Stereoselective Cycloaddition and Epoxidation of Enol Ethers by α-Peroxy Lactone as a Function of Steric and Stereoelectronic Effects

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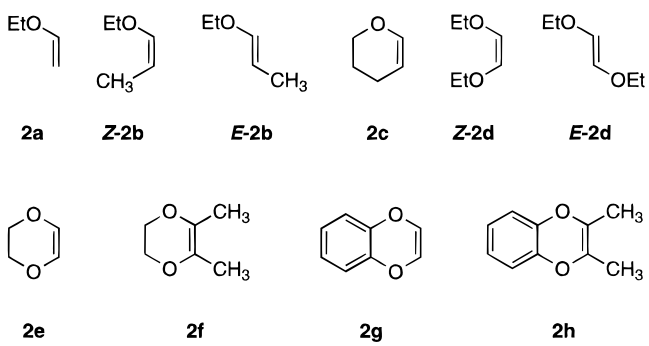
Received August 26, 1996[⊗]

The reaction of mono- and dioxy-substituted olefins **2** with dimethyl α-peroxy lactone **1** affords the cycloaddition products **3** and the epoxides **4** with a high degree of stereoretention of the initial olefin configuration. Only for the pyran **2c** is the *ene* product **5c** obtained. When the reaction is run in methanol as cosolvent, additionally the trapping products **6** are observed. The S_N2 reaction is found to be highly regioselective in all cases, as displayed by the cycloadducts **3** and the trapping products **6**. The preferred reaction mode has been found to be sensitive to steric effects. The product distribution is rationalized in terms of the diastereomeric 1,4-zwitterionic epoxonium intermediates ***syn***- and ***anti*-C**, which are proposed to arise from a side-differentiated S_N2 attack of the enol ether double bond on the peroxide bond of the α-peroxy lactone **1** through a perpendicular *spiro*-configurated transition state geometry. When the α-peroxy lactone **1** approaches the enol ether **2** from the oxy-substituted side, the ***syn*-C** epoxonium intermediate is formed, which leads to the epoxide **4** after release of the corresponding α-lactone. The latter oligomerizes to the polyester **8** or is trapped in methanol as the α-methoxy acid **9**. On the contrary, the ***anti*-C** epoxonium intermediate results by approach of the α-peroxy lactone **1** from the non-oxy-substituted side of the enol ether **2**, but the electronic repulsion between the lone pairs of the epoxonium and enol ether oxygens leads by ring opening of the epoxonium species to the coiled 1,6-zwitterion (U conformation). The latter is too short-lived for stereorandomization and closes to the cycloadducts **3** under high retention of the initial enol ether configuration, but is sufficiently long-lived to be trapped in methanol stereoselectively in form of the adducts **6**. These unprecedented results in the peroxide−olefin reaction are contrasted with the previously reported α-peroxy lactone **1** oxidation of alkenes. While the enol ethers **2** lead to the cycloadducts **3** with a high degree of stereoretention and the alkenes lead to extensive loss of the initial olefin geometry, for both trapping by methanol in form of the adducts **6** takes place, again with high stereoselectivity for the enol ethers but not for the alkenes. This mechanistic dichotomy requires different intermediates, namely, the epoxonium species **C** for the enol ethers and the stretched 1,6-dipole (W conformation) **A** for the alkenes, which both lead to the cycloadducts **3**, the former by way of the coiled 1,6-dipole (U conformation) **D**. For the enol ethers the epoxonium intermediate **C** is the precursor to the epoxide, while for the alkenes an independent concerted "butterfly" transition state geometry **B** applies in the epoxidation.

Introduction

We have recently reported[1] on the oxidation of di-, tri-, and tetrasubstituted alkenes by the α-peroxy lactone **1** (Scheme 1). As expected, the α-peroxy lactone **1** is considerably more reactive than the corresponding 1,2-dioxetanes[2] due to the activating polarization of the peroxide bond by the adjacent carbonyl group. Two different reaction modes were observed. On the one hand, cycloadducts and *ene* products were formed through the stretched 1,6-dipole (W conformation) **A** proposed to arise from S_N2 attack of the π nucleophile on the peroxide bond of α-peroxy lactone **1**, which is responsible for the extensive loss of the initial alkene geometry in the cycloaddition. On the other hand, more sterically encumbered alkenes gave epoxidation. The intervention of the 1,6-dipole is mandatory in view of the loss of stereochemistry in the cycloaddition, the formation of *ene* products, and the trapping in the presence of methanol. For the epoxidation we postulated a concerted mechanism with a "butterfly" transition state geometry[3] **B** (Scheme 1) rather than a stepwise pathway through a *bona fide* 1,4-dipolar epoxonium intermediate.

