

The Homolytic Ring Opening of Epoxides in the Liquid Phase

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Recent studies on homolytic ring opening of cyclic ethers, especially on that of epoxides, in the liquid phase have been summarized classifying them into two reaction types. 1. Ring opening after hydrogen abstraction from cyclic ethers including epoxides. 2. Ring opening of epoxides by free radical addition. As to 1, the effects of ring size and of substituents at epoxide ring-carbon on the ease of hydrogen abstraction are mainly discussed. As to 2, the possibility of free radical polymerization of epoxides and the problem of conjugative effect of substituents at ring carbon are considered.

INTRODUCTION

It has been shown that the homolytic reaction of cyclic ethers having an α -hydrogen atom proceeds through the initial formation of α -ethereal radicals by hydrogen abstraction. As in the case of aliphatic ethers, the resulting radicals undergo chain transfer (substitution), fragmentation and dimerization. Here, the fragmentation means the ring opening into α -keto alkyl radicals and this transformation corresponds to the fragmentation into alkyl radicals and carbonyl compounds in aliphatic ethers. Furthermore, another type of ring opening by free radical addition has been found in the peroxide-induced reaction of various epoxides, including tetrasubstituted derivatives. According to the view of known similarities among epoxide ring, cyclopropane ring and olefinic bond, such radical addition would be natural.

In this review, somewhat detailed discussions on these two types of ring-opening reactions of cyclic ethers, especially on those of epoxides will be given.

1. HYDROGEN ABSTRACTION FROM CYCLIC ETHERS AND RING OPENING OF THE RESULTING RADICALS

1a. Ring Opening after α -Hydrogen Abstraction from Epoxides

Like aliphatic ethers, epoxides undergo α -hydrogen abstraction to give the free radicals of type I (1,2-epoxy alkyl radicals) which might be stabilized by resonance as represented by the hybrid structure I'.



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The relative reactivities of cyclic ethers including various epoxides towards *tert*-butoxyl radical have been determined by Wallace and Gritter.¹³ They estimated the *tert*-butanol/acetone ratios in reaction products obtained by treatment of cyclic ethers with di-*tert*-butyl peroxide (DTBP) at 135°C. The results are shown in Table 1.

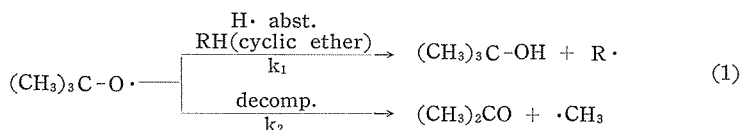


Table 1.

RH	Observed k_1/k_2	k_1/k_2 (relative to benzene)
Benzene	0.032	1.0
Propylene oxide	0.035	1.1
1,2-Epoxybutane	0.08	2.7
1,2-Epoxyoctane	0.21	7.0
Phenyl glycidyl ether	0.18	6.0
Styrene oxide	0.34	10.6
4-Methyl-3,4-epoxy-2-pentanone	0.10	3.3
Trimethylene oxide	0.045	1.4
Tetrahydrofuran	0.47	15.7
Tetrahydropyran	0.45	15.0

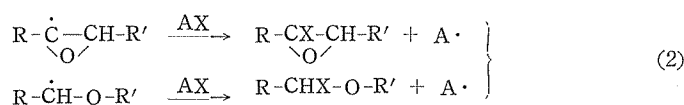
In comparison with alkylene oxides, the higher reactivity of styrene oxide or phenyl glycidyl ether is undoubtedly ascribed to high resonance stabilization of the resulting radical.

The effect of ring size on α -hydrogen abstraction is clearly indicated in the order of increasing reactivity 3-<4-<6-<5-membered, by a comparison of k_1/k_2 values. This order is in agreement with that on the reaction of cycloalkanes with methyl radical.²¹ A similar ring-size effect has also been found on α -hydrogen abstraction from five- and six-membered cyclic acetals.³¹

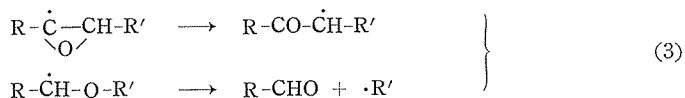
The extreme low reactivity of epoxide or trimethylene oxide is apparently due to its angle strain as follows: the bond angle in the ring is considerably less than the normal angle of 109°, therefore all bonds joined to ring atoms take on some sp^2 character, and this results in enhancement of C(ring)-H bond strength. The situation is very similar to the difficult formation of phenyl radical from benzene or of vinyl radical from ethylene.

