computer-calculated parameters for the pH-rate profile in Figure 2 as compared to those for the profile of Figure 1.

Conclusion

In agreement with model system studies[23] the present work demonstrates that a newly introduced intramolecular nucleophile in an enzyme is far more effective than the external nucleophile water. Specifically, α-toluenesulfonyl-α-CT which does not possess such an intramolecular nucleophile is unable to desulfonylate in the pH range near neutrality[24] through the attack of water catalyzed by the enzyme. However, the enzyme-catalyzed attack of the phenolic hydroxyl on the sulfonyl group in 2-hydroxy-5-nitro-α-toluenesulfonyl-α-CT is very effective. Thus, the enzyme appears to be able to utilize the proximity effect of the phenolic hydroxyl group in desulfonylation thereby greatly favoring kinetic control (re-formation of the sultone) rather than thermodynamic control (formation of sulfonic acid). By analogy, this enzyme model system lends credit to the pathway proposed for the re-formation of virgin soybean inhibitor from the acyl-trypsin produced by the interaction of trypsin with soybean trypsin inhibitor.[25] Therefore, it appears that the most powerful naturally occurring serine proteinase inhibitors probably form acyl-enzymes, but in order to maintain the efficiency of the inhibitor the destruction of the inhibitor by normal hydrolysis should be avoided. In other words, the re-formation of the native inhibitor by an intramolecular nucleophilic reaction should be favored. Thus, we suggest that the powerful naturally occurring serine proteinase inhibitors owe their efficiency to the presence of covalently bound leaving groups in the acyl enzymes produced by the reaction of the inhibitors with the enzymes.

Acknowledgment. This research was supported in part by a grant from the National Institute of General Medical Sciences. We wish to thank Professor F. J. Kézdy for helpful discussions.

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(23) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 8-35.

(24) D. E. Fahrney, Ph.D. Thesis, Columbia University, 1963.

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Communications to the Editor

Direct Reaction of Triphenyl Phosphite Ozonide with *cis*- and *trans*-Diethoxyethylenes[1]

Sir:

Triphenyl phosphite ozonide (**2**), formed at −78° by the addition of ozone to triphenyl phosphite[2] (**1**), decomposes spontaneously at −17° ($k_1 = 1.58 \times 10^{-3}$ sec^{-1} at −17° in CH_2Cl_2)[3a] to triphenyl phosphate (**3**) and singlet oxygen (eq 1 and 2).[3a-c] The singlet oxygen

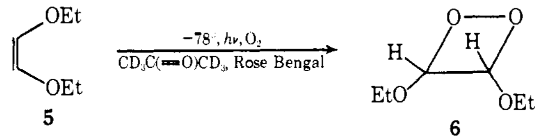
$$\underset{\mathbf{1}}{(C_6H_5O)_3P} + O_3 \xrightarrow{-78^\circ} \underset{\mathbf{2}}{(C_6H_5O)_3PO_3} \qquad (1)$$

$$\underset{\mathbf{2}}{(C_6H_5O)_3PO_3} \xrightarrow{-17^\circ} \underset{\mathbf{3}}{(C_6H_5O)_3PO} + {}^1O_2 \qquad (2)$$

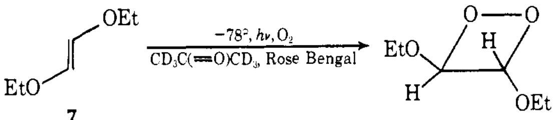
produced in this decomposition can be trapped by acceptors in solution to yield the characteristic singlet oxygen products.[3a-c,4a]

Recently, Bartlett and Mendenhall[4a] have shown that the ozonide **2** also undergoes a bimolecular reaction with tetramethylethylene (**4**) at −70°, at which temperature **2** is indefinitely stable, to form the same allylic hydroperoxide produced by photooxidation of **4**.[5] The corresponding reaction of the ozonide **2** with most dienes and substituted anthracenes either does not occur or is imperceptibly slow.[4a,b] These authors have also established that this reaction is not the result of a catalytic decomposition of the ozonide **2** by the olefin **4**.

