

their effective concentrations usually approach apparent concentrations. These aldehydes, as well as cyclohexanone and other ketones which readily undergo the Baeyer–Villiger rearrangement, may prevent ozonide formation when used in excess.

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Paul R. Story,* John A. Alford
John R. Burgess, Wesley C. Ray

Department of Chemistry, The University of Georgia
Athens, Georgia 30601

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Mechanisms of Ozonolysis. A New and Unifying Concept

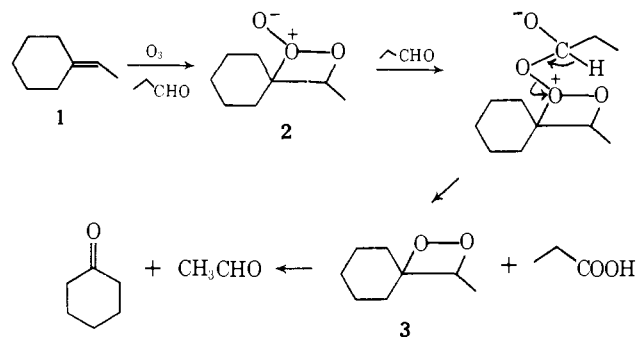
Sir:

In the preceding communication¹ we demonstrated that if the ozonolysis of typical aliphatic olefins is carried out in the presence of certain aldehydes and ketones, the formation of ozonides can be curtailed or prevented. The effect may be described as a reductive ozonolysis, with the added aldehyde or ketone being oxidized. An appropriate example is provided by the ozonolysis of ethylidenecyclohexane (**1**), which, in pentane or acetone solvent, at -78° using either ozone–oxygen or ozone–nitrogen, gives the normal ozonide, methyl cyclohexylidene ozonide, in 85% yield.

The addition of 1 molar equiv of propionaldehyde to the pentane–olefin solution prior to ozonolysis leads, as expected, to a good yield of both normal ozonide and the cross-ozonide, ethyl cyclohexylidene ozonide, in about equal quantities. Increasing the ratio of propionaldehyde to olefin, however, begins to decrease the total yield of ozonide until, finally, ozonolysis in propionaldehyde as the solvent gives no ozonide product. Cyclohexanone, acetaldehyde, and propionic acid are isolated, all in high yield.

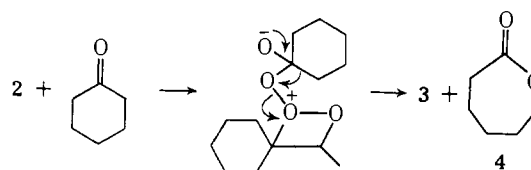
This result appears incompatible both with the Criegee zwitterion mechanism² and with our aldehyde–interchange mechanism.³ We submit, nonetheless, that these findings invalidate neither the Criegee mechanism nor our earlier mechanistic proposal,³ but, in fact, provide for the first time the basis for a unifying mechanistic rationale, one which serves to tie together the many seemingly diverse elements of the ozonolysis reaction.

It is apparent that an intermediate formed during the ozonolysis is reduced in Baeyer–Villiger fashion by added aldehyde or ketone. The intermediate which can most reasonably provide the observed results is the Staudinger molozonide (**2**),^{4,5} which see in the scheme below. Reduction of the molozonide (**2**) may occur, in what is essentially a Baeyer–Villiger oxidation of



the aldehyde; the dioxetane intermediate **3** would, of course, be expected to cleave rapidly to cyclohexanone and acetaldehyde.

If the same reaction is carried out in cyclohexanone as solvent, 6-hexanolide (**4**) results from Baeyer–Villiger rearrangement of cyclohexanone, which is prone to undergo such rearrangement. Acetone, on the other hand, does not readily undergo Baeyer–Villiger rear-

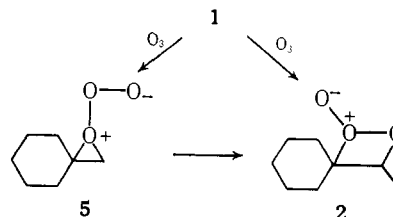


angement,⁶ and in this solvent ozonide forms normally.