On the fate of the 1,2-epoxyalkyl radicals the following two courses have been known, and the corresponding transformations in α -ethereal alkyl radicals are also shown for comparison.

Substitution:

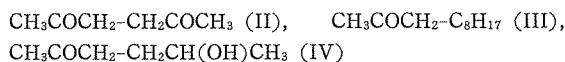


Fragmentation :



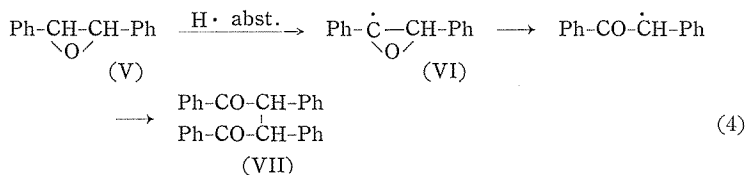
Walling and Fredrick⁴³ showed that the ultraviolet-initiated reaction of ethylene oxide and propylene oxide with *tert*-butyl hypochlorite at 0~70°C gave the corresponding α -chloro-epoxides in yields of 90 % and 45 %, respectively, and gave no ring-opening product. From this result it would appear that the reaction proceeds through Eq. 2.

On the other hand, in the DTBP-induced reaction of propylene oxide using 1-octene as a scavenger at 150°, Gritter and Wallace⁵⁾ obtained the following products:



In contrast to the preceeding result, no formation of a compound having epoxide ring was reported. The above three compounds suggest the intermediate formation of acetylonyl radical, probably through Eq. 3. The compounds III and IV would be formed by radical addition of the radical to 1-octene and propylene oxide, respectively. On the latter addition, details will be given in a later section. Considering from the reaction conditions, the homolytic ring opening of 1,2-epoxyalkyl radicals seems to occur at moderately high temperatures.

Recently, Huang and Lee⁶⁾ have found somewhat different behavior between *cis*- and *trans*-stilbene oxides (V) on the reaction of both isomers with DTBP to yield α,α' -dibenzoylbibenzyl (VII) through the radical VI.



The *cis* isomer gave approximately equal amounts of *meso*- and *dl*-VII (total yield: 57 %); whereas the *trans* isomer gave only the *meso* form in a slight yield, in addition to a considerable amount of a polymeric product (probably polyether). The higher reactivity of the *cis* isomer than the *trans* isomer would be ascribed to lesser steric crowding on hydrogen abstraction from the *cis* isomer. In contrast, the formation of polyether from the *trans* isomer may be explained as follows: the radical addition to the epoxide proceeds through much crowded transition state (see section 2c), and the reaction would be more favorable for less crowded *trans* isomer.

1b. Ring Opening after β -Hydrogen Abstraction from Epoxides

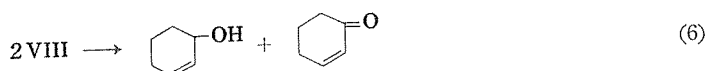
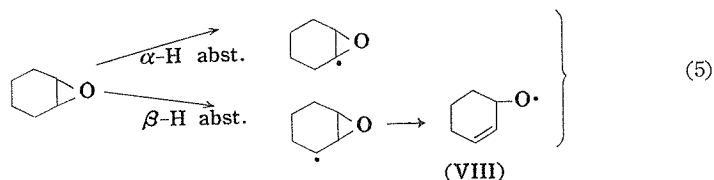
In addition to the facile α -hydrogen abstraction, the abstraction of a β -hydrogen atom would also be possible to some extent under appropriate conditions. This was confirmed by Sabatino and Gritter,⁷ who performed the reaction of some

epoxides with DTBP (in the absence of a scavenger) and obtained various products as shown in Table 2.

