Tetrahedron Letters No.11, pp. 1287-1292, 1968. Pergamon Press. Printed in Great Britain.

THE BAEYER-VILLIGER REACTION AS A SOURCE OF "ABNORMAL" OZONOLYSIS PRODUCTS

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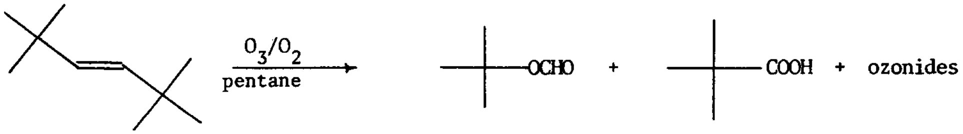
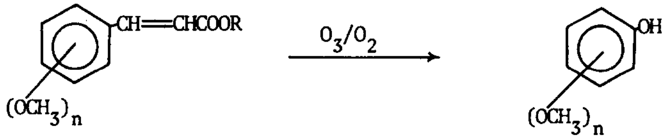
(Received in USA 13 November 1967)

Many so-called "abnormal" ozonolysis products obtained in inert solvents have been explained in terms of rearrangement of a Criegee zwitterion intermediate.(*1,2,3,4,5*) We present evidence here which indicates that products of this type are, more likely, the result of subsequent Baeyer-Villiger oxidations resulting from peracid produced during the ozonolysis.

The most frequently encountered "abnormal" ozonolysis is one in which cleavage of a carbon-carbon bond α to the double bond occurs, resulting in the isolation of either an ester and/or other products containing one less carbon than normally expected. Simple aliphatic olefins generally give low yields of rearranged products; *trans*-di-*t*-butyl ethylene, for example, gives only about 5% of *t*-butyl formate, as shown in Eq. 1(*6*). Cinnamic esters of the type (1), on the other hand, generally give significantly higher yields of the corresponding phenol(2).(*5a, 7*) In some of these cases, however, over-ozonization of the reaction mixture occurred and is probably responsible for part of the phenol(2).



(Eq.1)



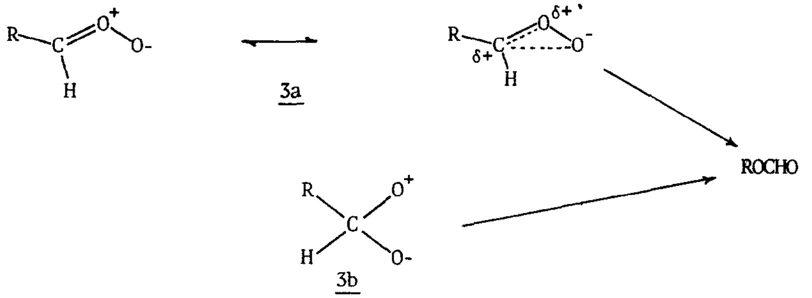
(Eq.2)

R = alkyl
n = 1-3

1

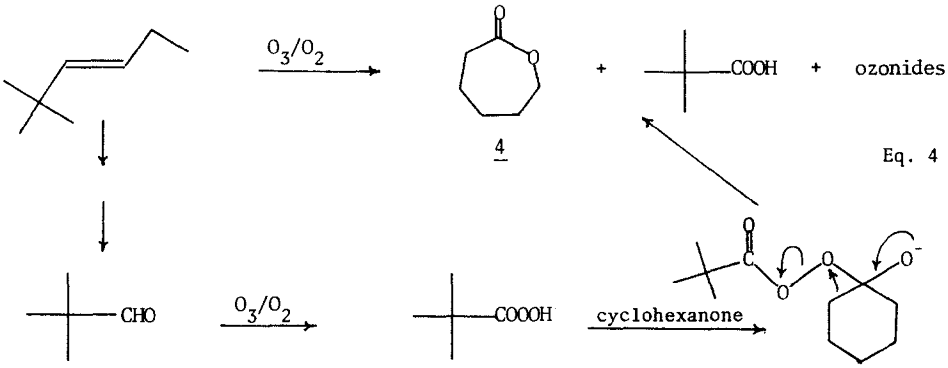
2

Formation of products of this type is usually interpreted as rearrangement of one of several formulations of the intermediate Criegee zwitterion (3) (*1,2*).



