

EtO group), 18.67 (q, $J = 128.2$ Hz, CH_3 from Me group), 47.26 (t, $J = 134.2$ Hz, C-4), 57.10 (t, $J = 146$ Hz, CH_2 from EtO group), 69.41 (t, $J = 151.4$ Hz, C-5), 105.90 (s, C-3); IR (CCl_4) 2990 (s), 2945 (s), 2890 (s), 1770 (vw), 1725 (vw), 1450 (w), 1395 (w), 1385 (s), 1305 (w), 1210 (s), 1165 (vs), 1125 (s), 1105 (s), 1065 (vs), 960 (w), 905 (w), 865 (s) cm^{-1} ; GC-MS (70 eV), m/e (relative intensity) 132 (M^+ , 6), 99 (100), 87 (61), 72 (25), 71 (29), 61 (8), 57 (11), 43 (88), 42 (13).

Synthesis of 2a from 3-Bromo-1-methoxypropyl Hydroperoxide (12) with Silver Oxide. 4-Bromo-1-butene, 270 g (20 mmol), was ozonized in 30 mL of methanol. The methanol was removed by using a water aspirator and the residual volatile products were removed on a vacuum line. The residue (3.30 g, 90%) 12 was dissolved in 50 mL of dichloromethane and treated with 5 g of silver oxide while cooling with an ice bath. After it was stirred for 12 h at 25 °C the reaction mixture was filtered, dichloromethane was removed, and the product was distilled at high vacuum. A yield of 1.67 g (16 mmol, 80%) of 2a was obtained.

Synthesis of Deuterium-Labeled Ethyl Vinyl Ethers 7a-e. To lithium aluminum hydride or deuteride (2.5 g, 66 mmol or 60 mmol) in 60 mL of diglyme 7 g (100 mmol) of ethoxyacetylene (6a) or ethoxyacetylene- d_1 (6b) was added dropwise. Intermittent cooling maintained the temperature between 35 and 40 °C. After an additional hour at room temperature deuterium oxide or water was added dropwise, while the reaction temperature was maintained between 20 and 30 °C. The reaction product was distilled under vacuum into a trap at -196 °C. Redistillation yielded the corresponding ethyl vinyl ethers 7a-e in yields between 3 and 3.7 g or 42-51%. The product was allowed to stand over calcium hydride for 12 h and was then stored at -16 °C under argon. ^1H NMR spectra of the labeled ethyl vinyl ethers are given in Table II. The stereospecificity in the products was nearly 100%.

Ozonolysis of Deuterated Ethyl Vinyl Ether. 7a-e, 500 mg (6.75 or 6.85 mmol), in 10 mL of pentane was ozonized at -78 °C. After the reaction mixture was degassed and warmed to 0 °C, it was treated with a solution of 178 mg (0.68 mmol) of triphenylphosphine and stirred 2 h at 25 °C. The solvent was removed with a water aspirator and the dioxolanes 8a-i were isolated by high-vacuum distillation. The results of the ^1H NMR

spectra are shown in Table III. Table V gives the ^{13}C NMR data for the labeled dioxolanes.

Decomposition Reactions of 3-Alkoxy-1,2-dioxolanes 2a-c. Approximately 300 mg of the respective dioxolane was stored in an evacuated sample bulb at 25 °C for 2 weeks. At that time, 2a and 2b were completely decomposed while appreciable amounts of 2c still remained. The volatile products were then distilled at room temperature on a vacuum line into a trap at -196 °C leaving an involatile residue (200 mg) which contained as the major product methyl β -hydroxypropionate²⁵ (9a) from 2a, ethyl β -hydroxypropionate²⁶ (9b) from 2b and undecomposed starting material from 2c. The volatile products were acetaldehyde, methyl formate, and methyl acetate (4:5:1) from 2a and acetaldehyde, ethyl formate, and ethyl acetate from 2b and 2c in a ratio of 4:4.5:1.5 and 6.5:2:1.5, respectively. There was also evidence for formaldehyde and traces of ethylene oxide. Acid-catalyzed rearrangements were carried out by dissolving 1-6 mmol of 2a-c in approximately 5 mL of dry methanol and ethanol and treating this overnight (stirring) with 200-500 mg of Amberlyst 15. After separation of the Amberlyst, the alcohol was removed by distillation at 20 torr. The product was distilled in a high vacuum and identified as methyl β -hydroxypropionate²⁵ (9a, 53%) from 2a, ethyl β -hydroxypropionate²⁶ (9b, 66%) from 2b and 1,1-diethoxybutan-3-one²⁷ (11c, 76%) from 2c.