To gain further mechanistic insight into the complexities and intricacies of the peroxide−olefin reaction,[4] we decided to examine the α-peroxy lactone **1** oxidation of the considerably more electron-rich enol ethers **2a**−**h**. We



2a ***Z*-2b** ***E*-2b** **2c** ***Z*-2d** ***E*-2d**

2e **2f** **2g** **2h**

anticipated that the higher nucleophilicity of the enol

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[⊗] Abstract published in *Advance ACS Abstracts,* November 1, 1996.

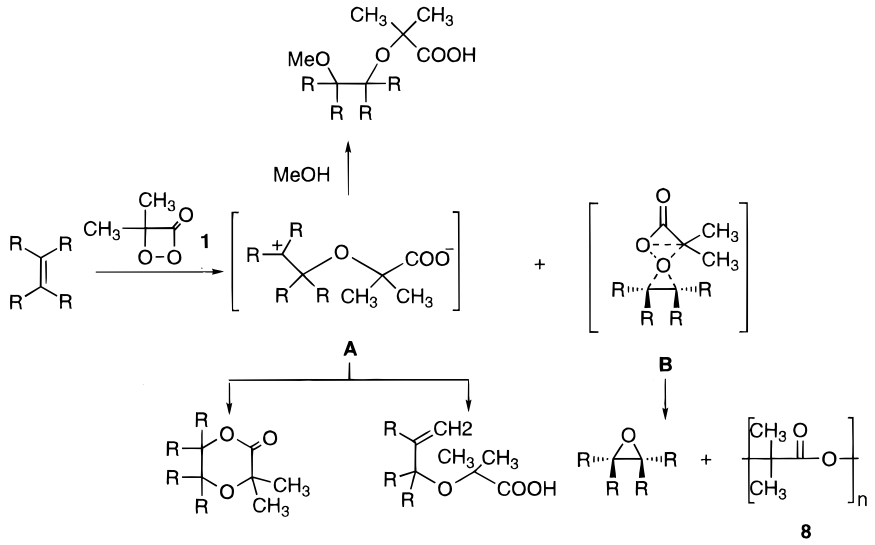
(1) Adam, W.; Blancafort, L. *J. Am. Chem. Soc.* **1996**, *118*, 4778−4787.

(2) Adam, W.; Andler, S.; Heil, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1365−1366.

(3) (a) Bartlett, P. D. *Rec. Chem. Progr.* **1950**, *2*, 47−51. (b) Baumstark, A. L.; McCloskey, C. J. *Tetrahedron Lett.* **1987**, *28*, 3311−3314.

S0022-3263(96)01645-3 CCC: $12.00

Scheme 1. Mechanism for the Reaction of α-Peroxy Lactone 1 with Alkenes in the Absence and Presence of Methanol



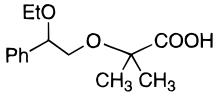
ethers **2** would favor the heterolysis of the peroxide bond, for which purpose we decided to compare the monooxy-substituted olefins **2a**−**c** with the dioxy-substituted derivatives **2d**−**h**. Moreover, the *Z*/*E* isomer pairs **2b** and **2d** were chosen to assess the stereochemical course of the cycloaddition, while the dioxenes **2e**−**h** were selected to study the influence on the product distribution of steric effects on the lateral sides of the double bond of the π nucleophile, by comparison of the methyl-substituted with the hydrogen-substituted enol ethers **2e** and **2f** and the flattening effect of the benzo substitution in substrates **2g** and **2h**. Furthermore, the methyl-substituted derivatives **2b**,**f**,**h** should be particularly prone for the *ene* reaction through proton abstraction. The unsymmetrical enol ethers **2a**−**c** should provide information on the regioselectivity of the oxidation. Analogous to the alkene nucleophiles, trapping experiments in methanol should allow us to probe the participation of any polar intermediate. Herein we present unprecedented results in the reaction of the α-peroxy lactone **1** with enol ethers **2**, which disclose marked differences in their mechanistic features compared with those of the alkenes. The most salient conclusion is that, in contrast to the previously studied alkenes,[1] for the enol ethers the intervention of the epoxonium intermediate **C** best rationalizes the initial encounter with the α-peroxy lactone **1**.