Eq. 3

The similarity between the rearrangement depicted in Eq. 3 and that usually written for the Baeyer-Villiger reaction (*8*) is quite clear. This particular reaction path, however, bears great resemblance to that first suggested by Baeyer and Villiger (*8*) for their reaction and later rejected by Doering and Dorfman on the basis of Oxygen-18 labeling experiments (*9*). In view of the seeming unsoundness of the mechanism outlined in Eq. 3 and the fact that ozone is well known to catalyze the oxidation of aldehydes to peracids (*10*), we have examined the possibility that those abnormal ozonolysis products which resemble normal Baeyer-Villiger products are, in fact, formed in a subsequent Baeyer-Villiger reaction. It seems quite likely that the peracid Baeyer-Villiger reaction has not been considered as a source of rearranged products previously because of the widely held opinion that aldehydes produced during an ozonolysis are not attacked as long as olefin is present. Our results clearly demonstrate this not to be the case (*11*).



Eq. 4

Ozonolysis of several very reactive, aliphatic olefins at <u>low ozone flow rates</u> (≅ 2% O_3/O_2) in the presence of cyclohexanone, which undergoes Baeyer-Villiger oxidation readily (*8*), has produced yields of the normal Baeyer-Villiger product, 6-hexanolactone (4) as high as 10%, based on ozone consumed. Neat cyclohexanone or cyclohexanone/chloroform was unaffected. Eq. 4 illustrates.

TABLE 1.

Ozonolysis of Olefins in Cyclohexanone/Chloroform Solution*

Olefin	% Olefin reacted before appearance of 4	% yield lactone	unreacted ozone
trans-2,2-dimethyl-3-hexene	62	3.2	0.30 mmole
trans-2,2-dimethyl-3-heptene	42	5.4	0.27 mmole
trans-2,5-dimethyl-3-hexene	83	2.7	0.28 mmole
trans-2,2,5,5-tetramethyl-3-hexene	ozonized to 2/3 completion in neat cyclohexanone	10.	nil

*Solutions consisted of 10 mmoles of olefin in 25 ml of a solvent obtained by diluting 50 ml of cyclohexanone to 250 ml with chloroform. Each solution was ozonized at 0°C at a rate of 0.62 mmole of ozone/min. for 1000 sec. (calculated time to completion = 968 sec.). Less than 5% of the olefin remained after completion.

In order to determine that oxidation of aldehydes could account for formation of lactone under these conditions the following aldehydes were ozonized.

TABLE 2.

Ozonolysis of Aldehydes

Aldehyde	% yield lactone (based on ozone used)
propionaldehyde	30
n-butyraldehyde	55
isobutyraldehyde	35
pivaldehyde	80

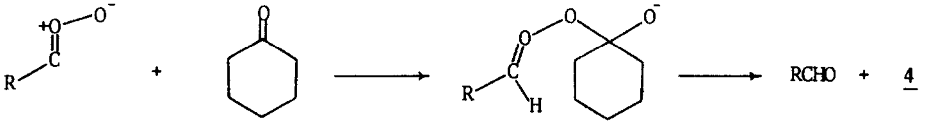
Aldehydes were ozonized in a solution of cyclohexanone and chloroform (see Table 1.) containing 20 mmoles of aldehyde at a rate of 0.75 mmole per minute for 600 sec. at 0°C.

The results presented here clearly demonstrate that aldehydes can be oxidized to peracid during ozonolyses and that the peracid so formed can account for the formation of "abnormal" products through a Baeyer-Villiger oxidation.