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Stereochemistry in the 1,3-Dipolar Cycloaddition Reactions of Formaldehyde Oxide- d_1 (HDCOO)

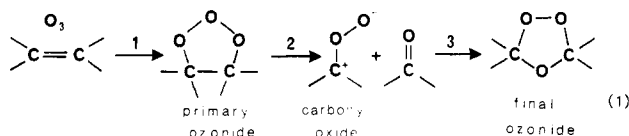
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Ozonolysis of *E,Z* pairs of ethyl vinyl- $2-d_1$ ether, ethyl vinyl- $1,2-d_2$ ether, styrene- $\beta-d_1$, and 1-hexene- $1-d_1$ were investigated in pentane and ester solvents and in the presence of added acetaldehyde and benzaldehyde. Different amounts of H,D stereoselectivity were found at C(5) in the resultant 1,2,4-trioxolanes and 1,2-dioxolanes. The deuterium atoms at C(5) in the predominant trioxolane isomers had the same configuration as in the starting alkenes but the opposite configuration in the predominant dioxolane isomers. The stereoselectivity was associated with syn-anti isomerism in the carbonyl oxide HDCOO. It was analyzed, in the context of the Criegee mechanism, as arising from competing transition states in the decomposition of the primary ozonide and in the recombination of the carbonyl oxide with a dipolarophile. It was shown that syn-anti equilibration was not important and that the stereodirective influence of the dipolarophile reacting with HDCOO decreases in the order ester > acetaldehyde > benzaldehyde.

The carbonyl oxide produced during ozonolysis of an alkene (eq 1) is an intriguing 1,3-dipole which has played



a central role in the mechanism of ozonolysis since the 1950's.¹ It has a sufficient lifetime, especially in polar

media, to escape the initial solvent cage and react with a variety of dipolarophiles. However, low steady-state concentrations have precluded its spectroscopic detection. In spite of this fleeting existence a good deal has been inferred

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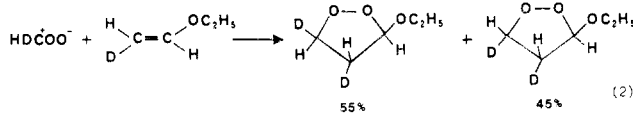
about its properties from indirect experiments.

Syn-anti isomerism was attributed to the carbonyl oxide in a seminal paper² which rationalized the stereoselective formation of cis and trans final ozonides. This isomerism has now been incorporated in all discussions of the reaction stereochemistry.^{1b,d,3} Theoretical calculations⁴ have also affirmed the concept of syn and anti isomerism. Most calculations,⁴ in agreement with inferences from experimental data,^{3a} indicate that the syn isomer is more stable for a single alkyl substituted carbonyl oxide.

Nevertheless the transitory existence of the carbonyl oxide and the puzzling nature of stereochemistry data especially with solvent and temperature changes^{1b,d,3} have impeded a clear understanding of the stereochemical properties of the carbonyl oxide. It has been difficult to determine the extent to which the partial randomization exhibited by the final ozonide cis/trans ratio arises from the following three possible sources: (1) stereoselective production of both carbonyl oxide isomers during cleavage of the primary ozonide; (2) partial syn-anti equilibration occurring after production, perhaps assisted by the solvent; (3) stereoselectivity in the recombination of the carbonyl oxide with the dipolarophile.

In this paper a series of experiments are described which provide some insight on these questions. Evidence is presented that the ozonolysis of stereospecifically deuterium labeled 1-alkenes produces an excess of one of the isomeric forms of HDCOO. This labeled carbonyl oxide is interesting since the energies of the syn and anti isomers are essentially identical, unlike the situation with alkyl substituted carbonyl oxides. Thus aspects of the ozonolysis reaction stereochemistry could be explored in the absence of steric influences from substituents on the carbonyl oxide. In particular, the questions of syn-anti equilibration and the stereoselectivity in the recombination of the carbonyl oxide with a dipolarophile could be examined from a new perspective.

These investigations were fostered by recent work on the synthesis of 3-alkoxy-1,2,4-trioxolanes (ozonides) and 3-alkoxy-1,2-dioxolanes by 1,3-dipolar cycloaddition reactions of the carbonyl oxide H_2COO with esters and enol ethers, respectively.⁵ This work showed that the cycloaddition of HDCOO to a stereolabeled vinyl ether such as (*E*)-ethyl vinyl-2-*d*₁ ether occurs with retention of configuration of the alkene hydrogen atoms at the C(3)-C(4) bond of the dioxolane but with incomplete randomization of the stereochemistry at C(5) (eq 2). The partial randomization



at C(5) was unexpected since previously reported reactions of HDCOO with carbonyl compounds to form 1,2,4-trioxolanes occurred with complete H,D randomization.⁶ The curious stereoselectivity at C(5) suggested some

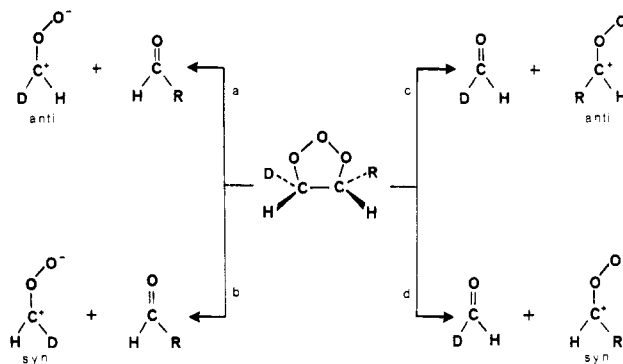


Figure 1. Cleavage paths for a 1-alkene-1-*d*₁ primary ozonide.