We must now deal with the observation that moderate concentrations of propionaldehyde do not prevent ozonide formation; e.g., equimolar quantities of olefin and propionaldehyde in pentane solvent lead to good yields of both normal and cross-ozonides. This situation suggests the presence of more than one competing intermediate.

For some time now it has been assumed that ozone addition to an olefinic double bond is of the 1,3-dipolar type.^{2,5,7} The results reported in the preceding communication are not consistent with that concept.¹

From the data now available we can propose that the initial addition of ozone to an olefinic bond is to give the peroxy epoxide (**5**), which we have previously termed the σ complex.³ The required Staudinger molozonide (**2**) is then formed from the σ complex. Alternatively, the Staudinger molozonide (**2**) may be produced directly through a 1,2-cycloaddition of ozone to the double bond; a concerted cycloaddition is not likely to be prohibitively forbidden.⁸



There are other reasons for preferring the initial formation of the peroxy epoxide (**5**). It is well known, for example, that many hindered olefins react with

(1) P. R. Story, J. A. Alford, J. R. Burgess, and W. C. Ray, *J. Amer. Chem. Soc.*, **93**, 0000 (1971).

(2) R. Criegee, *Rec. Chem. Progr.*, **18**, 111 (1957); R. Criegee in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience, New York, N. Y., 1962, p 29.

(3) P. R. Story, R. W. Murray, and R. D. Youssefyeh, *J. Amer. Chem. Soc.*, **88**, 3144 (1966); P. R. Story, C. E. Bishop, J. R. Burgess, R. W. Murray, and R. D. Youssefyeh, *ibid.*, **90**, 1907 (1968).

(4) H. Staudinger, *Chem. Ber.*, **58**, 1088 (1925).

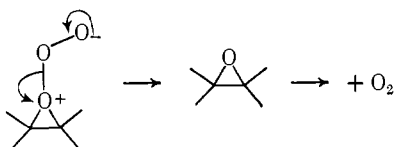
(5) P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958); see also, R. W. Murray, *Accounts Chem. Res.*, **1**, 313 (1968), and P. S. Bailey and A. G. Lane, *J. Amer. Chem. Soc.*, **89**, 4473 (1967).

(6) P. A. S. Smith in "Molecular Rearrangements," P. deMayo Ed., Interscience, New York, N. Y., 1963, p 577.

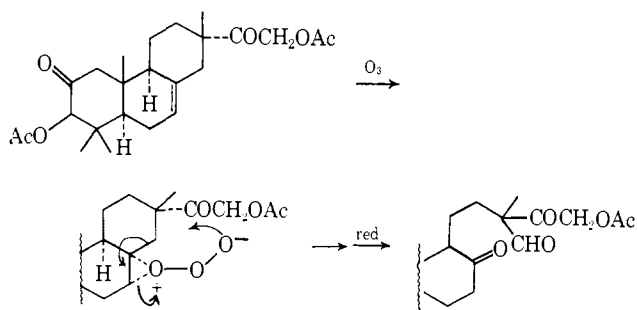
(7) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963); P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Amer. Chem. Soc.*, **88**, 4098 (1966).

(8) D. R. Kearns, *ibid.*, **91**, 6554 (1969).

ozone to produce, in some cases, significant quantities of epoxide.^{5,9} Such a reaction is most conveniently represented as loss of oxygen from the peroxy epoxide



In addition, certain "abnormal" ozonolyses, including those of several isopimarane derivatives, are best explained in terms of the rearrangement of the peroxy epoxide^{9,10}