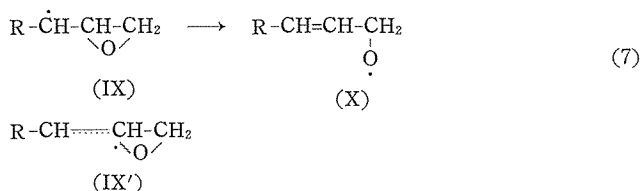
Table 2.

Reactant	Products (%)	Origin of Products
Cyclohexene oxide	Cyclohexanone (32)	α -H abstraction
	2-Cyclohexenone (9)	β -H abstraction
	2-Cyclohexenol (7)	β -H abstraction
1,2-Epoxybutane	2-Butanone (0.12)	α -H abstraction
	Crotonaldehyde (0.18)	β -H abstraction
	Crotyl alcohol (0.14)	β -H abstraction
Propylene oxide	Allyl alcohol (2)	β -H abstraction
Propylene sulfide	Thioacetone (0.15)	α -H abstraction
	Allyl mercaptane (0.30)	β -H abstraction
	Allyl disulfide (0.84)	β -H abstraction

The following scheme is a typical one to explain all the products from cyclohexene oxide.



Somewhat easier elimination of β -hydrogen would be associated with the gain of homo-allylic resonance, which can be represented by the hybrid IX'; and the isomerization to β,γ -unsaturated alkoxy radicals (X) may be favored. A quite similar explanation for the ring-opening reaction of cyclopropylmethyl radical⁹⁾ has been known well.



The chain termination would occur by disproportionation, which is shown in Eq. 6, since nearly equal amounts of unsaturated ketone or aldehyde and alcohol are isolated. Therefore, another termination by means of certain transfer agents seems to be less probable. It has also been shown that propylene sulfide undergo α - and β -hydrogen abstractions, but the chain termination after β -hydrogen transfer can occur by recombination of the thiyl radical, in contrast to epoxide.

1c. Ring Opening of 4-, 5- and 6-Membered Cyclic Ethers

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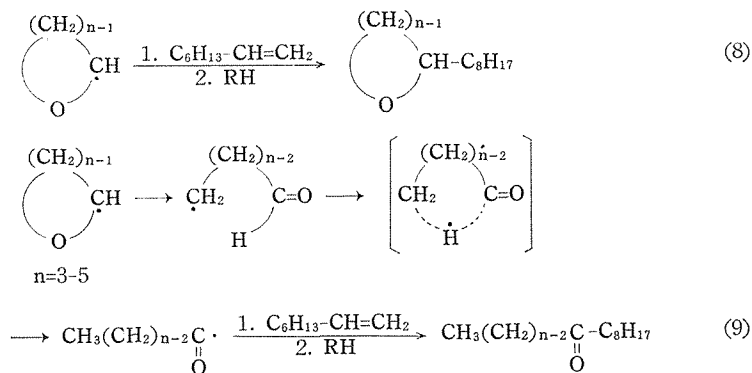
It is very interesting to know the reaction mode of other cyclic ethers, in comparison with that of epoxides. Some consideration on α -hydrogen abstraction from cyclic ethers has already been made in section 1a. Therefore, we shall mention here the following steps, especially the ring-opening reaction.

Wallace and Gritter⁹⁾ investigated the DTBP-induced reaction of trimethylene oxide, tetrahydrofuran and tetrahydropyran in the presence of 1-octene at 135~150°, and obtained α -dodecyl cyclic ethers and alkyl dodecyl ketones as products. The results are shown in Table 3.

Table 3.

Reactant	Products (%) (based on 1-octene consumed)
Trimethylene oxide	3-Undecanone (65)
Tetrahydrofuran	4-Dodecanone 2-Octyl-tetrahydrofuran } (79)
Tetrahydropyran	5-Tridecanone 2-Octyl-tetrahydropyran } (49)

The formation of the ethereal adduct can be understood by Eq. 8, and the ketonic adduct would be produced by Eq. 9.