preferential syn-anti isomerism in the carbonyl oxide formation and stereoselectivity in its subsequent reaction with the enol ether. This motivated us to examine the reactions of HDCOO more thoroughly and particularly to look for stereoselective effects in 1,2,4-trioxolanes as well as at C(5) in any 1,2-dioxolanes which are formed during the ozonolysis of enol ethers.^{5b,c} The stereochemistry between C(3) and C(4) in the dioxolane resulting from cycloaddition to the alkene will not be discussed in this paper; this process is stereospecific and has been discussed previously.^{5c}

Results and Discussions

Several pairs of stereolabeled 1-alkenes were employed to study the reactions of HDCOO, including ethyl vinyl-2-*d*₁ ether (1a,b), ethyl vinyl-1,2-*d*₂ ether (1c,d), styrene- β -*d*₁ (2a,b), and 1-hexene-1-*d*₁ (3a,b) (see Chart I). Besides normal ozonide and dioxolane formation, cross ozonide formation between HDCOO and added carbonyl compounds was also investigated using acetaldehyde, benzaldehyde, ethyl formate, and ethyl acetate as the dipolarophiles. The low dipolarophilicities of the esters led to their use as the reaction solvent while pentane was the solvent in other ozonolyses.

The yields of the cis/trans isomeric 1,2,4-trioxolanes and 1,2-dioxolanes from product isolation and ¹H NMR are shown in Table I. The stereoassignment in the dioxolanes is based on NOE experiments and is discussed elsewhere.^{5c} Although all the trioxolanes were known, a stereochemical assignment of their ¹H NMR spectra has been reported only for 5c and 5d.⁷ The stereoassignment for the deuterated alkoxy ozonides (4a etc.) was established by correlating NMR intensity changes with microwave intensity changes where the isomer assignment is clear.⁸ The complete stereochemical assignment used in the present work is shown in Table II. It uniformly assigns the downfield hydrogen atom at C(5) cis to the substituent at C(3).

Ozonolysis of ethyl vinyl ether 1a-d (runs 1-4) in pentane gave trioxolanes 4 and dioxolanes 8 in similar yields as nonlabeled alkenes. The relative ratios of the stereoisomers for the ethoxy trioxolanes 4a,b and 4c,d, showed a remarkable 3:1 excess for one isomer. The major isomer always had the same configuration for the deuterium atom at C(5) in the trioxolane (cis or trans relative to OEt) as in the starting alkene. In the dioxolane, the isomer ratio was 1.22:1 and the deuterium atom at C(5) for the major

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(8) Isotopic shifts and intensity differences in the microwave spectra of the cis and trans isomers of $\overset{\ominus}{C}HDOOCH(OCH_3)\overset{\ominus}{O}$ result in a stereo-isomer identification which can be correlated unambiguously with ¹H NMR assignments^{5c} for alkoxy ozonides. Soltis, M. B.; Kuczkowski, R. L., unpublished results.

Table I. Trioxolane and Dioxolane Products (Yields and Isomer Ratios) from Ozonolysis of Deuterated 1-Alkenes

run ^a	alkene	solvent	trioxolanes (rel amt)	yield, %	dioxolanes (rel amt)	yield, %
1	1a	pentane	4a (76) 4b (24)	8	8c (45) 8d (55)	73
2	1b	pentane	4a (25) 4b (75)	6	8f (56) 8e (44)	62
3	1c	pentane	4c (77) 4d (23)	7	8a (43) 8b (57)	75
4	1d	pentane	4c (25) 4d (75)	5	8h (55) 8g (45)	64
5	2a	pentane	5a (50) 5b (50)	84		
6	2b	pentane	5a (50) 5b (50)	88		
7	3a	pentane	6a (50) 6b (50)	78		
8	3b	pentane	6a (50) 6b (50)	81		
9	1a	ethyl acetate	4a (73) 4b (27)	4	8c (43) 8d (57)	41
			4e (77) 4f (23)	10		
10	1b	ethyl acetate	4a (28) 4b (72)	4	8f (54) 8e (46)	44
			4e (23) 4f (77)	10		
11	1c	ethyl acetate	4c (69) 4d (31)	2	8a (45) 8b (55)	49
			4e (79) 4f (21)	9		
12	1d	ethyl acetate	4c (28) 4d (72)	4	8h (55) 8g (45)	49
			4e (24) 4f (76)	11		
13	1a	ethyl formate	4a (77) 4b (23)	28	8c (46) 8d (54)	51
14	1d	ethyl formate	4a (26) 4b (74)	33	8h (56) 8g (44)	51
15	2a	ethyl formate	4a (75) 4b (25)	5		
			5a (53) 5b (47)	71		
16	2b	ethyl formate	4a (24) 4b (76)	5		
			5a (48) 5b (52)	69		
17	3a	ethyl formate	4a (72) 4b (28)	2		
			6a (50) 6b (50)	55		
18	3b	ethyl formate	4a (32) 4b (68)	2		
			6a (50) 6b (50)	65		
19	1c	pentane, CH ₃ CHO	7a (61) 7b (39)	15		
20	1d	pentane, CH ₃ CHO	7a (38) 7b (62)	15		
21	2a	pentane, CH ₃ CHO	7a (59) 7b (41)	47		
			5a (53) 5b (47)	14		
			5c (32) 5d (68)	8		
22	2b	pentane, CH ₃ CHO	7a (40) 7b (60)	47		
			5a (48) 5b (52)	14		
			5c (31) 5d (69)	8		
23	1a	pentane, C ₆ H ₅ CHO	5a (57) 5b (43)	67		
24	1b	pentane, C ₆ H ₅ CHO	5a (45) 5b (55)	64		
25	3a	pentane, C ₆ H ₅ CHO	5a (56) 5b (44)	3		
			6a (49) 6b (51)	72		
26	3b	pentane, C ₆ H ₅ CHO	5a (44) 5b (56)	4		
			6a (50) 6b (50)	72		

