isomerization problem.

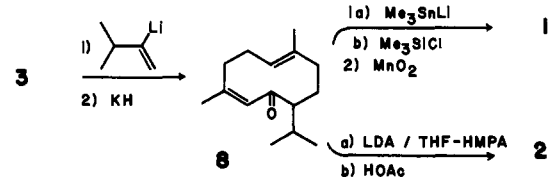
Our approach to the task was based on the following working hypothesis. Conjugate addition of some very bulky nucleophile to **5** should yield adducts existing largely in the kinetic conformation **5a** or in what appears to be the thermodynamic conformation **5b**.[11] Once thermodynamic equilibrium has been established, preferential elimination from **5b** leading to the desired *E* enone **7** would be expected if the elimination transition state geometry were reactant-like or if its energy of activation were small relative to the conformational interconversion barrier leading back to **5a**.[12]



Based on the above analysis, we have developed a kinetic 1,4 addition/elimination sequence for the isomerization of **5** to **7**. Conjugate addition of trimethylstannyllithium (THF, −78 °C) and silylation of the resulting enolate gave the stannyl enol silyl ether **6**.[13] Conversion to the desired (*E*,*E*)-cyclodecadienone **7** was easily accomplished by mild oxidation. Although a variety of oxidants[14] could be used, we found that the Attenburrow[15] manganese dioxide (1.5 g of MnO_2/mmol of **6**, CH_2Cl_2, 30 min, 25 °C) was particularly effective for smooth preparation of **7** (70% yield from **5**; ir (neat) 1680, 1610 cm^{-1}; NMR (δ^{CCl_4}) 5.44 (1 H, br s), 4.78 (1 H, br t, J = 7.5 Hz), 1.89 (3 H, br s), 1.20 (3 H, br s)).[5] No starting *Z*,*E* dienone could be detected by TLC or NMR.



To illustrate the potential of our approach we have applied the above procedures to the total synthesis of (±)-acoragermacrone (**1**) (four steps) and (±)-preisocalamendiol (**2**) (three steps). Addition of 2-lithio-3-methyl-1-butene[16] (THF, −78 °C) to isopiperitenone (**3**) followed by oxy-Cope rearrangement as before gave the known isoacoragermacrone[3c,5] (**8**) in 73% yield. Isomerization via the above organotin addition/oxidation sequence yielded (±)-acoragermacrone (**1**, 71% yield, mp 26 °C) and approximately 5% **8**. Alternatively, **8** could be deconjugated by kinetic enolate protonation[17] to yield (±)-preisocalamendiol (**2**, 76% yield).[18] These racemic materials had spectroscopic properties identical with those reported for the naturally occurring substances.[19]



Acknowledgment. I wish to thank the Research Corporation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their support.

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(10) Cf. E. N. Marvell and W. Whalley, *Tetrahedron Lett.*, 509 (1970).
(11) The parallel double-bond conformation for 1,6-cyclodecadienes has been suggested previously.[2c,3e] Molecular models suggest that both torsional and Van der Waals interactions would favor conformation **5b**.
(12) In this regard, barriers to conformation interconversion of the closely related 1,5-cyclodecadienes are known to be large based on peak coalescence temperatures in the NMR; *e.g.*, I. Horibe, K. Tori, K. Takeda, and T. Ogino, *Tetrahedron Lett.*, 735 (1973), and references cited therein.
(13) Cf. W. C. Still, *J. Am. Chem. Soc.*, in press.
(14) These agents included *m*-chloroperbenzoic acid, *p*-periodic acid, and anhydrous ferric chloride.
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(16) Prepared from the corresponding bromide by exchange with *tert*-butyllithium; cf. D. Seebach and H. Neumann, *Chem. Ber.*, **107**, 847 (1974).
(17) Cf. M. W. Rathke and D. Sullivan, *Tetrahedron Lett.*, 4249 (1972).
(18) It is interesting that the major by-product in this operation is **1** (10–20% yield). The result can be explained by a mechanism analogous to that used to rationalize the isomerization of **5** to **7**.
(19) Structures were confirmed by IR, NMR, and TLC comparison with authentic **8** and by IR comparison with authentic **1**. I wish to thank Professor Shosuke Yamamura of Meijo University for a sample of authentic isoacoragermacrone and for an IR spectrum of natural acoragermacrone.
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Resonance Raman Study of Oxyhemocyanin with Unsymmetrically Labeled Oxygen