We now report that triphenyl phosphite ozonide (**2**) is able to imitate another reaction of singlet oxygen, the 1,2 cycloaddition to vinylene diethers to yield 1,2-dioxetanes. Singlet oxygen produced photochemically adds stereospecifically to *cis*- and *trans*-diethoxyethylenes (**5** and **7**) to give the dioxetanes **6** and **8**, respectively.[6a,b] The ozonide **2** also yields **6** and **8** from **5** and **7**, but in its stereochemical course the reaction contrasts sharply with the stereospecific behavior of free singlet oxygen. The bimolecular reaction at −78°, in trichlorofluoromethane, of the ozonide **2** with **5** and with **7** yields the same mixture of the two isomeric dioxetanes



5 **6** (3)



7 **8** (4)

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(1) Presented in part at the 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970.

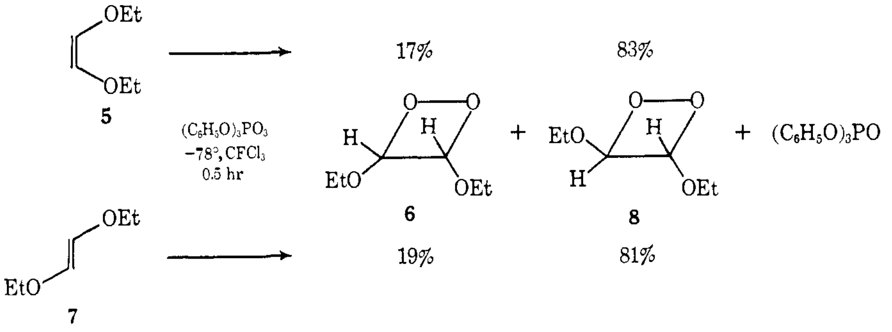
(2) Q. E. Thompson, *J. Amer. Chem. Soc.*, **83**, 845 (1961).

(3) (a) R. W. Murray and M. L. Kaplan, *ibid.*, **91**, 5358 (1969); (b) R. W. Murray and M. L. Kaplan, *ibid.*, **90**, 527 (1968); (c) E. Wasserman, R. W. Murray, M. L. Kaplan, and W. A. Yager, *ibid.*, **90**, 4160 (1968).

(4) (a) P. D. Bartlett and G. D. Mendenhall, *ibid.*, **92**, 210 (1970). (b) 2,5-Dimethylfuran reacts slowly with **2** at −70° to give a mixture of products.[4a]

(5) C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968), and references therein.

(6) (a) P. D. Bartlett and A. P. Schaap, *J. Amer. Chem. Soc.*, **92**, 3223 (1970). (b) Mazur and Foote have reported the addition of singlet oxygen to tetramethoxyethylene: S. Mazur and C. S. Foote, *ibid.*, **92**, 3225 (1970).



(5)

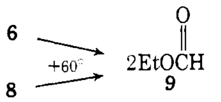
6 and 8 within the limits of the nmr method (eq 5). As expected, the less sterically hindered *trans*-diethoxydioxetane (8) is the major component of the mixture.

A solution of triphenyl phosphite ozonide (2) was prepared by the slow addition of 0.744 g (2.40 mmol) of triphenyl phosphite (base washed and redistilled) to 10 ml of dry $CFCl_3$ at −78° continuously saturated with ozone. Following the addition, dry nitrogen was bubbled through the solution to remove all ozone. With a precooled syringe, 0.55 ml of the solution (0.13 mmol of the ozonide) was added to an nmr tube which was held in liquid nitrogen and contained 14 mg (0.12 mmol) of the olefin (5 or 7) which had been collected by preparative vpc and was >99% pure. The material was melted by placing the tube in a Dry Ice–acetone bath and was then stirred with a glass rod. After 0.5 hr at −78°, tetramethylsilane was added to the solution and its pmr spectrum recorded at −78°. The spectrum indicated the complete consumption of the starting olefin and the formation of the mixture of the two dioxetanes. The pmr absorptions reported in Table I for the dioxetanes are identical with those found for authentic 6 and 8 under the same conditions.[6a] The ^{31}P nmr spectrum exhibited only the absorption of triphenyl phosphate at +17.3 ppm relative to 85% H_3PO_4 external, indicating that the products did not contain phosphorus, differently bonded.