Results

α-Peroxy lactone **1** was synthesized according to the published procedure[5] and was obtained as deuteriochloroform or 1,1,1-trichloroethane solution. $CDCl_3$ was used for the determination of the product distribution at the analytical scale, while CH_3CCl_3 was used for preparative purposes. The trapping experiments were run in a 1:1 mixture of the α-peroxy lactone solution and methanol. The results of the analytical scale reactions are summarized in Table 1.

Beside the catalytic decomposition of the α-peroxy lactone **1** into acetone, two kinds of products were obtained in the reaction with enol ethers **2**, namely, the cycloadducts **3** and the epoxides **4** (Scheme 2). Independent synthesis of the epoxides **4a**, **4c**, ***cis*-4d**, **4e**, **4f**, and **4h**[6] by dioxirane epoxidation of the corresponding olefins allowed their identification or confirmation of their absence in the α-peroxy lactone oxidations by comparison of their spectral data with that of the authentic material. Epoxides ***trans*-4d** and **4g** were identified by the characteristic ^{1}H NMR signals at δ 4.69 (singlet) and 5.06 (singlet). Isolation and full characterization of the epoxides **4** were not possible due to their thermal lability and decomposition during Florisil chromatography. The cycloadducts **3** were isolated and their structures assigned on the basis of their spectral and analytical data. Thus, the lactone functionality of the 1,4-dioxan-2-ones **3** displays the characteristic IR band at 1720−1765 cm^{-1} and a carbonyl ^{13}C NMR resonance between δ 170.7 and 173.0, while the acetal ring positions show typical chemical shifts between δ 5 and 6 in the ^{1}H NMR and between δ 90 and 105 in the ^{13}C NMR spectra.

To determine the regioselectivity of the cycloaddition for the unsymmetrical enol ethers **2a**−**c**, the cycloadduct **3a** was allowed to react with an excess of phenylmagnesium bromide, which in accordance to an established literature precedent[7] yielded the acid **10a** from nucleophilic attack of the Grignard reagent at the alkoxy−acyloxy acetal functionality. The regiochemical assign-



10a

ment of the ***cis*-** and ***trans*-3b** cycloadducts was determined by analogy of its spectral data with those of the cycloadduct **3a**; the alkoxy−acyloxy acetal ^{13}C NMR resonances for ***cis*-** and ***trans*-3b** appear at δ 102 and 105 *vs* 100.3 for **3a**. For comparison, the alkoxy-alkoxy acetal carbon atoms for ***cis*-** and ***trans*-3d** show ^{13}C NMR shifts at δ 93. For cycloadduct **3c**, beside the similarity

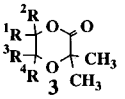
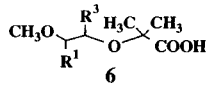
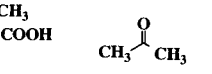
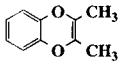
(4) (a) Greene, F. D.; Rees, W. W. *J. Am. Chem. Soc.* **1958**, *80*, 3432−3437. (b) Adam, W.; Griesbeck, A.; Kappes, D. *J. Org. Chem.* **1986**, *51*, 4479−4481. (c) Adam, W.; Hadjiarapoglou, L.; Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W., Ed.; John Wiley & Sons Ltd.: Chichester, 1992; pp 195−220.

(5) Adam, W.; Alzérreca, A.; Liu, J.-C.; Yany, F. *J. Am. Chem. Soc.* **1977**, *99*, 5768−5773.

(6) Adam, W.; Hadjiarapoglou, L.; Wang, X. *Tetrahedron Lett.* **1991**, *32*, 1295−1298.