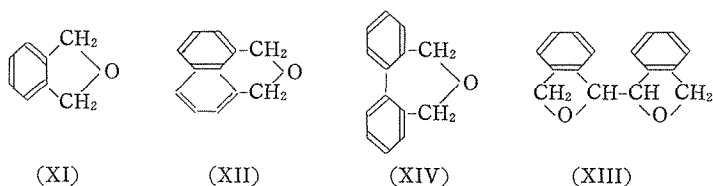


The conversion of ω -formyl alkyl radicals into acyl radicals seems to be an intramolecular hydrogen transfer, which probably proceeds in a "cage". English¹⁰⁾ and German¹¹⁾ chemists have already made detailed discussions on such transfer process. Moreover, this interesting rearrangement would be characteristic for four-membered and larger. (Compare Eqs. 9 and 3). Trimethylene oxide, unlike five- and six-membered cyclic ethers, gave only the corresponding ketone and this clearly results from a high angle strain.

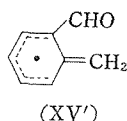
Similar reaction modes of other cyclic ethers such as cyclic acetals,^{3,15)} dioxane,¹²⁾ morpholine¹³⁾ and α -perhydroxy cyclic ethers¹⁴⁾ have also been reported recently.

Some examples in which the steric inhibition suppresses the ring opening of the α -ethereal cyclic radicals have been found by Huang and Lee.⁶⁾ In the DTBP-induced reaction, phthalan (XI) and naphthalan (XII) gave the corresponding dimers

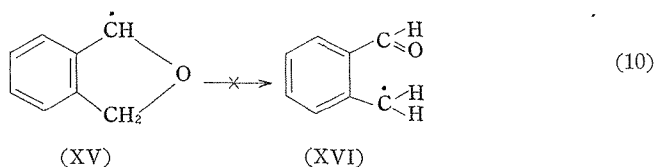
having the structure of α,α' -bis(cyclic ether) type, such as XIII, whereas diphenan (XIV) gave a rearranged cyclic alcohol.



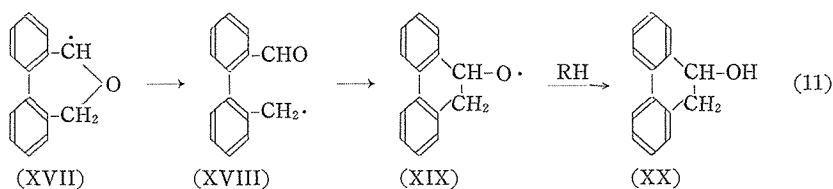
In this reaction, if the initially-formed α -ethereal radicals undergo the ring opening, the resulting benzyl-type radicals would be somewhat stable, because of the gain of resonance, such as XV'.



However, such ring opening is not found except in the case of XIV. As a reasonable explanation, the suppression of the resonance due to the interference between sterically too closed formyl and methylene groups may be considered.



An experimental support on such inhibition has been given. Thus, in the DTBP-induced reaction of *o*-tolualdehyde, the formation of 2-methyl-benzoyl radical, not 2-formyl benzyl radical, was observed, notwithstanding that the dissociation energies of benzylic C-H linkage in toluene and of formyl C-H linkage in benzaldehyde were approximately equal. On the other hand, in the case of XIV, the absence of steric inhibition, *i.e.*, the lack of coplanarity of two benzene rings in a benzyl-type radical XVII, would facilitate the ring opening of XVII.



2. THE RING-OPENING OF EPOXIDES BY FREE RADICAL ADDITION

2a. The Ultraviolet Photolysis of Epoxides

In ultraviolet photolysis of epoxides in the gas phase, the intermediate forma-

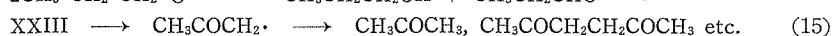
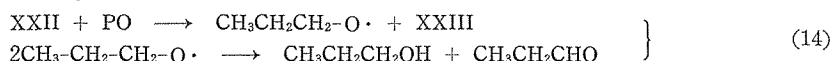
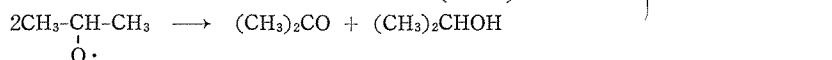
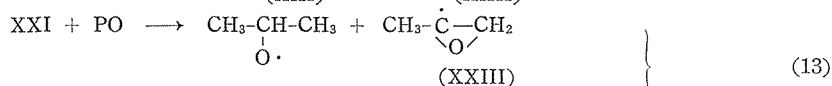
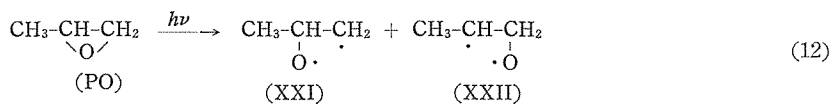
tion of diradicals was suggested. Gritter and Sabatino¹⁶³ subsequently studied the liquid-phase photolysis of some epoxides in expectation of recognizing the diradicals, which would be formed by the cleavage of C-O linkage¹⁷², and of knowing the effect of substituent on the orientation of cleavage. The results are shown in Table 4.

