$k_H/k_D = 1.65$ (50 cal/D).[5] In the case of the terminal bromoallene, **1d**, $k_H/k_D = 1.23$ (44 cal/D) for CD_3 substitution at C-3 in 70T at 60°. These data strongly support the proposal that terminal haloallenes as well as trisubstituted haloallenes react *via* charge-delocalized cationic intermediates under initially neutral conditions.

The α-secondary isotope effect observed upon deuterium substitution at the reaction center $k_H/k_D = 1.22$ represents one of the largest α-secondary isotope effects yet reported. For saturated chlorides, such as 1-phenylethyl chloride, Shiner has suggested that values of $k_H/k_D = 1.15$ (83 cal/D) are to be considered a maximum for limiting solvolysis.[6] Shiner has also noted that these "limiting" maxima vary with the leaving group. Thus, the α effect reported here is to be compared with that for bromide as the leaving group, $k_H/k_D = 1.125$ (70 cal/D).[7] Larger α effects are observed in the solvolysis of secondary propargyl brosylates[6] and furylmethylcarbinyl *p*-nitrobenzoate.[8] Shiner has suggested that $k_H/k_D \simeq 1.23$ for oxygen leaving groups in saturated systems be considered comparable to the lower maximum effects observed with the halides.[7]

We are unable to assess the magnitude of the limiting α effect to be expected for an $sp^2 \rightarrow sp$ hybridization change from the data reported here. However, it is possible to estimate this maximum from a consideration of the exchange equilibrium constants for the reactions shown below.[9] These calculations imply that the iso-

$$CH_3CH_3 + CH_2{=}CHD \rightleftharpoons CH_3CH_2D + CH_2{=}CH_2 \quad K = 1.075$$

$$CH_2{=}CH_2 + DC{\equiv}CH \rightleftharpoons CH_2{=}CHD + HC{\equiv}CH \quad K = 1.257$$

tope effect for $sp^2 \rightarrow sp$ hybridization is 1.257/1.075 = 1.17 times that for an $sp^3 \rightarrow sp^2$ change. Assuming a maximum $k_H/k_D = 1.125$ for Br^- leaving from a saturated halide, this predicts that the maximum α-isotope effect to be expected for solvolysis of a vinyl or allenyl bromide is 1.32.[10] Thus it appears that larger α-isotope effects may be observed for systems on which digonal cations are implicated.

We are continuing work in this area by varying solvent, temperature, and structure in order to assess the degree of limiting character in these solvolyses as well as to test the prediction that digonal cations assume a linear geometry.[11]

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(5) V. J. Shiner, Jr., and G. S. Kriz, Jr., *J. Amer. Chem. Soc.*, **86**, 2643 (1964).

(6) V. J. Shiner, Jr., in "Isotope Effects in Chemical Reactions," C. J. Collins and N. S. Bowman, Ed., ACS Monograph 167, Van Nostrand-Reinhold, New York, N. Y., 1970, pp 105–120.

(7) V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *J. Amer. Chem. Soc.*, **90**, 418 (1968).

(8) D. S. Noyce and G. V. Kaiser, *J. Org. Chem.*, **34**, 1008 (1969).

(9) S. R. Hartshorn and V. J. Shiner, Jr., *J. Amer. Chem. Soc.*, **94**, 9002 (1972).

(10) In fact, a more appropriate exchange equilibrium constant required for prediction of this maximum is that for the reaction $CH_2{=}C{=}CHBr + DC{\equiv}CH \rightleftharpoons CH_2{=}C{=}CDBr + HC{\equiv}CH$. The calculations on this system are being attempted.

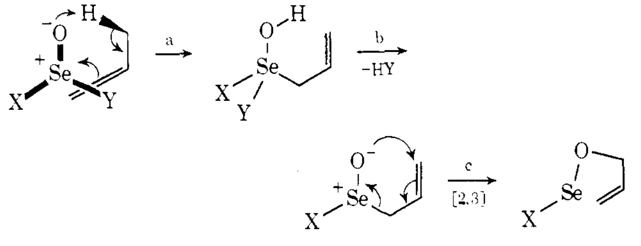
(11) J. E. Williams, R. Sustmann, L. C. Allen, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **91**, 1037 (1969).