Sir:

We wish to report the results of a resonance Raman spectroscopic investigation of the reaction between hemocyanin, a copper-containing respiratory protein, and a mixed isotope molecular oxygen. Recently, we determined that the O-O stretching vibration of the protein-bound O_2 occurs at 744 cm^{-1} in *Cancer magister* hemocyanin and at 749 cm^{-1} in *Busycon canaliculatum* hemocyanin and shifts to 704 and 708 cm^{-1}, respectively, when >90 atom % $^{18}O_2$ is employed in place of atmospheric oxygen.[1] These frequencies indicate that oxygen is bound as a peroxide ion in oxyhemocyanin and that oxygen binding is an oxidative addition process in which O_2 is reduced and the two Cu(I) centers of colorless deoxyhemocyanin are converted to the blue Cu(II) state. Magnetic susceptibility measurements on oxyhemocyanin place the lower limit of exchange coupling at 625 cm^{-1} for the antiferromagnetically coupled cupric dimers.[2]

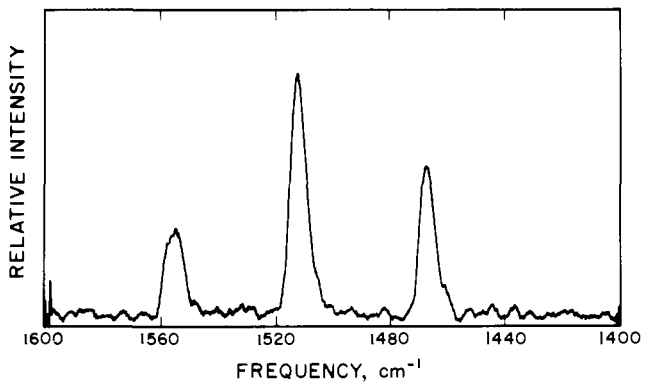


Figure 1. Gas phase Raman spectrum of molecular oxygen (55 atom % ^{18}O). The spectrum is a signal average of 12 repetitive scans subjected to a 25-point computer smoothing using the Savitzky-Golay technique (A. Savitzy and M. J. E. Golay, *Anal. Chem.*, **36**, 1627 (1964)). Excitation, spike-filtered 514.5-nm laser radiation, 0.2 W, 90° scattering geometry, single pass; slit width, 8 cm^{-1}; scan rate, 1.0 cm^{-1}/s; digitizing increment, 0.2 cm^{-1}.

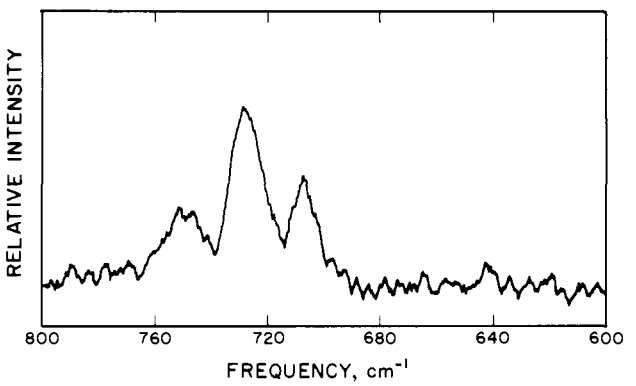


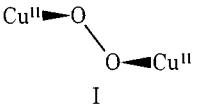
Figure 2. Resonance Raman spectrum of *B. canaliculatum* hemocyanin oxygenated with 55 atom % ^{18}O gas. The spectrum is a signal average of 50 repetitive scans subjected to 25 point smoothing. Excitation, spike-filtered 530.9-nm laser radiation, 30 mW at the sample, ~180° scattering geometry; slit width, 10 cm^{-1}; scan rate, 0.5 cm^{-1}/s; digitizing increment, 0.2 cm^{-1}.

