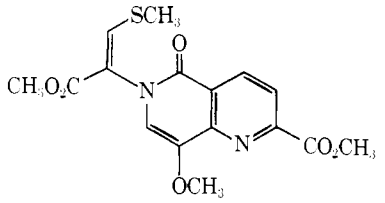

2

ramethyl berninamycinate hydrate is by cleavage of the thiazole ring system. In view of the pyridine ring the likely site of hydrolytic cleavage of the thiazole ring system in **1** is the S-C(10b) bond. Thus, structure **2** is assigned for tetramethyl berninamycinate hydrate.

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Supplementary Material Available: structure factors and atomic coordinates (15 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Presented in part at the 170th National Meeting of the American Chemical Society, Chicago, Ill., Aug 1975; *cf.* Abstract No. ORGN 20. (b) Taken in part from the Ph.D. Thesis of J. M. Liesch, University of Illinois, Urbana, 1975.
(2) M. E. Bergy, J. H. Coats, and F. Reusser, U.S. Patent 3 689 639 (23 Jan 1969); *Chem. Abstr.*, **77**, 150582 (1972).
(3) F. Reusser, *Biochemistry*, **8**, 3303 (1969).
(4) Even after drying at 0.02 Torr for 24 h at 110 °C the anhydrous acid could not be obtained. Calcd for $C_{12}H_6N_2O_5S \cdot 0.2H_2O$: C, 49.04; H, 2.19; N, 9.53; S, 10.91. Found: C, 48.93; H, 2.30; N, 9.46; S, 10.93. The molecular weight corresponding to $C_{12}H_6N_2O_5S$ is 290. Electron impact mass spectra of berninamycinic acid vary due to decomposition. The field desorption mass spectrum[5] of ammonium berninamycinate showed only fragmentation peaks at *m/e* 246 ($M - NH_3 - CO_2$) and 202 ($246 - CO_2$).
(5) K. L. Rinehart, Jr., J. C. Cook, Jr., K. H. Maurer, and U. Rapp, *J. Antibiot.*, **27**, 1 (1974).
(6) A program called LSAM by P. Main and M. M. Woolfson, Department of Physics, University of York, York, England, 1972, was used.
(7) A listing of the final values for the atomic coordinates and for the x-ray structure factors will appear following these pages in the microfilm edition of this volume of the journal. See paragraph at end of paper regarding supplementary material.
(8) University of Illinois Fellow, 1971–1973; Mobil Foundation Fellow, 1973–1974; Uniroyal Fellow, 1974–1975.
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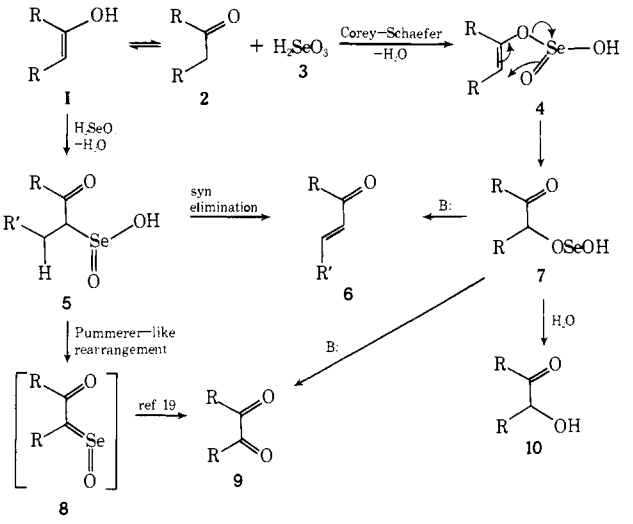
Selenium Dioxide Oxidation of Ketones and Aldehydes. Evidence for the Intermediacy of β-Ketoseleninic Acids

Sir:

Olefins, ketones, and aldehydes are the three organic functional groups most often subjected to oxidation by selenium dioxide. We previously established that olefin oxidations proceed via allylseleninic acids,[1] and we now present evidence that the selenium dioxide oxidation of ketones and aldehydes to α-diketones and glyoxals also involves an organoselenium species.

Scheme I



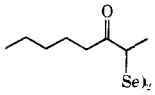
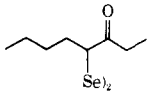
Our mechanism (Scheme I) proposes that the key intermediate in this sequence is the β-ketoseleninic acid **5** formed by electrophilic attack of selenous acid, **3**, on the enol **1**;[2] Pummerer-like[3] decomposition yields the α-diketone **9**. For comparison, Scheme I also includes the mechanism proposed by Corey and Schaefer[4] which is widely accepted at this time, but does not involve an organoselenium intermediate. Ample precedent exists for the formation of carbon-selenium bonds during selenium dioxide oxidations,[5] and, in several cases, the putative β-ketoseleninic acid intermediate appears to have been trapped by a second molecule of the substrate.[5d-f]