^a Starting materials. Runs 1–6: 7.67 mmol of 1a, 7.12 mmol of 1b, 5.14 mmol of 1c, 9.46 mmol of 1d, 2.1 mmol of 2a, 2.38 mmol of 2b in 10 mL of C₅H₁₂. Run 7: 15.3 mmol of 3a, 25 mL of C₅H₁₂. Run 8: 9.41 mmol of 3b, 20 mL of C₅H₁₂. Runs 9–12: 4.68 mmol of 1a, 4.79 mmol of 1b, 4.05 mmol of 1c, 4.86 mmol of 1d in 10 mL of EtOAc. Runs 13–18: 5.62 mmol of 1a, 4.86 mmol of 1d, 8.38 mmol of 2a, 8.38 mmol of 2b, 3.17 mmol of 3a, 3.81 mmol of 3b in 10 mL of EtOCHO. Run 19: 6.3 mmol of 1c, 17.6 mmol of CH₃CHO, 15 mL of C₅H₁₂. Run 20: 6.75 mmol of 1d, 19.8 mmol of CH₃CHO, 15 mL of C₅H₁₂. Run 21–22: 10.0 mmol of 2a or 2b, 37.7 mmol of CH₃CHO, 20 mL of C₅H₁₂. Run 23: 6.44 mmol of 1a, 24.9 mmol of PhCHO, 20 mL of C₅H₁₂. Run 24: 2.87 mmol of 1b, 11.1 mmol of PhCHO, 10 mL of C₅H₁₂. Run 25: 3.94 mmol of 3a, 20 mmol of PhCHO, 21 mL of C₅H₁₂. Run 26: 4.10 mmol of 3b, 20 mmol of PhCHO, 21 mL of C₅H₁₂.

Table II. ¹H NMR Assignment (δ) for Ring Protons or Methyl Substituents in Trioxolanes 4–7

trioxolane	R ₁	R ₂	R ₃
4h	5.47 s	4.93 s	6.08 s
5e	5.39 s	5.31 s	6.02 s
6c	5.19 s	5.03 s	5.13 t
7c	5.18 s	5.04 s	5.26 q
4g	5.41 s	5.04 s	1.66 s
5c	1.55 d	5.57 q	6.06 s
5d	5.60 q	1.52 d	6.02 s

isomer had the opposite configuration as the alkene. In the case of styrene 2a,b (runs 5, 6) as well as in the case of 1-hexene 3a,b (runs 7, 8) ozonolysis gave a 1:1 mixture of the corresponding ozonides 5a,b and 6a,b. This is consistent with the results obtained earlier by Murray et al. who first ozonized labeled 1-hexenes.^{6a}