The nonheme iron respiratory protein, hemerythrin, exhibits several similarities to hemocyanin. In the oxygenated protein the O-O stretching frequency is observed at 844 cm^{-1}, indicating that oxygen binding to hemerythrin also involves an oxidative addition process that yields O_2^{2-} bound to two Fe(III).[3] Furthermore, the two Fe(III) atoms in oxyhemerythrin are also antiferromagnetically coupled.[4] In an elegant experiment, Kurtz et al.[5] used oxyhemerythrin containing unsymmetrically labeled O_2 to demonstrate that the two oxygen atoms in the bound peroxide moiety are not equivalent. We have now obtained resonance Raman data for oxyhemocyanin which differ significantly from those in the hemerythrin study and indicate that, in contrast to hemerythrin, the oxygen atoms bound to hemocyanin appear to be equivalent.

A representative gas-phase Raman spectrum of mixed-isotope oxygen (Miles Laboratories, 55.11 atom % ^{18}O) in the O_2 stretching region is shown in Figure 1. The peaks corresponding to ^{16}O-^{16}O, ^{16}O-^{18}O, and ^{18}O-^{18}O vibrations exhibit intensity ratios[6] of 0.71:1.63:1.00, in excellent agreement with the ratios expected from the analytical composition (0.66:1.63:1.00). The full band widths at half-maximum intensity (FWHM) of the three peaks are 8.3, 7.6, and 7.3 cm^{-1} (±0.5 cm^{-1}), respectively.

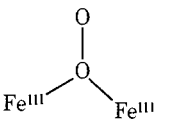
Busycon canaliculatum hemocyanin was prepared as previously described.[1] Hemocyanin samples for this study were lightly pelleted (20 min at 325 000g), deoxygenated, and equilibrated with the oxygen-isotope mixture. The resonance Raman spectrum in the 600-800-cm^{-1} region (Figure 2) shows three peaks at 749, 728, and 708 cm^{-1}. The relative intensities of these three peaks, based on peak heights, are 0.66:1.63:1.00, respectively, and lie well within the standard deviations, *s*, of the intensity ratios observed in the free gaseous mixture. The measured peak widths (FWHM) are 16.8, 14.5, and 12.5 cm^{-1} (±1 cm^{-1}), respectively, for the spectrum obtained with 10.0-cm^{-1} slits and 15.0, 11.7, and 9.9 cm^{-1} (±1 cm^{-1}), respectively, for a spectrum recorded with 6.0-cm^{-1} slits. The greater width of the 749-cm^{-1} peak is due to its overlap with an ~760-cm^{-1} vibrational mode of the protein itself that was clearly revealed in the $^{18}O_2$ hemocyanin samples in our previous studies.[1,7]

The excellent agreement in peak intensity ratios from protein and gaseous samples strongly suggests that only one species contributes to the 728-cm^{-1} peak in oxyhemocyanin. However, a curve-fitting analysis of 10-cm^{-1} slit resolution Raman peaks shows that a splitting of 3 cm^{-1} or less would not have been detectable in the intensity ratios. Although the peak widths are more difficult to quantitate, they show only slight evidence for broadening of the central peak. Since even the maximum probable splitting for oxyhemocyanin is considerably less than the 5-cm^{-1} splitting observed for oxyhemerythrin,[5] it is likely that the bound oxygens are spectroscopically equivalent in oxyhemocyanin. The structure which best explains the collective spectral properties and molecular orbital description of the active site of hemocyanin is the previously proposed nonplanar, μ-dioxygen bridged geometry (I).[1]

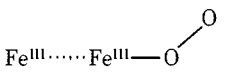


I

In the oxyhemerythrin study, the width of the bound ^{16}O-^{18}O peak at 822 cm^{-1} is nearly twice that of the two flanking peaks (844 and 798 cm^{-1}) and its height is diminished accordingly.[5] These data could only be consistent with nonequivalent oxygens in the Fe_2O_2 site, as suggested by structures II and III. Thus, the resonance Raman spectroscopic data indicate that oxygen is coordinated differently in these two respiratory proteins.[8]