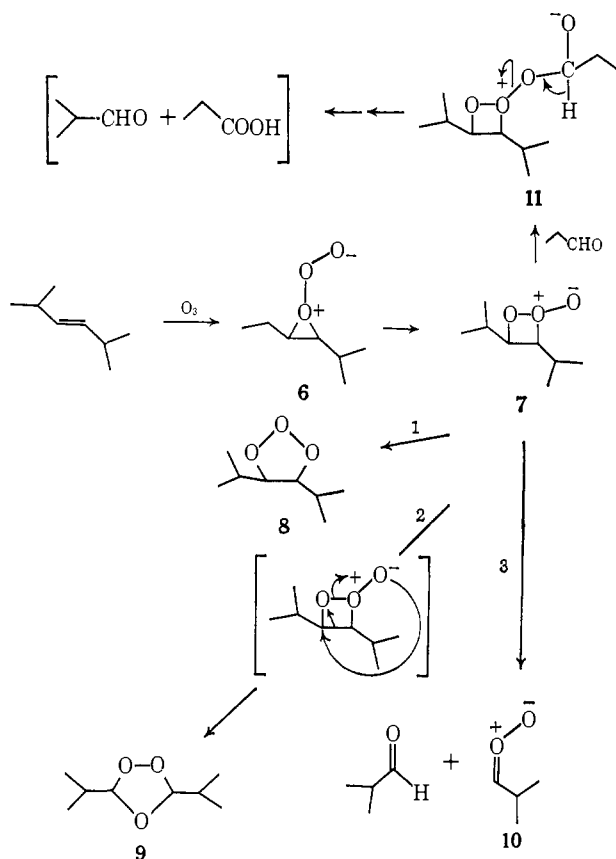
Assuming, then, the initial formation of a peroxy epoxide in the ozonolysis of a typical olefin, it becomes possible to understand the results reported in the preceding communication.¹ For the case of *trans*-diisopropylethylene, the peroxy epoxide (6) will rapidly rearrange to the Staudinger molozonide (7). In the presence of relatively low concentrations of aldehyde the molozonide (7), which reasonably would have a rather short lifetime, is not trapped and reduced to any significant degree. The competing reaction, *i.e.*, opening of the molozonide, may then lead to three possibilities: (1) formation of the 1,2,3-trioxolane (8), (2) rearrangement, intramolecularly in Baeyer-Villiger fashion, to ozonide (9), or (3) cleavage to the Criegee zwitterion (10). Ozonides, then, may be formed in at least three different ways. For this particular olefin, ozonized in the presence of 1 equiv of acetaldehyde-¹⁸O, we know that most of the cross-ozonide must be formed through the 1,2,3-trioxolane (8), and probably by its reaction with acetaldehyde-¹⁸O.³ Cross-ozonide can also be formed in one other way, and that is through the Criegee zwitterion.

By contrast, in situations where aldehyde is present in great excess, the Staudinger molozonide (7) is trapped and the resulting Baeyer-Villiger intermediate 11 fragments to yield two molecules of aldehyde and one molecule of acid. If the reacting solvent is a ketone, rearrangement takes place to yield lactone rather than acid.

We must now account for the observation that *cis*-diisopropylethylene and certain other olefins yield some ozonide even in propionaldehyde solvent. Two reasonable possibilities present themselves. For a *cis*

(9) C. R. Enzell and B. R. Thomas, *Tetrahedron Lett.*, 391 (1964); 225 (1965).

(10) The ozonolysis of Feist's acid has also been interpreted in this fashion [A. T. Bottini and J. D. Roberts, *J. Org. Chem.*, 21, 1169 (1956)]. However, the structure of the product(s) derived on ozonolysis of this acid (the ester thereof) has now been questioned by Erickson [R. E. Erickson and G. D. Mercer, *Amer. Chem. Soc., Div. Polymers, Prepr.*, 16, A54 (1971)]. It seems probable that the Erickson products can be explained by a similar rationale.