Table 4.

Epoxide	Product	Origin*	Conversion (%)
Propylene oxide	Acetone	C ₁ -O cleavage	0.28
	Isopropyl alcohol	C ₁ -O cleavage	0.21
	Propionaldehyde	C ₁ -O cleavage	0.01
	Propyl alcohol	C ₂ -O cleavage	0.01
	2,5-Hexanedione	C ₁ -O cleavage(and dimerization)	0.22
Styrene oxide	Acetophenone	C ₁ -O cleavage	0.03
	2-Phenyl-ethanol	C ₂ -O cleavage	0.14
	1-Phenyl-ethanol	C ₁ -O cleavage	0.13

* C₁ means primary ring carbon atom and C₂ means secondary one.

The following mechanism was proposed for the reaction of propylene oxide:



From this study, it was found that the C(primary)-O to C(secondary)-O cleavage ratio was ca. 25:1 with propylene oxide, and ca. 1:1 with styrene oxide. In the former, the preferential cleavage of C(primary)-O linkage is not readily explained, whereas in the latter, as will be mentioned later, the enhanced cleavage of C(secondary)-O linkage would be attributed to the conjugative effect of phenyl group attached to ring carbon atom.

2b. The Free Radical Polymerization of Epoxides having Some Hydrogens on the Ring

In the peroxide-induced reaction of propylene oxide, the formation of 1:1 adduct of acetyl radical and the epoxide (see section 1a) is of interest to us, because it involved the ring-opening attack of the radical on ring carbon and if the attack of the resulting alkoxy radical occurs successively, the formation of a polyether would be possible. Indeed, a considerable amount of non-distillable residue, like a polymeric product, was obtained occasionally in some radical reactions of epoxides.¹⁸⁾ In addition, the radical copolymerizations of ethylene oxide with some perfluoroolefins have also been known.¹⁹⁾

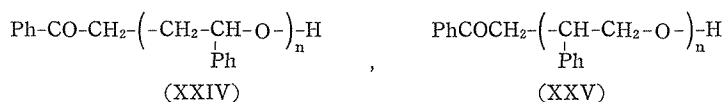
Recently, the authors²⁰⁾ have examined the possibility of homopolymerization of styrene oxide (SO) or phenyl glycidyl ether using DTBP as an initiator. In general, the degree of polymerization was not so high. The structures of the obtained polymers were based on infrared and chemical analyses. Some results are shown in Table 5.

Table 5.

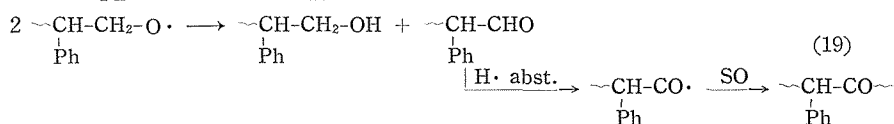
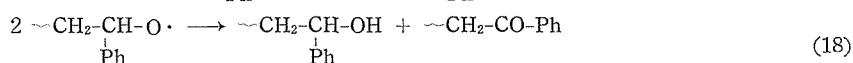
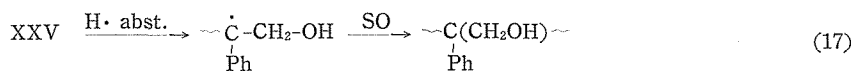
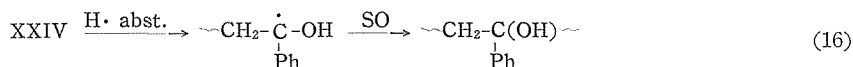
Epoxide*	Molar Ratio of Epoxide/DTBP	Temp. (°C)	Polymer (%)	M.W.	$[\eta]$	OH group (unit/molecule)	CO group
SO	2.5	140-145	21	2000	0.07	1.8	1.5
SO	10	135-143	9.6	1800	0.05	2.0	1.6
PGE	10	145-155	7.7	1200	—	1.8	1.8
SO	10(BPO)	80- 81	21	1300	—	1.0	0.85

* So: styrene oxide, PGE: phenyl glycidyl ether.