Table I. Pmr Data (δ, in $CFCl_3$ relative to TMS)

cis-Diethoxyethylene (**5**)	5.12, s, 2 H; 3.73, q, 4 H; 1.25, t, 6 H
trans-Diethoxyethylene (**7**)	6.12, s, 2 H; 3.55, q, 4 H; 1.22, t, 6 H
cis-Diethoxydioxetane (**6**)	5.87, s, 2 H; 3.88, m, 4 H; 1.29, t, 6 H
trans-Diethoxydioxetane (**8**)	5.62, s, 2 H; 3.74, m, 4 H; 1.29, t, 6 H
Triphenyl phosphate (**3**)	7.20

The pmr spectrum was unchanged from −78° to ambient temperature; heating to +60° decomposed the dioxetanes 6 and 8 to 2 mol of ethyl formate (9) as has been reported for 6 and 8 generated *via* photooxidation (eq 6).[6a]

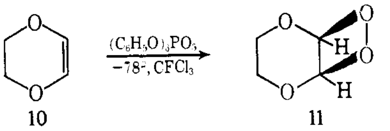


$$\mathbf{6},\ \mathbf{8} \xrightarrow{+60^\circ} 2\mathrm{EtOCH{=}O}\ \ \mathbf{9} \qquad (6)$$

It was established that 5 and 7 are not isomerized by any trace impurities that might have been formed in the synthesis of the ozonide with the observation that the olefins are stable at room temperature in an aliquot of the ozonide solution which had been allowed to decompose thermally prior to the addition of the olefin.

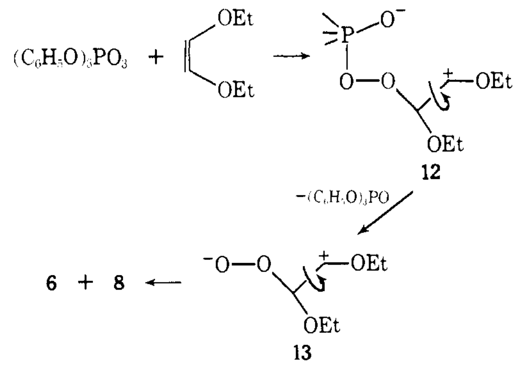
Further, an aliquot of the ozonide solution at −78° was added to a solution of recrystallized *cis*-diethoxydioxetane (6)[6a] in $CFCl_3$ at −78°. The resulting solution was allowed to warm slowly to room temperature with the expected evolution of oxygen observed. Analysis by pmr showed that the dioxetane was neither decomposed nor isomerized, indicating its stability under the reaction conditions as well as to singlet oxygen.

The direct reaction at −78° in $CFCl_3$ of 2 with *p*-dioxene (10) was similarly carried out. This reaction proved to be very slow in contrast to the reaction with the acyclic olefins 5 and 7; there was 58% reaction of the *p*-dioxene in 32 hr at −78° (pmr of *p*-dioxene dioxetane (11):[7] δ 5.90, s; AA′BB′ multiplets at δ 3.97 and 4.53). A competitive reaction of 5 and 10 with the ozonide has established that as a lower limit 5 is more than 50 times as reactive as 10 toward the ozonide. A similar result was obtained in a competitive photooxidation of 5 and 10: $k(\mathbf{5})/k(\mathbf{10}) = 151$.[8]



(7)

A plausible mechanism for the donation of oxygen by the ozonide to the vinylene diethers 5, 7, and 10 is given in eq 8: rotation about the bonds indicated in dipolar intermediates 12 and 13 would account for the formation of both isomeric dioxetanes. The complete rotational equilibration observed in this reaction is surprising inasmuch as this does not generally obtain in cycloadditions *via* 1,4 dipoles[9a,b] or 1,4 biradicals.[10]



(8)

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[7] The photooxidation of *p*-dioxene to give the dioxetane has been carried out and will be reported shortly.

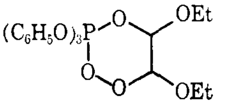
[8] P. D. Bartlett, G. D. Mendenhall, and A. P. Schaap, *Ann. N. Y. Acad. Sci.*, in press.

[9] (a) S. Proskow, H. E. Simmons, and T. L. Cairns, *J. Amer. Chem. Soc.*, 88, 5254 (1966); (b) P. D. Bartlett, *Quart. Rev., Chem. Soc.*, in press.

[10] P. D. Bartlett, *Science*, 159, 833 (1968).

Therefore the possibility of rotation in the two successive intermediates is attractive. In addition, loss of triphenyl phosphate from **12** should leave **13** in an extended conformation with a resulting greater aptitude for rotation.

An intermediate such as **14** is probably not involved in this reaction as it would probably be no less stable than the ozonide **2** and therefore should have been observable at −78° by nmr.



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Further work on the direct reactions of triphenyl phosphite ozonide with vinyl ethers and other olefins is in progress.