Selenium Dioxide Oxidations of Olefins. Trapping of the Allylic Seleninic Acid Intermediate as a Seleninolactone

Sir:

A recently proposed mechanism (Scheme I) for the oxidation of olefins by selenium dioxide suggested an initial ene addition of an $>Se^{+}{-}O^{-}$ moiety (step a) followed by dehydration, or its equivalent (step b), and a [2,3] sigmatropic shift (step c) of the resulting allylseleninic acid.[1]

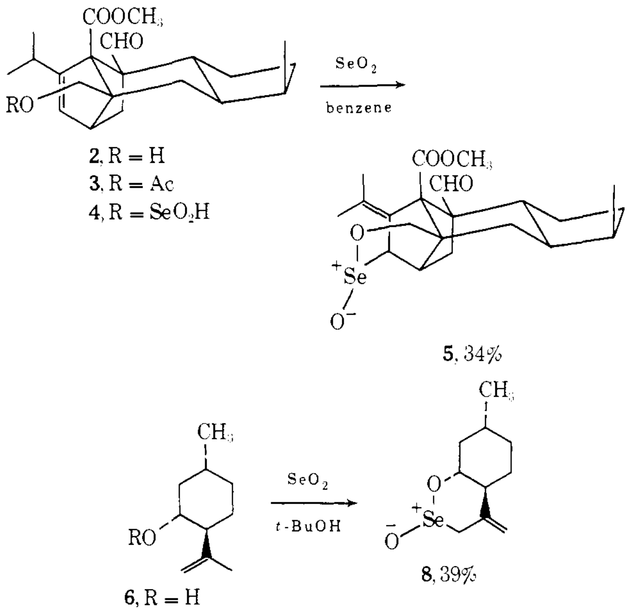
Scheme I



X, Y = OH, OAc, or OR

Having previously[1] provided support for the [2,3] shift, we now report evidence in favor of the initial ene reaction by demonstrating that with appropriate substrates, such as **2** and **6**, the intermediates can be trapped as seleninolactones (Scheme II).

Scheme II



2, R = H
3, R = Ac
4, R = SeO₂H

5, 34%

6, R = H
7, R = SeO₂H

8, 39%

Treatment of sordaricin methyl ester **2**[2,3] with sele-

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(1) K. B. Sharpless and R. F. Lauer, *J. Amer. Chem. Soc.*, **94**, 7154 (1972).

(2) D. Hauser and H. P. Sigg, *Helv. Chim. Acta*, **54**, 1178 (1971).

(3) A. Vasella, Ph.D. Thesis, ETH Zürich, No. 4814, 1972. Independent evidence for the structure **2** is available from X-ray analysis of a degradation compound carried out in the group of Professor O. S. Mills, Manchester.

nium dioxide for 52 hr in refluxing benzene gave the seleninolactone **5** in 34% yield: mp 192–194 dec; $[\alpha]^{20}\text{D}$ −500 (*c* 0.749, $CHCl_3$); uv$_{max}$ (C_2H_5OH) 210 (ϵ 7400) and 255 mμ (sh, ϵ 1300); ir (KBr) 3035, 1719, 1712 (C=O), and 879 cm^{-1} (Se=O); nmr ($CDCl_3$) δ 10.0 (s, 1, C(O)*H*), 4.32 (d, 1, *J* = 13 Hz, C*H*O–), 3.96 (d, 1, *J* = 13 Hz, C*H*O), 3.82 (s, 3, CH_3O), 3.67 (s, 1, *W*/2 = 4 Hz, C*H*Se), 3.01 (d, 1, *J* = 6 Hz, bridgehead C*H*CSe), 1.78 (s, 3), 1.58 (s, 3), and 0.77 ppm (d, 3, *J* = 6.6 Hz); mass spectrum[4] *m*/*e* (rel intensity) 440* (0.1) (M^+), 424* (0.05) ($M - O^+$), 408* (0.15) ($M - CH_3OH^+$), 3.80 (0.1), 378 (0.05), 344 (14) ($M - OSe^+$), 343 (48) ($M - HOSe^+$), 315 (13), 283 (53), 268 (27), 18 (100).

Anal. Calcd for $C_{21}H_{28}O_5Se$: C, 57.40; H, 6.42; mol wt, 439. Found: C, 57.07, 57.76; H, 6.30, 6.60; mol wt, 439.