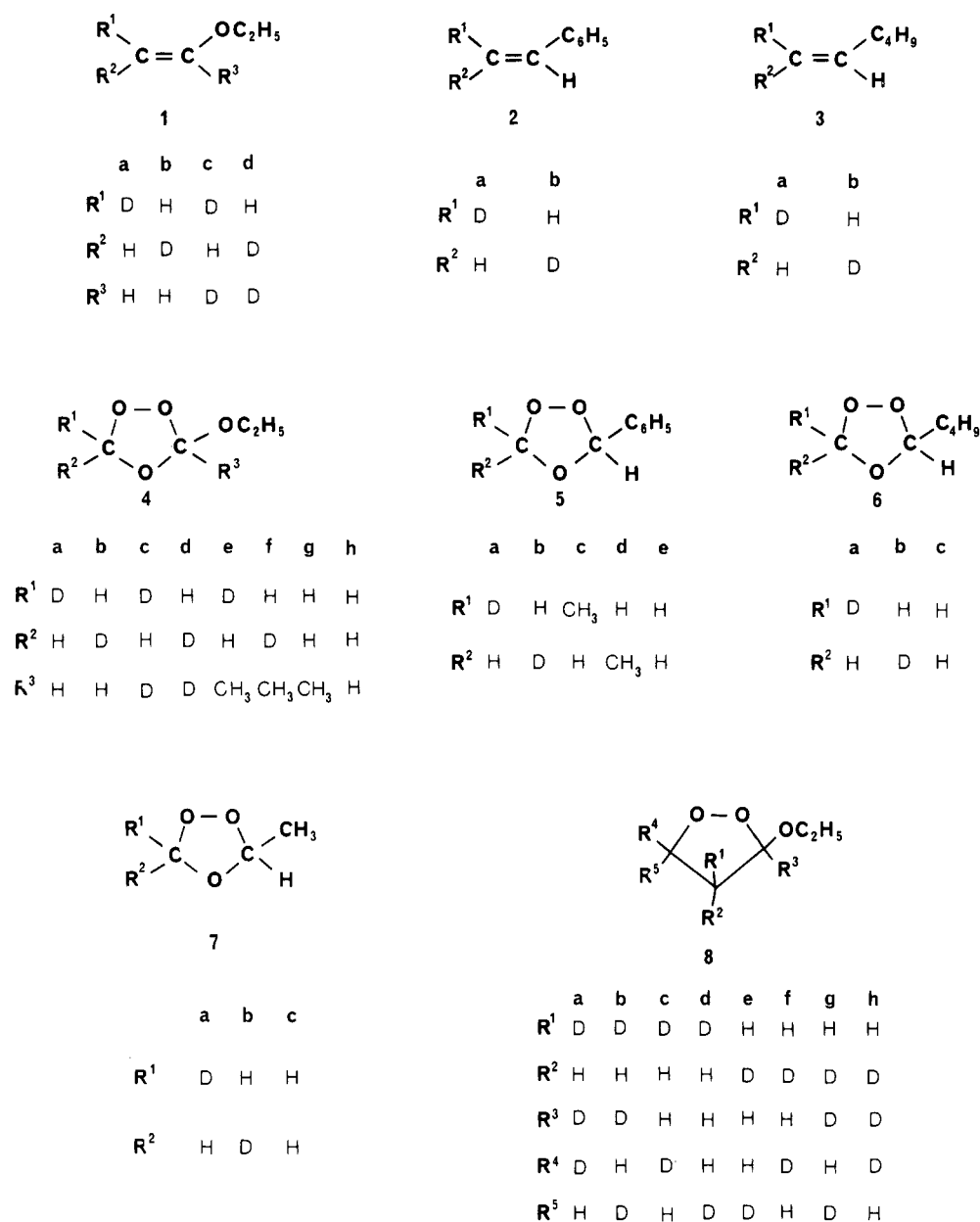
The different product stereoselectivity obtained from ethyl vinyl ether compared to styrene and 1-hexenes should be explicable in the context of the three-step Criegee mechanism of ozonolysis¹ (eq 1). An important distinction is that ethyl vinyl ether primary ozonide cleaves only in the direction of HDCCO^{5c} (i.e., paths c and d in Figure 1 do not occur significantly), while the cleavage is bidirectional for styrene⁹ and 1-hexene.¹⁰ For example, the ratio

of pathways a + b and c + d is 40:60 in the case of styrene. Thus, the ozonides 4a,b to 4c,d are formed only from HDCCO and ethyl formate while approximately 60% of the ozonides 5a,b (and similarly for 6a,b) are formed from PhHCCO and HDCCO and 40% from HDCCO and PhHCO. Since HDCCO cannot transfer any stereochemical information, at least 60% of the final ozonides (5 or 6) must have complete H,D randomization at C(5) of the trioxolane. This means that the ratios of 4a/4b, 4c/4d and 5a/5b, 6a/6b depend 100% and 40%, respectively, upon (1) any excess in the syn or anti HDCCO carbonyl oxide isomers produced in the second step of the Criegee mechanism (path a vs. b in Figure 1), (2) the extent of any subsequent syn-anti equilibration in the carbonyl oxide with or without solvent assistance, and (3) activation energy differences for competing stereoisomer transition states in the third step of the Criegee mechanism.

Some information on these factors can be inferred by comparing various results in Table I. Ozonolysis of the two pairs 1a,b and 1c,d in ethyl acetate (runs 9–12) com-

(9) Fliszár, S.; Renard, J. *Can. J. Chem.* 1970, 48, 3002.(10) While 1-hexene primary ozonide has not been examined, all other similar alkyl substituted 1-alkene primary ozonides show bidirectional cleavage.⁹

Chart I



pared to pentane (runs 1–4) gave expected changes in the product distribution, viz., less dioxolane and normal ozonide and a significant amount of cross ozonide (4e,f). No significant change in the normal ozonide cis:trans ratio (2.5:1) and only a slightly larger ratio for the cross ozonide (3.4:1) were observed. The differences in solvent polarity and nucleophilicity between ethyl acetate and pentane and the invariance in the ozonide ratios 4a:4b, 4c:4d, and 4e:4f are evidence for kinetic stability toward syn-anti equilibration for HDCOO.¹¹ Of course, it should be noted that there is no enthalpic driving force towards isomerization since both carbonyl oxides have essentially the same energy. Ozonolysis of 1a or 1d in ethyl formate (runs 13, 14)

also showed no differences in the ozonide ratios 4a:4b or 4c:4d compared to ozonolysis in pentane although the overall yield of trioxolane was higher.