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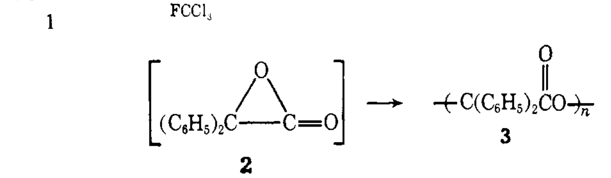
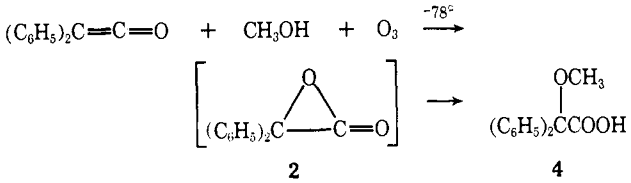
α-Lactones from Diphenylketene and Di-*tert*-butylketene

Sir:

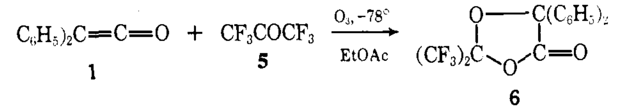
Persuasive evidence exists that α-lactones occur as intermediates in certain displacement[1,2] and free-radical[3–5] reactions. In view of past observations that ozone is an epoxidizing agent toward highly hindered alkenes,[6–8] we ozonized diphenylketene (**1**) in chlorotrifluoromethane (Freon 11) at −78°. A white, insoluble precipitate appeared at once. It was dissolved in chloroform and reprecipitated by pouring into petroleum ether; yield of purified product, 49%. Its ir spectrum, determined in chloroform solution, was identical with that of the benzilic acid polyester previously obtained from the thermal decomposition of di-*tert*-butylperoxy diphenylmalonate.[4] A determination with the vapor phase osmometer[9] gave a molecular weight of 6483, corresponding to $n = 31$ in formula **3**. Polyester **3** gave satisfactory elemental analyses. With methanol in refluxing benzene **3** yielded α-methoxydiphenylacetic acid (**4**), mp 106–107°, identified by ir.

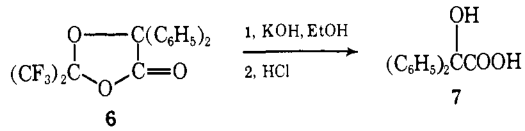


At temperatures as low as −100° the precipitate of **3** was immediate on oxonization of **1**, showing that the diphenylacetolactone (**2**) was of exceedingly short life. It could, however, be trapped in two ways. When **1** was added slowly to a solution of excess ozone in methanol at −78°, **4** resulted in a yield of 60%. Since methanol did not react with the polyester **3** under the conditions of the reaction or work-up, it is clear that the precursor of **3** had been intercepted by methanol in this experiment.

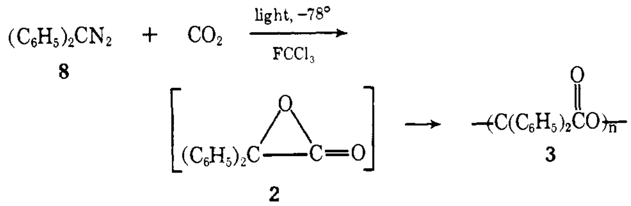


In another experiment at −78°, ozone was passed into an emulsion of **1**, ethyl acetate, and hexafluoroacetone (**5**). The product **6** could be distilled at 143° and passed unchanged through vpc at 155°, showing that it is neither a peroxylactone[10] nor an allene ozonide. The structure of **6** was confirmed by alkaline hydrolysis to benzilic acid (**7**), mp 151–152°, neut equiv 228, and by elemental analysis, ir (C=O at 1830 cm^{-1}), and mass spectrum (strong parent peak and parent −CO$_2$; base peak $C_6H_5CO^+$; prominent $(C_6H_5)_2CO^+$ peak).





A second way to produce an α-lactone is, in principle, the addition of a carbene to carbon dioxide. Diphenyldiazomethane (**8**) dissolved sufficiently in liquid carbon dioxide at room temperature in a sealed tube to yield a pink solution whose color did not fade, indicating the absence of any thermal reaction. However, when photolyzed at −78° in a slurry of Dry Ice and fluorotrichloromethane, **8** yielded **3** in 40% yield; this **3** was again converted into **4** by methanol in refluxing benzene.



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(2) E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.*, **70**, 841 (1948).

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(8) P. S. Bailey and A. G. Lane, *J. Amer. Chem. Soc.*, **89**, 4473 (1967).

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