Our principal objection to the mechanism of Corey and Schaefer arises from our observation[1a] that selenium II esters such as **7** hydrolyze very rapidly to alcohols (**10**). Furthermore, in their kinetic study of the oxidation of deoxybenzoin, Corey and Schaefer explicitly excluded the intermediacy of such a ketol on the basis that oxidation of benzoin to benzil proceeds at only one-twentieth the oxidation rate of deoxybenzoin. We therefore do not consider **7** to be a likely intermediate.[6]

To date, we have been unable to isolate a β-ketoseleninic acid (**5**). We have sought instead to generate this species in situ by the oxidation of α,α′-diketodiselenides[7a] and observe the resulting organic products. To eliminate the possibility that β-ketoseleninic acids thus formed might revert to selenous acid and ketone which could conceivably afford diketone by some alternate mechanism, we synthesized the two isomeric α,α′-diketodiselenides **16** and **17**.[8] As indicated in Table I, ozonolysis at 25° of each isomer afforded the corresponding α-diketone only (**16** → **11** and **17** → **12**);[9] careful GLPC analysis[10] revealed no crossover products. We submit this as evidence that the carbon-selenium bond remains intact until the Pummerer rearrangement effects oxidation of the α-carbon, and we propose the selenine **8** as a likely intermediate. Selenines have not yet been characterized, but Barton[11] has demonstrated that oxidation of di-*tert*-butyl selenoketone gives the corresponding ketone, presumably via a selenine intermediate, and Strating[12] has reported that the analogous sulfine groups readily hydrolyze to ketones.

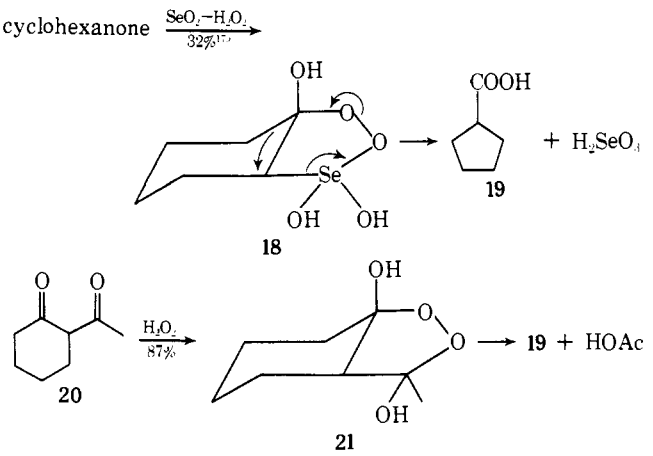
Although the yields of α-diketones are low (Table I) for the ozonolysis of **16** and **17**, selenium dioxide oxidation of the parent ketone, 3-octanone, in hot 70% acetic acid gave

Table I

Substrate	Oxidant	Products, % yield[a] 2,3-Octanedione 11	3,4-Octanedione 12	1-Octen-3-one 13	4-Octen-3-one 14
3-Octanone, 15	SeO_2[b]	10.5[c]	3.5[c]	Trace	Trace
 16	O_3[d]	34	<0.6	...	...
	H_2O_2[e]	2	0	2	0
 17	O_3[d]	<0.6	28	...	...
	H_2O_2[e]	0	1	0	3

[a] Yields determined by GLPC using an internal standard; see ref 9. [b] 70% HOAc, 100°, 4 h. [c] Isolated yield. [d] EtOAc, 25°, 30 min; lower yields were obtained in CCl_4 at 0°.[7] [e] THF, 65°, 5 min.

Scheme II



only a 14% isolated yield of a 3:1 mixture of the diketones **11** and **12.**

In addition to this evidence for the Pummerer-like rearrangement of β-ketoseleninic acids, we have observed[13] several examples of Pummerer products from alkyl phenyl selenoxides similar to those reported by Okamoto[14a] and Reich.[14b]

Investigations of alkyl phenyl selenoxide eliminations have demonstrated that this process proceeds via syn elimination,[15] and we believe that analogous decomposition of β-ketoseleninic acids explains the formation of dehydrogenated products frequently observed as by-products of selenium dioxide oxidations of carbonyl compounds. Indeed, treatment of each α,α′-diketodiselenide with hydrogen peroxide[7b] afforded both the α-diketone and the α,β-unsaturated ketone (Table I);[16] again, no crossover products were detected.[10] These observations support our mechanism for the reaction of **5** to give both **6** and **9**.

Finally, the β-ketoseleninic acid intermediate suggests a reasonable mechanism for the unusual oxidative rearrangement observed during selenium dioxide oxidations of ketones in the presence of hydrogen peroxide.[17] Scheme II demonstrates this mechanism for cyclic ketones which afford ring-contracted acids such as **19**. Intermediate **18** bears a noteworthy resemblance to that (**21**) proposed for the remarkably similar process involving 2-acetylcyclohexanone (**20**) and hydrogen peroxide.[18]

Acknowledgment. We thank the National Institutes of Health (GM21686-01) and Hoffmann-La Roche for support of this research.