It is remarkable that the cross ozonide ratio 4a:4b from ozonolysis of 2a or 2b in ethyl formate (runs 15, 16) is the same as from 1a or 1b and is only slightly different from 3a or 3b (runs 17, 18). However, the normal ozonide ratio 5a:5b and 6a:6b are 1.1:1 and 1:1, respectively. These results clearly imply that the production of HDCOO from all the pairs of isomeric 1-alkenes is highly stereospecific if not 100% and that the carbonyl compound in the recombination, step three, affects the final ozonide stereoselectivity. In order to examine the influence of the carbonyl compound, ozonolyses with added aldehyde were carried out and the cross ozonide cis:trans ratios were determined. Ozonolysis of 1c or 1d in pentane in the presence of an excess of acetaldehyde (2.8 M, runs 19, 20) gave a small amount (15%) of propylene ozonide 7a,b. The major isomer was produced in an excess of 1.5:1 and had the same configuration for the deuterium atom at C-5 in the trioxolane as in the starting alkenes 1c or 1d. From ozonolysis of 2a or 2b in pentane in the presence of excess

(11) There is general agreement among calculations¹² that barriers to syn-anti interconversion for a carbonyl oxide are high (>25 kcal). Such barriers should preclude equilibration given their short lifetime and the low reaction temperature. Therefore solvent interactions, such as coordination at the carbon atom by a nucleophilic solvent, are necessary to provide an equilibration pathway.^{3a} The chosen solvents were different enough to expect some change if they participate in any partial equilibration.

(12) See Table XXI in ref 1d.

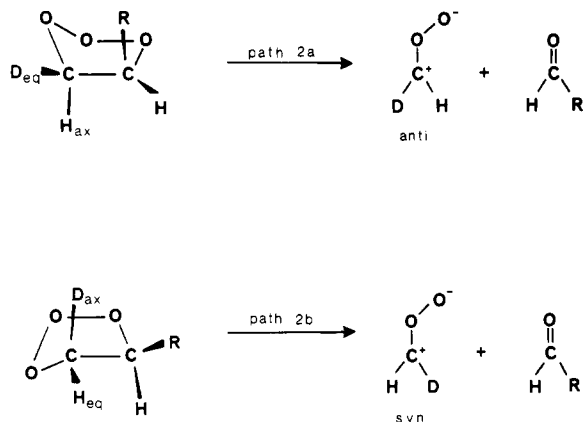


Figure 2. Two possible envelope transition states for primary ozonide cleavage to *syn*- or *anti*-carbonyl- d_1 oxide; R = OEt, Ph, C_4H_9 .

acetaldehyde (3.8 M, runs 21, 22), two pairs of *cis*,*trans* cross ozonides as well as the normal ozonide were obtained. For propylene ozonide (7a,b) the major isomer was produced in an excess of 1.44:1 in good agreement with that obtained from 1c and 1d. For 3-methyl-5-phenyl ozonide (5c,d) the same *cis*:*trans* ratio of 1:2.17 was obtained from both alkenes 2a,b. Ozonolysis of 1a or 1b in pentane in the presence of an excess of benzaldehyde (3.8 M, runs 23, 24) gave a high yield of 5a,b. The major isomer was produced in an excess of 1.27:1 with the same configuration for the deuterium atom at C(5) as in the starting alkenes 1a and 1b. Ozonolysis of 3a,b in pentane in the presence of excess benzaldehyde (5 M, runs 25, 26) gave a low yield of cross ozonide and a high yield of normal ozonide. For the normal ozonide, no significant excess of either isomer could be observed. However, for the cross ozonide, the major isomer was produced in an excess of 1.27:1, which is the same value obtained from 1a or 1b. These results indicate that the stereodirective influence arising from the carbonyl dipolarophile in the third step of the Criegee mechanism decreases in the order ester > acetaldehyde > benzaldehyde. Although the order between acetaldehyde and benzaldehyde may appear counter to intuition, methyl also appears to have a greater stereoeffect than phenyl when *cis*/*trans* ratios in some other ozonide systems are examined.¹³

The results in Table I show that a *cis* (*trans*) configuration for D and R (either OR, Ph, or C_4H_9) in the alkene results in a more abundant *cis* (*trans*) stereoorientation in the trioxolane products with the exception of the normal ozonides from styrene (2a,b) and 1-hexene (3a,b). For the dioxolane products, a *cis* (*trans*) alkene gave a slightly more abundant *trans* (*cis*) product at C(5) (relative to the substituent on C(3)). A plausible rationale for this stereoselectivity considers the transition states expected for the three-step Criegee mechanism proceeding as a concerted 1,3-dipolar cycloaddition, cycloreversion, and cycloaddition, respectively.^{1d,3b} The formation of the primary ozonide is, of course, stereospecific.^{1c} For the decomposition of the primary ozonide, an exaggerated envelope transition state will be assumed based on simple orbital alignment arguments^{1d} and more detailed energy calculations.^{3c} The two possible envelope conformations leading to HDCOO are illustrated in Figure 2 starting with a *cis*-alkene. It is evident that the three kinds of alkenes (1a, 2a, 3a, etc.)