Unfortunately most investigations of abnormal ozonolyses have involved an oxidative workup of the reaction mixture; for if, indeed, a subsequent Baeyer-Villiger reaction is reasonable for the abnormal product then the carboxylic acid produced in this reaction also constitutes an abnormal product. Peracid oxidation of aldehydes, in fact, generally leads to formation of acid; rearrangement occurs to an appreciable extent only in the case of those aldehydes which contain substituents prone to migration, such as *t*-butyl or aryl (*8*). If we also note that negatively substituted peracids are more reactive in Baeyer-Villiger oxidation (*8*), we see that it becomes possible to draw a correlation between the nature of olefinic substituents and the probability of the observation of abnormal products on the basis of the Baeyer-Villiger reaction.

It becomes clear, then, why, for example, di-isopropyl ethylene leads to no observable abnormal product while *trans*-di-*t*-butyl ethylene, on the other hand, gives a low yield of the abnormal formate and methoxylated cinnamates (1) give still higher yields of abnormal products. It also becomes clear why ozonolysis of (1) gives a higher yield of the phenol than does ozonization of the corresponding methoxylated benzaldehyde.

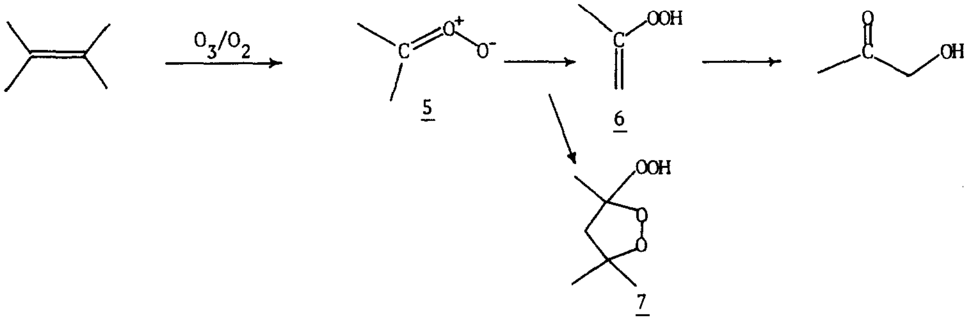
The possibility exists, of course, that lactone (4) could arise by action of zwitterion on cyclohexanone in a Baeyer-Villiger type reaction (Eq. 5) (*12*). Although it would be extremely difficult to test this possibility for monosubstituted zwitterions, we have done so for a dialkyl zwitterion. Ozonolysis of tetramethylethylene to completion in neat cyclohexanone at 0°C and at room temperature does not yield a trace of lactone (4). We conclude that the zwitterion Baeyer-Villiger reaction is unlikely in these cases.



Eq. 5

While the results reported here demonstrate a high probability that a subsequent Baeyer-Villiger reaction can account for abnormal products in ozonolyses, they do not demonstrate that zwitterion rearrangement to acid or ester does not occur. It would seem difficult, in fact, to account for very high yields of abnormal products such as in the case of (1) to give phenol(2) in yields as high as 48% by a peracid oxidation alone without extensive over-ozonization. We note, however, that Bernatek has demonstrated that carboxylic acids react with ozonides to produce peracids.*(13)*.

Thus while no definitive evidence exists concerning rearrangement of zwitterions to acids or esters, we have recently reported evidence for a zwitterion(5) tautomerization to a vinyl hydroperoxide(6) followed by rearrangement to hydroxyacetone; alternatively, 1,3-dipolar addition of 5 to 6 yields a peroxyhydroperoxide(7).*(14)* This general reaction scheme must also, therefore, be considered as a potential source of abnormal products in evaluating an ozonolysis reaction.



In conclusion, we submit that the weight of the evidence holds that many "abnormal" ozonolysis products are normal Baeyer-Villiger products generated by the action of peracid formed in the reaction by ozone/oxygen oxidation of aldehyde. This would suggest, since ozone alone does not generate peracids from aldehydes *(10)*, that rearrangements could be minimized by utilizing ozone/nitrogen mixtures in ozonolysis. This possibility is being investigated further.

ACKNOWLEDGEMENT:

We thank the Public Health Service, National Center For Air Pollution Control, for support of this work through Grant AP00505.

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