II



III

Such differences in oxygen coordination are quite reasonable in view of the following information on metal-metal distances in these proteins. (1) The x-ray crystallographic data on *Themiste dyscritum* hemerythrin indicate an Fe···Fe separation of less than 3 Å (L. H. Jensen, personal communication). (2) The Cu···Cu distance calculated from EPR spectra of NO hemocyanin is ~ 6 Å.[9] (3) The Cu···Cu separation of I falls in the range 3.5 to 5.0 Å based upon a model with Cu-O = 2.0 Å, O-O = 1.5 Å, and variable Cu-O-O and dihedral angles.[1]

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(7) J. S. Loehr, T. B. Freedman, and T. M. Loehr, *Biochem. Biophys. Res. Commun.*, **56**, 510 (1974).
(8) Similar results have been obtained by D. M. Kurtz, Jr., D. F. Shriver, and I. M. Klotz (personal communication) on oxyhemocyanin from *Limulus polyphemus*. With the 9-cm^{-1} FWHM observed in their spectra, they estimated that a splitting of 3 cm^{-1} or less could not have been detected.
(9) A. J. M. Schoot-Uiterkamp, H. van der Deen, H. J. C. Berendsen, and J. F. Boas, *Biochim. Biophys. Acta*, **372**, 407 (1974).
(10) The computerized Raman instrumentation consists of a Jarrell-Ash 25-300 spectrometer newly equipped with an RKB, Inc. "Polydrive". Data are collected in core of a Computer Automation 24K computer, and stored on magnetic disks using a Computer Automation dual floppy-disk subsystem. We are using a Tektronix 4010 graphics terminal and 4610 Hard Copy Unit.
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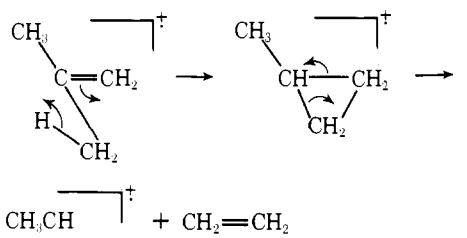
Specific Loss of Ethene from Gaseous 2-Methylpropene Radical Cations in the Picosecond Time Frame. Field Ionization Kinetics

Sir:

Numerous mass spectrometric investigations have emphasized the rich complexity in the gas-phase ion chemistry of $(C_4H_8)^{+\cdot}$ isomers,[2] which when understood will serve as a welcome model for other unsaturated hydrocarbon systems. A pressing requirement to advance the present level of understanding is a mechanism for the facile interconversion of branched and straight-chain structures, and there has been discussion as to the possible involvement of methylcyclopropane intermediates.[2d,h] In this communication, field ionization kinetics (FIK)[3] results are presented for the loss of ethene from 2-methylpropene-*2*-^{13}C and from 2-methylpropene-*1,1*-$[^2H]_2$; these are processes which of necessity involve skeletal rearrangement. These results reveal the intriguing facts that the loss of ethene from 2-methylpropene at short times (picoseconds) following FI is a specific process and that there is an apparent localization of charge during the decomposition. The interpretation proposed here firmly implicates methylcyclopropane-type intermediates in skeletal rearrangements of the $(C_4H_8)^{+\cdot}$ system.

The kinetics of formation of *m/e* 28 and 29 from 2-methylpropene-*2*-^{13}C following FI are shown in the Figure 1a. These two fragments correspond to the fragment *m/e* 28 in the unlabeled compound, attributed to loss of C_2H_4 from the molecular ion.[2c] With 2-methylpropene-*2*-^{13}C, the three fragments *m/e* 40, 41, and 42 are observed corresponding to the two fragments *m/e* 40 (M − CH_4) and 41 (M − CH_3) with the



(1)