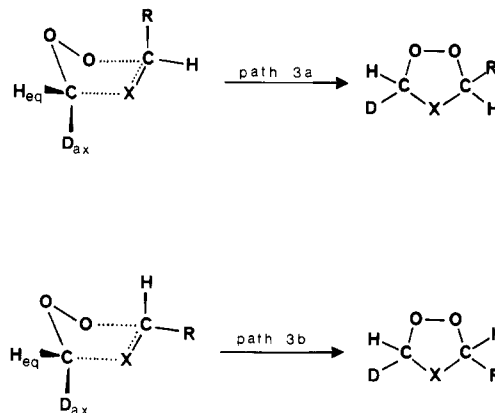


Figure 3. Two possible envelope transition states for recombination of the *syn*-carbonyl- d_1 oxide with the dipolarophile; X = O, R = OEt, CH_3 , Ph; X = CH_2 , R = OEt.

produce the same HDCOO isomer in at least a 3:1 ratio but it is difficult to infer with any certainty whether this preference is for path 2a or 2b. Pathway 2b should have the lower energy if across the ring interactions between the envelope flap and the R substituent are significantly repulsive. This premise is incorporated as a working hypothesis in the subsequent discussion. Thus an excess of *syn* over *anti* HDCOO would be produced. It can be further argued that the stereoselectivity at this stage is even higher than the 3:1 ratio mentioned above¹⁵ although this premise is not critical to the subsequent rationale.

In the recombination step, two envelope-like transition states are again possible as illustrated in Figure 3 for *syn*-HDCOO. Considering ozonide formation first, the dipolarophile must be an ester or aldehyde. As in the primary ozonide decomposition, path 3b is preferred if the interaction of the substituent on the dipolarophile with the carbonyl oxide flap is to be minimized. However, the data also indicate that the stereoselectivity in this step is variable and dependent on the nature of the R group. These differences must arise from interactions between the carbonyl oxide with the dipolarophile and reside in small energetic differences for the two isomeric transition states. Thus a larger excess for one of the isomeric trioxolanes is found when R is an ethoxy group and a smaller excess when R is methyl or phenyl. This can be interpreted to signify that lone pair interactions of the ethoxy group with the carbonyl oxide are important in the transition state (perhaps the early influence of an exo-anomeric effect). Also, π -electron interactions between the phenyl group and carbonyl oxide which might lead to high stereoselectivity are apparently not very significant. In summary, the successive preference for paths 2b and 3b provides a consistent rationale for the stereoselectivity observed for all the ozonide pairs in Table I except those associated with styrene and hexene ozonides (e.g., runs 5–8). We will return to these latter cases subsequently.

In the dioxolane formation, the dipolarophile is an alkene specifically an enol ether. It is apparent that the

(13) The *cis*:*trans* 2-butene cross ozonide ratio from propylene can be as high as 4:1.^{3d} The highest reported *cis*:*trans* stilbene cross ozonide ratio from styrene is 2:1.¹⁴ See other examples in ref 14.

(14) Fliszár, S.; Carles, J. *Can. J. Chem.* 1969, 47, 3921.

(15) The average ratio 4x/4y (runs 1–4, 9–18) is 74.5/25.5 or approximately 3/1. This is the lower limit for the ratio of the two pathways in Figure 2 and necessitates that the recombination of HDCOO with the ester be stereospecific. The upper limit of 1/0 (a single pathway) is also a possibility with the recombination stereoselective. Some stereoselectivity is apparent in the recombination of HDCOO with the other two dipolarophiles and therefore it seems likely to be a factor in the recombination with the ester. It also appears somewhat more acceptable to assume that the three alkene primary ozonides cleave predominantly by one pathway than for each to fortuitously cleave in two directions by the same 3 to 1 ratio. Hence, the ratio of the two cleavage directions for the primary ozonide is probably somewhat above the lower limit for all three kinds of alkenes.

alternative path 3a must now have the lower energy since the preferred stereochemistry at C(5) is reversed from ozonides. Compared to the ozonide stereorations, a modest 0.5-kcal reversal in the relative energies for the paths 3a and 3b would account for the dioxolane stereorations. On closer inspection, significant structural and electronic differences exist between enol ethers and esters or aldehydes, any of which might readily affect the energetics of the cycloaddition reaction.¹⁶ The most important factor is probably the lower polarity for the C=C bond compared to the C=O bond. This would impact on steric interactions since the closeness of approach and flexibility in the transition states should be different for dioxolane and trioxolane formation.

It has been noted above that the stereoselectivity in the final ozonides is virtually absent in the ozonolysis of 1-hexene-1-*d*₁ and styrene- β -*d*₂ (runs 5–8). This arises partly because one pathway to ozonide formation (RCHO + HDCO) randomizes the stereochemistry. In the case of styrene, 60% of the final ozonide occurs by this process. Run 23 implies that the other path (HDCO + PhHCO) is modestly stereoselective (57/43). These figures would imply that the ratio of the H,D styrene ozonide isomers should be 52/48 when starting with stereolabeled styrene. This is close to the observed result for runs 15, 16, 21, and 22 and only slightly different from runs 5 and 6. Similar figures for the 1-hexene cleavage directions and the stereoinfluence of C₄H₉CHO are not available but presumably the loss of stereochemistry in the 1-hexene-1-*d*₁ system has a similar origin.