Infrared data suggested that the polymer would be a polyether having a head to tail structure. Since the acylmethyl radical derived from α -ethereal radical is a chain initiator, the following two structures (XXIV and XXV) would be expected.



But the matter appeared to be complicated by the following factors: the slow propagation rate due to the considerably high activation energy for ring opening and the facile fragmentation and disproportionation of the growing alkoxy radical at high temperature. In fact the polymer obtained by the benzoyl peroxide-induced polymerization at low temperature showed the expected hydroxyl number. A low carbonyl value seems to imply the additional contribution of benzoyl radical as a initiator. However, in the DTBP-induced polymerization, the carbonyl and hydroxyl groups in the polymer were estimated to be more than one unit per molecule, unexpectedly. Thus, it became apparent that its structure should be represented in somewhat modified forms. The following transformations would be considered.



The presence of two ketonic absorptions (corresponding to aliphatic ketone and benzoyl ketone) in the infrared spectra of the polymer strongly supports that the

radical attack can occur on both carbon atoms of the ring. In view of Gritter's observation of an exclusive attack on primary ring carbon atom in homolytic reaction of propylene oxide, we cannot overlook an attack on secondary ring carbon atom in this reaction.

As a conclusion, the peroxide-induced polymerization of epoxides is practically impossible because of the facile disproportionation and hydrogen abstraction of the growing alkoxy radical at high temperatures which cause short chain termination and branching.

2c. A Free Radical Addition to Tetrasubstituted Epoxides

To know the mode of homolytic ring opening of epoxides precisely, an attempted decomposition of epoxides which have no ring hydrogen would be desirable. The authors²¹⁾ have examined the DTBP-induced reaction of α,β,β -trimethylglycidates (XXVI a and b) in the liquid phase. The isolated products are summarized in Table 6.

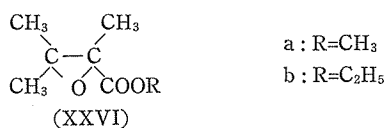


Table 6.

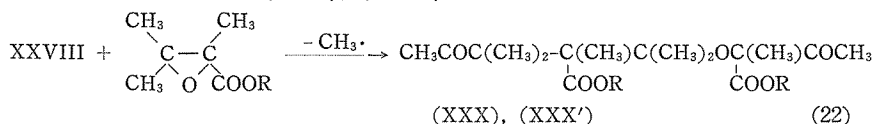
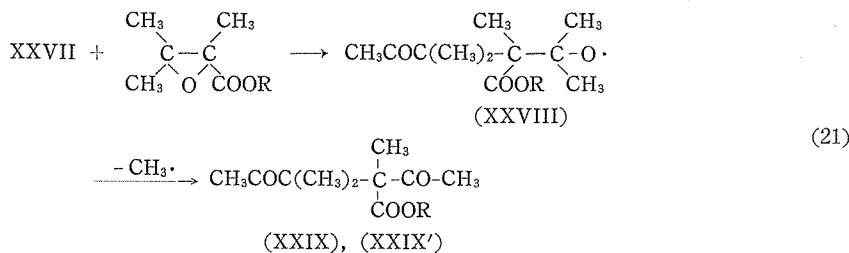
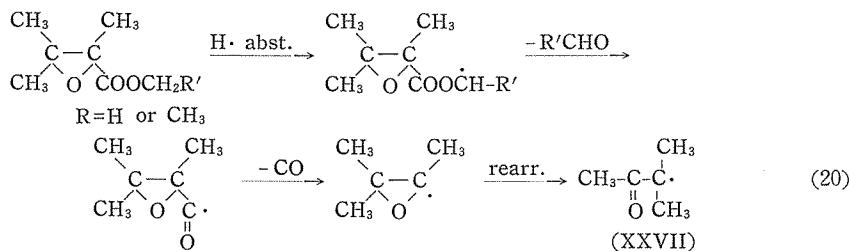
Products from the glycidate XXVIa	bp/mmHg	Yield (%)
Acetone and t-BuOH	t-BuOH/acetone=0.56	
CH ₃ COCH ₂ CH ₂ COCH ₃ (XXXI)	80-85°/23	2
CH ₃ COCH ₂ C(CH ₃)COCH ₃ (XXXII)	82-85°/0.5	1.6
CH ₃ COC(CH ₃) ₂ C(CH ₃)COCH ₃ (XXIX)	110-113°/0.5	3.4
CH ₃ COC(CH ₃) ₂ C(CH ₃)C(CH ₃) ₂ OC(CH ₃)COCH ₃ (XXX)	131-132°/0.03	1.6
Oligomer		13.7
Products from the glycidate XXVIb	bp/mmHg	Yield (%)
Acetone and t-BuOH	t-BuOH/acetone=0.66	
CH ₃ COC(CH ₃) ₂ C(CH ₃)COCH ₃ (XXIX')	63-65°/0.01	4.4
CH ₃ COC(CH ₃) ₂ C(CH ₃)C(CH ₃) ₂ OC(CH ₃)COCH ₃ (XXX')	103-105°/0.01	6.2
Oligomer		17.4