Under identical reaction conditions the acetate **3** was recovered unchanged, suggesting that reaction of the olefinic alcohol **2** proceeds *via* the selenous acid half-ester **4**.[5]

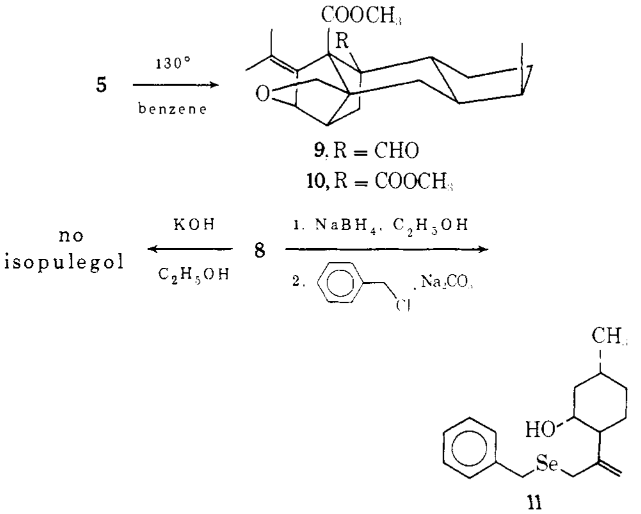
When purified[6] *l*-isopulegol (**6**) ($[\alpha]^{25}\text{D}$ −22°) was treated with 0.5 equiv of selenium dioxide in *tert*-butyl alcohol for 15 min at 80°, colorless crystals began to precipitate. After cooling to room temperature, filtration afforded pure seleninolactone **8**[7] in 39% yield: mp 170–172 dec; $[\alpha]^{20}\text{D}$ +275° (*c* 1.0, C_2H_5OH); uv$_{max}$ (C_2H_5OH) 209 (ϵ 3910) and 241 mμ (ϵ 1880); ir (KBr) 896, 1636, and 3095 cm^{-1} (>C=CH_2), 842 and 970 cm^{-1} (>Se=O); nmr (CD_2Cl_2) δ 5.16 (1, *W*/2 = 5.5 Hz, CH_2=), 5.04 (1, *W*/2 = 5.5 Hz, CH_2=), 4.06 (octet, 1, *J* = 4.1, 9.5, and 10.5 Hz, C*H*O), 3.82 (doublet of triplets, 1, *J* = 11.6 and 0.6 Hz, respectively, C*H*Se), 3.21 (d, 1, *J* = 11.6 Hz, C*H*Se), 2.1–1.1 (m, 8), and 0.94 ppm (d, 3, *J* = 6 Hz). Decoupling experiments confirm that the protons at δ 3.82 and 3.21 ppm are splitting each other. Mass spectrum[4] (70 eV) *m*/*e* (rel intensity) 248* (16) (M^+), 232* (4) ($M - O^+$), 152 (4) ($M - SeO^+$), 151 (17) ($M - HOSe^+$), 135 (100) ($M - HO_2Se^+$).

Anal. Calcd for $C_{10}H_{16}O_2Se$: C, 48.59; H, 6.52; O, 12.95; Se, 31.94; mol wt, 247. Found: C, 48.64; H, 6.33; O, 13.17; Se, 31.70; mol wt, 240 in $CHCl_3$.

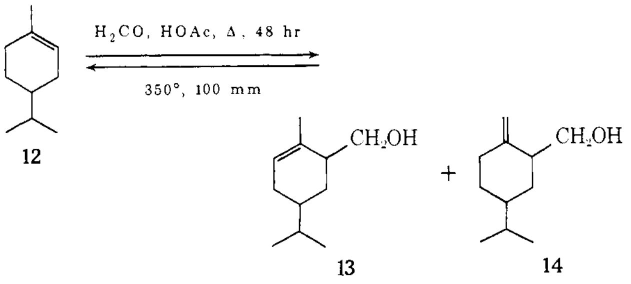
^{77}Se (spin ½, 7.5% abundance) couples with the proton which absorbs at δ 3.21 to give the expected satellites (*J* = 10.1 Hz)[8] each of which integrate for 3.7% of the larger peak. This splitting confirms the presence of an H–C–Se structural unit. A similar pattern expected for the proton at δ 3.82 is obscured by the presence of other signals.

The chemical transformations of **5** and **8** shown in Scheme III also support the assigned structures. Pyrolysis of the seleninolactone **5** in benzene at 130° afforded the ether **9** in 59% yield. Oxidation of the ether **9** to the corresponding acid followed by esterification with diazomethane gave the ester **10**, which is also available from **2** by another route.[3] The unusual thermal elimination of "SeO" from **5** to give the allylic ether **9** does not appear to be a general reaction for these seleninolactones; for, under identical pyrolytic conditions, **8** gave a complex mixture in which none of the expected ether could be found. Reductive benzylation[9] of **8** gave the hydroxyselenide **11**.[10] This observation and the fact that no isopulegol could be obtained from **8** upon treatment with base further support the seleninolactone structure **8** and are inconsistent with the half-ester structure **7** previously proposed for this substance by Sakuda.[7]

Scheme III



We propose that the seleninolactones **5** and **8** are formed by intramolecular ene reactions from the corresponding half-esters **4** and **7**.[11a] The present results strongly suggest that the general mechanism for oxidation of olefins by selenium dioxide is as shown in Scheme I. It is well known[11b] that there are strong orientational effects in the ene additions of other dipolar enophiles, such as carbonyls.[12] Consideration of such effects as they relate to Scheme I suggests that all the unusual orientational and stereochemical features



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[4] Peaks in the mass spectrum which show the Se isotope pattern are starred (*). The *m*/*e* reported for this cluster is for the highest intensity ion, *i.e.*, for the ion containing ^{80}Se.