It may be noted that these concepts can also be extended to account for the invariant cis:trans ratio for 3-methyl-5-phenyl cross ozonide (5c,d) obtained from either 2a or 2b in the presence of acetaldehyde (runs 21, 22). This suggests that only one carbonyl oxide is formed; i.e., the configuration of the D substituent does not influence the amount of *syn-anti*-PhHCOO produced from cleavage of the respective primary ozonides. This is reasonable; in fact, the phenyl seems likely to occupy an equatorial site in the envelope transition state resulting in *anti*-PhHCOO. If more *anti*-PhHCOO is produced regardless of the starting alkene and if the interactions with the Ph and the substituent on the dipolarophile are minimized in the recombination step, then the observed excess of the *trans*-ozonide 5d can be explained.¹⁸

The above stereorationale is generally in accord with the current concepts and framework employed to analyze the ozonolysis of alkyl substituted alkenes.^{3,19,20} The ster-

eeffects associated with HDCO are perhaps the most definitive evidence yet for *syn* and *anti* carbonyl oxide forms.²¹ The evidence for little *syn-anti* equilibration is not unexpected. Arguments that deemphasize this process have frequently been made.^{1d,2,4a,d} Nevertheless, the role of solvent^{3d} and complexation^{3a} in other examples is too striking to easily generalize this result to alkyl substituted systems. Our inference that step two in the Criegee mechanism has high stereoselectivity for 1-alkenes and that most (perhaps all) of the observed stereoselectivity in the products arises in step three presents a different view of the stereocourse of the reaction than heretofore. The implicit presumption has been that stereoselectivity in both steps two and three contributes to products which are partially randomized. Such a reaction profile is probably still applicable to other *cis* and *trans* disubstituted alkenes where the bulk of ozonolysis studies have been performed. Obviously the presence of only one substituent on the 1-alkene places its primary ozonides in a special category. Perhaps the most useful aspect of this study will prove to be the method devised to make large amounts of one HDCO isomer. As shown here, this can be used to study the stereoinfluence of the dipolarophile apart from any steric effects associated with a carbonyl oxide substituent. In order to employ this most effectively, it would be desirable to ascertain more clearly whether the stereocourse in Figure 2 results in the *syn* or *anti* form. It may be possible to shed light on this question by careful consideration of the R substituent and its properties or by careful transition-state calculations.

Experimental Section

The general procedure and equipment used in this study is the same as described in the preceding paper.^{5c} ¹H NMR spectra were obtained with a Bruker WM-360 spectrometer in CDCl₃.

Materials. The synthesis of the stereospecifically labeled ethyl vinyl ethers has been described.^{5c} Labeled styrenes and 1-hexenes were prepared by analogy to methods described in the literature.^{23,24} The starting materials for preparing labeled styrene were phenylacetylene, a 1.0 M solution of diisobutylaluminum hydride in hexane, and 99.8 atom % D₂O; 1-hexene, a 0.5 M solution of 9-BBN in THF, and D₂O were used for labeled 1-hexene. All chemicals were procured from Aldrich. The isotopic purity of the samples was >96%.

Ozonolysis Procedure. Approximately 3–15 mmol of alkene was ozonized at –78 °C in 10–15 mL of solvent. Fast warmup to room temperature (25 °C) was followed by removal of the solvent with a water aspirator. The products were then separated from any involatile residue by distillation in a high vacuum line. In some runs the volatile products were further separated by fractional condensation using high vacuum line techniques. Yields were determined by weighing combined with ¹H NMR (Table II) analysis for product distributions and isomeric ratios. The amounts of starting materials and product yields are given in Table I.

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(16) Isolelectronic ethyl vinyl ether and ethyl formate have two stable conformations.¹⁷ In the former, the *cis* isomer (heavy atom coplanar) is more stable and the second nonplanar conformer is 0.8 kcal higher. In the latter, this energy difference is 0.2 kcal. Their dipole moments are 0.98 and 1.98 D, respectively, and their dipolarophilic C=C and C=O bonds differ by 0.13 Å.

(17) (a) Riveros, J. M.; Wilson, E. B. *J. Chem. Phys.* 1967, 46, 4605. (b) Owen, N. L.; Sheppard, N. *Spectrochim. Acta* 1966, 22, 1101. (c) Owen, N. L. *J. Phys. Chem.* 1979, 83, 1483.

(18) It has been proposed that other 1-alkenes^{1d,3d,19} also preferentially produce *anti* carbonyl oxides although there is not agreement on this point.^{3c} The preferential formation of *trans*-3-methyl-5-phenyl ozonide is an exception to the usual tendency of *anti* carbonyl oxides to give *cis*-ozonides.^{1d}

(19) Lattimer, R. P.; Kuczkowski, R. L.; Gillies, C. W. *J. Am. Chem. Soc.* 1974, 96, 348.

(20) Our analysis chose envelope-like transition states which may be too idealized.^{3b} Presumably an analogous interpretation might be constructed choosing nonenvelope (twisted) transition states along the lines discussed by Bailey and Ferrell.^{3a,b}

(21) Although the cyclic dioxirane isomeric form of H₂COO and HDCO has been observed spectroscopically,²² such a symmetric structure cannot account for the stereochemical observations.

(22) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* 1978, 100, 5117.

(23) Wood, J. T.; Arney, J. S.; Cortes, D.; Berson, J. A. *J. Am. Chem. Soc.* 1978, 100, 3855.

(24) Brown, H. C.; Scouten, C. G.; Liotta, R. J. *J. Am. Chem. Soc.* 1979, 101, 96.