The above results give us the following four interesting informations.

1. The attacking radical on epoxide was an α -acylmethyl type radical.
2. Along with a 1:2 adduct from acylmethyl free radical with the glycidate, considerable amount of an oligomer having a similar structure was obtained. This clearly indicates the presence of propagation with *t*-alkoxy radical.
3. In the reaction of the methyl ester XXVIa, the compounds having acetonyl end-group were isolated, but in the case of ethyl ester XXVIb no such adduct was found.

4. The attacking position on the glycidate was preferentially α -carbon atom joined to ester group.

A most reasonable reaction course would be given as follows:



Equation 20, which leads to the formation of α,α -dimethyl acetonyl radical (XXVII), seems to be established without question, because the formation of carbon monoxide and aldehyde has been ascertained and a structural unit of $\text{CH}_3\text{COC}(\text{CH}_3)_2$ is contained in many products (XXIX, XXIX', XXX and XXX'). The first step of this reaction is, of course, hydrogen abstraction from ester groups, and the expectation that the reactivity of ethyl ester would be higher than that of methyl ester is fulfilled by a higher *t*-BuOH/Acetone ratio in the reaction of the ethyl ester. Somewhat difficult abstraction of hydrogen atom from methyl ester causes the formation of acetonyl radical from acetone (formed from DTBP) to some extent. The compounds XXXI and XXXII correspond to the products derived from this radical.

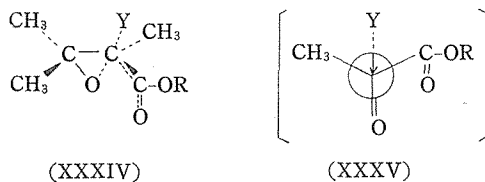
The structure of all adducts shows that the attack of α -acylmethyl radicals occurs on the α -carbon of the epoxides exclusively to produce a *tert*-alkoxyl radical XXVIII. The compounds XXIX and XXIX' correspond to the demethylation products from XXVIII. (Eq. 21). The addition of XXVIII to the glycidates would lead to XXX and XXX' (Eq. 22).

In this reaction, no adduct derived from *tert*-butoxyl radical, $(\text{CH}_3)_3\text{CO}\cdot$ (XXXIII), is formed, though XXXIII is similar in structure to XXVIII. There is no adequate explanation on this point, but less reactivity of XXXIII might be due to its increased stabilization over XXVIII.

Finally, we shall consider the problem why the preferential attack can occur on the ring carbon joined to phenyl (see section 2b) or ester group. The contribution of such conjugative groups would be possible in the transition state, as pictured

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below, and therefore a SH-2 attack by radical Y from the back side of epoxy oxygen will be necessary, in which ethereal O, attacking radical Y and ester CO groups must become coplanar with the α -carbon atom.



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