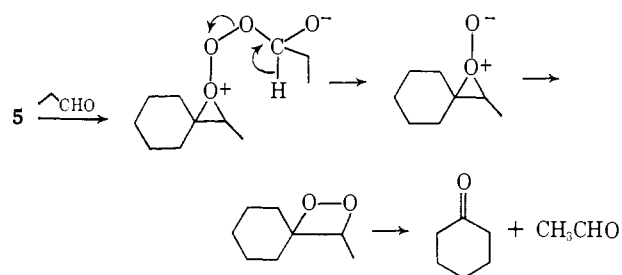
olefin, either the Staudinger molozonide is not formed or it has such a short lifetime that it cannot be effectively trapped with excess aldehyde. It is also possible, of course, that the σ complex can rearrange directly to both the Staudinger molozonide and to the 1,2,3-trioxolane in competing processes. For this and similar olefins the facts are: (1) under ordinary conditions, high yields of ozonide are obtained; (2) the *cis/trans* ratio for the ozonide is greater than one; (3) using acetaldehyde-¹⁸O, most of the cross-ozonide appears to be formed *via* the 1,2,3-trioxolane-aldehyde reaction;^{3,11} (4) ozonolysis of a 50:50 mixture of *cis*-3,4-dideuterio-3-hexene and unlabeled *cis*-3-hexene revealed that approximately 60% of the resulting ozonide was formed through an intramolecular process.¹¹ It is not unreasonable, of course, that such a molozonide should have a shorter lifetime than that of the corresponding *trans* isomer.

Both *cis*- and *trans*-stilbene are obviously in a different category. For this olefinic system, which almost certainly yields ozonide *via* the Criegee zwitterion,¹² the cross-ozonide is formed in propionaldehyde in almost the same yield as that of the normal ozonide in inert solvents. It is also noteworthy that ozonolysis of the stilbenes in cyclohexanone yields no lactone. Thus, it would appear that the Staudinger molozonide, in this case, readily cleaves to the Criegee zwitterion, with ozonide resulting therefrom. *It should be pointed out that intramolecular rearrangement (Baeyer-Villiger) of the Staudinger molozonide and its cleavage to the Criegee zwitterion are, of course, complementary and competing pathways of the one reaction.*

(11) W. C. Ray, unpublished results.

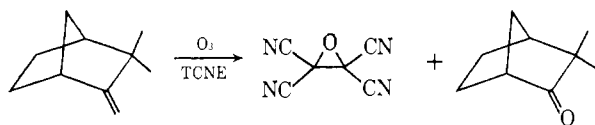
(12) C. E. Bishop, D. D. Denson, and P. R. Story, *Tetrahedron Lett.*, 5739 (1968).

An interesting alternative to the intermediacy of the Staudinger molozonide must also be considered. It is possible that the Staudinger molozonide is not the species reduced by excess aldehyde or ketone but that reduction of the σ complex occurs, *e.g.*



The resulting perepoxide is the same intermediate considered by Kearns⁸ for singlet oxygen-olefin reactions. Rearrangement of the perepoxide to the corresponding dioxetane followed by scission to the carbonyl compounds would account for the results reported here.

It is noteworthy that a reaction which, at least phenomenologically, corresponds to the observations reported here has been described by Criegee.¹³ Criegee observed that the ozonolysis of several olefins in the presence of tetracyanoethylene resulted in high yields of tetracyanoethylene oxide and the carbonyl compounds derived from cleavage of the olefin.¹³ In view of the present findings it would appear likely that tetracyanoethylene is also intercepting and reducing a primary ozonide.



The new information and interpretation offered here require a critical reexamination of the literature dealing with the ozonolysis reaction. The new data very likely offer the key to correlation and explanation of the great number of seemingly unrelated ozonolysis reactions.

Acknowledgment. We thank the National Air Pollution Control Administration for support of this work through Grant No. AP 00505.

(13) R. Criegee and P. Gunther, *Chem. Ber.*, **96**, 1564 (1963).