References and Notes

(1) (a) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **94**, 7154 (1972); (b) D. Arigoni, A. Vasella, K. B. Sharpless, and H. P. Jensen, *ibid.*, **95**, 7917 (1973); (c) H. P. Jensen and K. B. Sharpless, *J. Org. Chem.*, **40**, 264 (1975).

(2) Whether or not the enol serves as an intermediate is as yet unresolved (R. A. Jerussi in "Selective Organic Transformations", Vol. 1, B. S. Thyagarajan, Ed., Wiley-Interscience, New York, N.Y., pp 304–307). However, an ene reaction between the ketone and selenous acid to give **4**[4] followed by a [1,3] shift would also afford the β-ketoseleninic acid **5**. We have observed that allyl selenium compounds undergo a facile [1,3] shift (K. B. Sharpless and R. F. Lauer, *J. Org. Chem.*, **37**, 3973 (1972)).

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(4) E. J. Corey and J. P. Schaefer, *J. Am. Chem. Soc.*, **82**, 918 (1960).

(5) (a) J. S. Baran, *J. Am. Chem. Soc.*, **80**, 1687 (1958); (b) J. N. Marx and L. R. Norman, *Tetrahedron Lett.*, 2867 (1973); (c) K. Florey and A. R. Restivo, *J. Org. Chem.*, **22**, 406 (1957); (d) H. Stamm and K. Gossrau, *Chem. Ber.*, **66**, 1558 (1933); (e) F. E. King and D. G. I. Felton, *J. Chem. Soc.*, **274** (1949); (f) D. S. Breslow and H. Skolnick, *Chem. Heterocycl. Compd.*, **2**, 1301 (1966).

(6) We have found, however, that acid-catalyzed selenium dioxide oxidation of isobutyrophenone (chosen for its inability to give α-dicarbonyl products) yields 21% of the corresponding α-ketol in addition to 61% of the expected α,β-unsaturated ketone. If an intermediate such as **7** were involved, as this result might suggest, one would expect ketol to be the major product, especially considering that under the reaction conditions, the authentic ketol is stable and affords no α,β-unsaturated ketone. However, we propose that under the vigorous conditions required for this oxidation (19 h in refluxing 5% aqueous dioxane with catalytic sulfuric acid), ketol arises via a competing [1,2] shift of the β-ketoseleninic acid intermediate **5**. We have observed that primary seleninic acids undergo such [1,2] shifts to give alcohols in ~50% yield when refluxed in benzene in the presence of acid.[13] Although the presence of ketol can be rationalized by either mechanism, the formation of enone is best explained by syn elimination of **5**; even assuming that **7** could resist hydrolysis, dehydration of α-ketols is notoriously difficult and we do not envision the elimination of HOSeOH from **7** as being significantly more facile. To the best of our knowledge, this special case is the first reported example of a ketol as the product of a selenium dioxide oxidation.

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(8) The previously unknown α,α′-diketodiselenides were prepared from the corresponding α-chloroketones by displacement with KSeCN in DMF followed by reduction to the diselenide using NH_4OH in acetone (H. Frerichs, *Arch. Pharm.*, **241**, 177 (1903)). The α-chloroketones were prepared using the procedure of J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946). The required 2-chlorohexanoic acid was synthesized in 81% yield using the procedure of H. H. Guest, *ibid.*, **69**, 300 (1947).

(9) Each α-diketone was isolated by preparative GLPC and its ir spectrum compared to that of an authentic sample prepared in turn by $KMnO_4$–Ac_2O oxidation of *E*-2-octene or *E*-3-octene (K. B. Sharpless, R. F. Lauer, O. Repic, A. Y. Teranishi, and D. R. Williams, *J. Am. Chem. Soc.*, **93**, 3303 (1971)). Derivatization with *o*-diaminobenzene afforded the corresponding quinoxaline, shown to be identical (mixture melting point) with the authentic derivative: quinoxaline from **11**, mp 44.0–44.5°; quinoxaline from **12**, mp 33.5–34.0°.

(10) GLPC analysis permitted detection of 2% of each α-diketone or α,β-unsaturated ketone in the presence of the other isomer (3% FFAP, ⅛ in. × 6 ft column at 50°).

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(13) K. B. Sharpless, K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer, and M. W. Young, *Chem. Scr.*, in press.

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(15) K. B. Sharpless, M. W. Young, and R. F. Lauer, *Tetrahedron Lett.*, 1979 (1973).

(16) Each α,β-unsaturated ketone was isolated by preparative GLPC and its ir and NMR spectra compared to those of authentic samples prepared by the method of K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95**, 6137 (1973).

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(19) The decomposition of the selenine to ketone may proceed either by attack of water at the α-carbon as postulated for the Pummerer rearrangement of sulfoxides[3b] or by intramolecular transfer of oxygen via closure of the selenine to an oxaselenirane followed by expulsion of selenium.

(20) Camille and Henry Dreyfus Teacher–Scholar Grant Recipient; Alfred P. Sloan Fellow, 1973–1975.

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