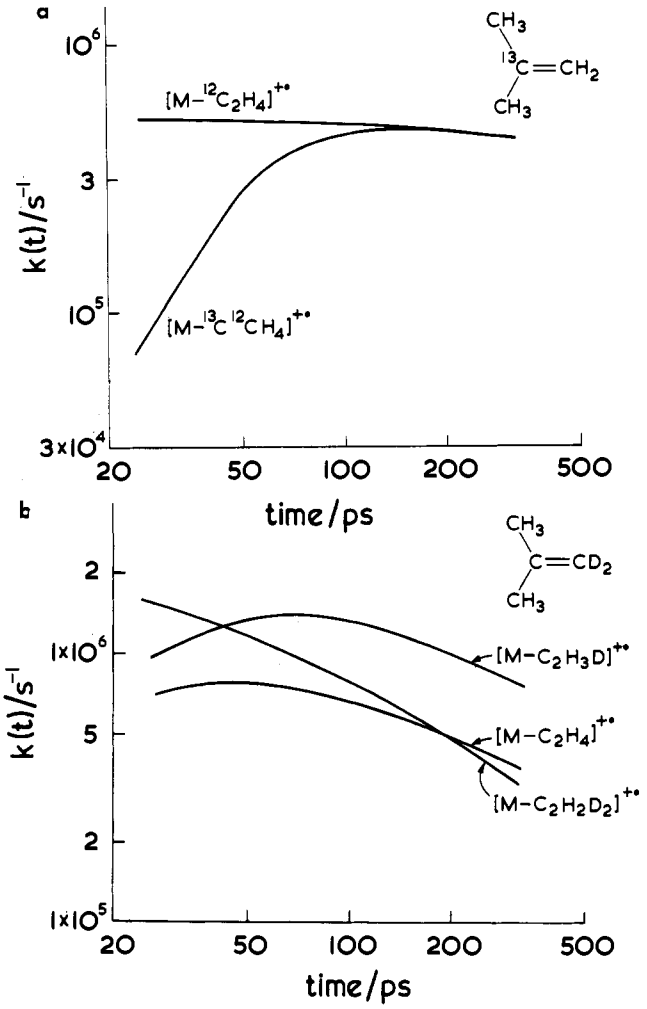


Figure 1. Normalized rates k_t for the loss of ethene from the radical cations produced by field ionization of (a) 2-methylpropene-*2*-^{13}C and (b) 2-methylpropene-*1,1*-$^2H_2$. Normalization is with respect to the measured molecular ion current.[3] To obtain these data, corrections have been made for unlabeled 2-methylpropene impurity, natural isotopic abundance, and fragments formed from $(M + 1)^+$ species. Statistical confidence limit in the *ratio* of the rates at any time is ±10%.

unlabeled compounds. Knowing the kinetics of formation of the latter, it is possible to deduce that with the labeled compound there is specific (>95%) formation of *m/e* 42 (M − $^{12}CH_3$) and 41 (M − $^{12}CH_4$) at times <40 ps. On moving to longer times, there is a gradual loss of specificity until at 200–300 ps both processes (loss of methyl and methane) exhibit "carbon randomization". The specific formation at short times of *m/e* 28 (M − $^{13}CCH_4$) from 2-methylpropene-*2*-^{13}C seemingly splits the molecule into halves; yet the charge remains on one half in preference to the other. The sensitivity of the instrument was also sufficient to measure *m/e* 28, 29, and 30 from 2-methylpropene-*1,1*-$[^2H]_2$ (in an earlier FIK study[2i] of this compound only *m/e* 41, 42, and 43 were intense enough to measure), and results are shown in the Figure 1b. Again there is a trend toward specificity (i.e., loss of neutral $C_2H_2D_2$) as time decreases.

The results (Figure 1) are taken as evidence for a specific reaction channel effecting loss of ethene from the 2-methylpropene ion.[4] That the specificity decreases with time is attributed to isomerization prior to decomposition. The lower specificity at 25 ps with 2-methylpropene-*1,1*-$[^2H_2]$ as compared to 2-methylpropene-*2*-^{13}C is explained on the grounds that hydrogen rearrangements (for example, 1,3 allylic hydrogen shifts[2i]) are faster than skeletal rearrangements. The labeling shows that, in the loss of ethene, C-2 forms part of the