Paul R. Story,* John A. Alford
Wesley C. Ray, John R. Burgess

Department of Chemistry, The University of Georgia
Athens, Georgia 30601

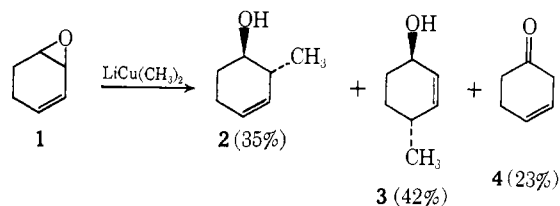
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Reaction of 1,3- and 1,4-Cyclohexadiene Monoepoxides with Methylorganometallic Reagents

Sir:

The title epoxides exhibit several interesting features in their reactions with common methylorganometallic reagents. For example, 1,3-cyclohexadiene monoepoxide (**1**), while not showing the high regioselectivity (preferred 1,4 addition) noted earlier with butadiene monoepoxide,^{1,2} on treatment with lithium dimethyl-

cuprate³ gives both direct-opening product **2** and conjugate-addition product **3** with complete trans stereospecificity.⁴



The stereochemistry of **2** and **3** was established by catalytic reduction of the crude product mixture from which the unsaturated ketone **4** had been removed.⁵ Analysis by vpc of the reduction product allowed the determination of upper limits on *cis*-2-methylcyclohexanol (<1%) and *cis*-4-methylcyclohexanol (<1%). Direct opening of **1** exclusively at the allylic rather than the homoallylic position is in agreement with earlier reports.^{1,2} Anti opening to give **2** is expected on the basis of an analogous stereochemical result with cyclohexene oxide.⁷ The formation of rearrangement product **4** also finds precedent in the cyclohexene oxide reaction, which gave approximately 20% cyclohexanone.⁷

The exact mechanisms of reactions involving lithium dialkylcuprates remain unknown, in spite of extensive study, particularly by House and coworkers.⁸ Nucleophilic attack on **1** by the copper center to give a complex which subsequently decomposes with methylation⁸ would fit the available data. Regardless of the mechanistic details, the net result is the apparent nucleophilic addition of a methyl group to **1**; as such, the conjugate addition might be appropriately considered as an S_N2' process. However, the classical S_N2' mechanism should lead to *cis*⁹ rather than the observed *trans* product **3**.¹⁰ Because of the limited

(3) H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952).

(4) All new materials have been characterized by C and H analyses, spectral methods, and conversion to known materials.

(5) Cyclohexanol, generated by reduction of **4**, would have interfered with the already difficult vpc analysis of *cis*- and *trans*-2- and -4-methylcyclohexanols. Compound **4** was removed by preparative vpc and shown by infrared and nmr analysis to be free of alcohol contaminants which might have exhibited identical retention times.

The structure of **2** was established by nmr (two low-field vinyl hydrogens), through reduction to *trans*-2-methylcyclohexanol, and by demonstrating that it differed from the other two conceivable *trans*-2-methylcyclohexenols.⁶

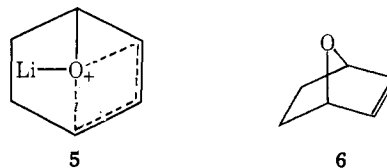
(6) B. Rickborn and R. P. Thummel, *J. Org. Chem.*, **34**, 3583 (1969). A sample of mixed (vpc separable) *cis*- and *trans*-6-methyl-2-cyclohexenols was available from this work. The alternate isomer is described in the present paper.

(7) R. W. Herr, D. M. Wieland, and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 3813 (1970).

(8) (a) H. O. House, W. L. Respass, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966), and references therein; (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968); (c) G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969); the reaction between (-)-2-bromobutane and lithium diphenylcuprate was shown to occur with predominant (84-92%) inversion.

(9) G. Stork and W. N. White, *ibid.*, **78**, 4609 (1956).

(10) Rearrangement product **4** presumably arises *via* a lithium ion catalyzed carbonium ion process.¹¹ Products **2** and **3** might also arise from an intermediate such as **5**. To test this possibility, the isomeric



(1) R. J. Anderson, *J. Amer. Chem. Soc.*, **92**, 4978 (1970).

(2) R. W. Herr and C. R. Johnson, *ibid.*, **92**, 4979 (1970).