[5] For evidence that such esters are easily formed see S. Astin, A. C. C. Newman, and H. L. Riley, *J. Chem. Soc.*, 391 (1933).

[6] Commercial *l*-isopulegol (Aldrich Chemical Co.) was purified according to the procedure of Sakuda (ref 7).

[7] Compound **8** is identical (same spectral and physical properties) to a substance isolated under identical reaction conditions by Sakuda: Y. Sakuda, *J. Sci. Hiroshima Univ., Ser. A-2*, **25**, 207 (1961). Sakuda concluded that this organoselenium compound was the half-ester **7**. The present work, however, reveals that the material is actually the much more interesting seleninolactone **8**.

[8] This *J* is of the expected magnitude based on known ^{77}Se–C–H coupling. See M. Lardon, *J. Amer. Chem. Soc.*, **92**, 5063 (1970).

[9] This reductive benzylation procedure was used by Mock and McCausland to characterize a seleninolactone of similar structure: W. L. Mock and J. H. McCausland, *Tetrahedron Lett.*, 391 (1968).

[10] This selenide (**11**) gave spectral and analytical data consonant with the assigned structure.

[11a] Similar intramolecular ene reactions of carbonyl compounds have been observed: N. H. Anderson, H.-S. Uh, S. E. Smith, and P. G. M. Wuts, *J. Chem. Soc., Chem. Commun.*, 956 (1972); (b) H. M. R. Hoffman, *Angew. Chem., Int. Ed. Engl.*, 568 (1969).

[12] Ohloff found the ene reaction of formaldehyde with (+)-carvomenthene (**12**) to be completely stereospecific and reversible. Thus pyrolysis of either of the two product alcohols **13** or **14** gave back the starting olefin (**12**) in optically pure form (O. Ohloff, *Chem. Ber.*, **93**, 2673 (1960)).

of selenium dioxide oxidations can now be adequately explained for the first time. With the exception of Wiberg's mechanism,[13] a common fault in all previously proposed mechanisms[14] was that they considered the oxygen end of the >Se=O dipole to be the electrophile; whereas, it is clearly the selenium atom which is the most electron deficient center in species such as **1**.

Acknowledgment. We are indebted to Dr. Daniel D. Troficante for obtaining a Fourier transform pmr spectrum of **8**. We are grateful to the National Science Foundation (GP-30485X), Hoffmann-La Roche Inc., and the Mobil Foundation for support of this research at M.I.T. and to Sandoz AG, Basel for financial assistance at the ETH.

(13) K. B. Wiberg and S. D. Nielsen, *J. Org. Chem.*, **29**, 3353 (1964).

(14) For a recent review of selenium dioxide oxidations see R. A. Jerussi in "Selective Organic Transformations," Vol. 1, B. S. Thyagarajan, Ed., Wiley-Interscience, New York, N. Y., 1970, Chapter 6, p 301.

(15) NSF Predoctoral Fellow, 1970–1973.

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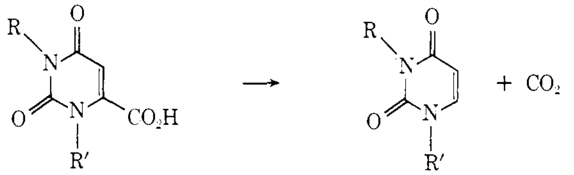
Mechanism of Decarboxylation of 1,3-Dimethylorotic Acid. A Possible Role for Orotate Decarboxylase

Sir:

The efficient enzymatic decarboxylation of orotidine 5′-phosphate (**1**) to uridylic acid (**2**), a central metabolic reaction in pyrimidine biosynthesis,[1] is mechanistically interesting because the types of stabilization usually associated with biochemically facile decarboxylations are not apparent for the pyrimidone ring of **1**.[2,3] We wish to report a study of the mechanism of decarboxylation of 1,3-dimethylorotic acid (**3**) which provides evidence that decarboxylation of this model compound can proceed *via* a zwitterionic intermediate and thereby to suggest a specific chemical role for orotate decarboxylase.

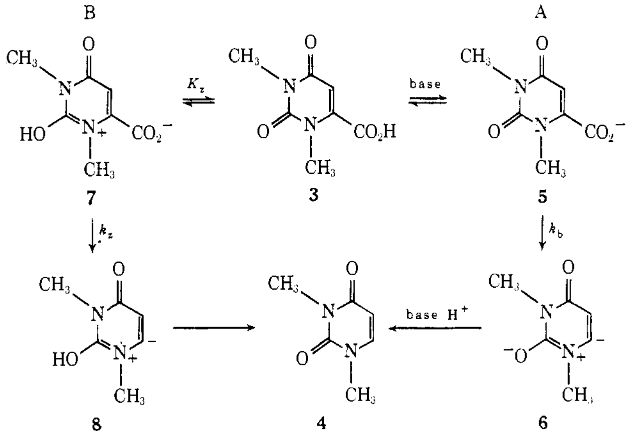


1, R = H; R′ = ribose 5′-phosphate
3, R = R′ = CH_3

2, R = H; R′ = ribose 5′-phosphate
4, R = R′ = CH_3

The conversion of 0.05 *M* **3** to 1,3-dimethyluracil (**4**) proceeds efficiently in sulfolane at 206°. The rate of evolution of carbon dioxide can be studied as a function of added base, concentration, and isotopic substitution. With added diethylaniline the observed pseudo-first order rate constant smoothly increases from 0.76 × 10^{-3} to 3.1 × 10^{-3} sec^{-1} as the base is increased from 0 to 0.7 *M*. The latter rate constant represents a plateau which is invariant up to 2 *M* base. The degree of ionization of the carboxylic acid, measured by the relative conductance of these solutions extrapolated to 206° from measurements at 50, 100, and 150°, also rises from essentially zero to a maximum over the same range of base concentrations.[4] These data imply that the carboxylate anion is chiefly responsible for decarboxylation in the presence of base while the low conductance in the absence of base suggests that the formally neutral acid undergoes decarboxylation in neat sulfolane.[5] Decarboxylation of an undissociated species is further required by the invariance of the first-order rate constant for CO_2 evolution from **3** as its initial concentration is varied between 0.01 and 0.25 *M*[6] in neat sulfolane. The fact that the formally neutral form of **3** which undergoes decarboxylation probably does not involve a transition state with simultaneous carbon–carbon and oxygen–hydrogen bond cleavage is revealed by the decarboxylation of carboxydeuterio **3**, which proceeds at the same rate (0.78 × 10^{-3} sec^{-1} ± 0.06 × 10^{-3} sec^{-1}) as the protio species.[7]

A dual pathway process consistent with these observations is shown below. In basic solution (path A) the carboxylate anion undergoes decarboxylation to the dipole-stabilized carbanion **6**, an intermediate which



(1) P. Reichard, *Advan. Enzymol.*, **2**, 263 (1959); C. C. Cheng and B. Roth, *Progr. Med. Chem.*, **7**, 285 (1970); G. Schmidt, *Annu. Rev. Biochem.*, **33**, 667 (1969); G. Crosbie, "The Nucleic Acids, III," J. Davidson and E. Charaguff, Ed., Academic Press, New York, N. Y., 1960, p 327.

(2) Stabilization in most biochemically important decarboxylations is considered to be provided by π delocalization of the residual electron pair or by bond making concerted with bond breaking, often in an electrocyclic process.[3]

(3) T. C. Bruice and S. Benkovic, "Bioorganic Mechanisms," Vol. 2, W. A. Benjamin, New York, N. Y., 1966, pp 188–194; M. L. Bender, "Mechanisms of Homogeneous Catalysis from Protons to Proteins," Wiley-Interscience, New York, N. Y., 1971, pp 165–175, 586–594.

(4) A slight decrease observed in the conductivity as the concentration of base is further increased is attributed to the decrease in dielectric constant of the medium.

(5) Moreover, if only the carboxylate anion were reacting in neat sulfolane, the observed rate constant would necessitate an unprecedented degree of ionization (25%) in that solvent: J. Coetzee and R. Bertozzi, *Anal. Chem.*, **45**, 1064 (1973).

(6) Since the equilibrium constant (*K*) for acid ionization = $[\alpha/(1-\alpha)]c$, if *c*, the total concentration of the acid plus its carboxylate anion, decreases, the fraction of ionization, α, will increase if *K* is significantly different from zero.

(7) F. Westheimer, *Chem. Rev.*, **61**, 265 (1961); for some decarboxylations in which deuterium isotope effects are observed see D. Bigley and J. Thurman, *J. Chem. Soc. B*, 436 (1968).