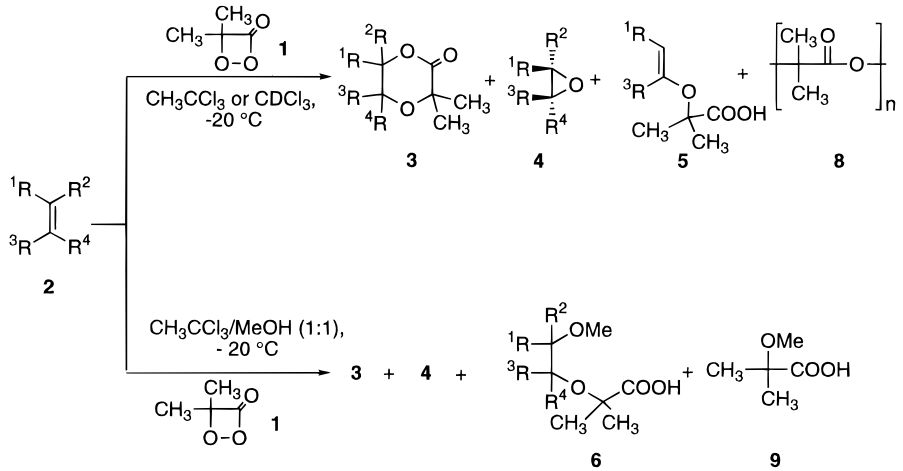
(7) (a) Shostakovskii, M. F.; Kulibekov, M. R. *Zh. Obshch. Khim.* **1958**, *28*, 2339−2341. (b) Nützel, K. In *Methoden der Organischen Chemie*; Müller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1973; Bd. XIII/2a, p 329.

Table 1. Product Studies[a] of the Reaction of α-Peroxy Lactone 1 with Enol Ethers 2

						product distribution [%][b]			
				time	m.b.[c]				
entry	2		solvent	[min]	[%]	3 cycloaddition[d]	4 epoxidation	6 trapping	decomposition
1		(**2a**)	$CDCl_3$	300	74	60	-	-	14
2		(**Z-2b**)	$CDCl_3$	20	92	92 (78:22)	-	-	-
3		(**E-2b**)	$CDCl_3$	20	90	84 (9:91)	-	-	6
4		(**2c**)	$CDCl_3$	15	92[e]	44 (*cis*)	-	-	26
5			CH_3CCl_3/CH_3OH	5	96	43 (*cis*)	-	53 (87:13)[f]	not determ.
6		(**Z-2d**)	$CDCl_3$	5	95	53 (92:8)	39[g]	-	3
7			$CDCl_3/CD_3CN$	5	97	67 (93:7)	10[g]	-	20
8			CH_3CCl_3/CH_3OH	5	94	48 (>90:10)	13[h]	33 (75:25)[i]	not determ.
9		(**E-2d**)	$CDCl_3$	5	81	59 (2:98)	13[g]	-	9
10			$CDCl_3/CD_3CN$	5	71[k]	42 (12:88)	<5[g]	-	29
11			CH_3CCl_3/CH_3OH	5	60	31 (*trans*)	21[h]	21 (40:60)[i]	not determ.
12		(**2e**)	$CDCl_3$	5	95	55 (*cis*)	-	-	36
13			CH_3CCl_3/CH_3OH	5	91	24 (*cis*)	-	67 (80:20)[i]	not determ.
14		(**2f**)	$CDCl_3$	5	91	59 (*cis*)	-	-	32
15		(**2g**)	CH_3CCl_3	30	83	36 (*cis*)	31[l]	-	16
16		(**2h**)	$CDCl_3$	5	86	31 (*cis*)	17[m]	-	38

[a] At −20 °C, in CH_3CCl_3 or $CDCl_3$; for trapping experiments in 1:1 CH_3CCl_3/CH_3OH. [b] Product distribution in $CDCl_3$ determined by ^1H NMR spectroscopy with hexamethyldisiloxane as internal standard (in CH_3CCl_3 by ^1H NMR analysis of the crude product mixture after distillation of the solvent). [c] Mass balance (m.b.) refers to 100% consumption of α-peroxy lactone **1**. [d] *Cis:trans* ratio of the cycloadducts indicated in parenthesis. [e] Contains 22% of *ene* product **5c** (cf. Scheme 2). [f] *Cis:trans* ratio (*d.r.*) of the trapping products. [g] Oligomeric ester **8** not quantified due to overlapping with other signals. [h] Yield estimated in terms of methoxy ester **9**, trapping product of the α-lactone. [i] Stereochemistry of the diastereomers not determined. [k] Contains 13% of undetermined side products. [l] Also 29% of oligomeric ester **8** detected. [m] Yield estimated in terms of oligomeric ester **8**; epoxide not directly quantified due to overlapped signals with other products.

Scheme 2. Conditions and Products for the Reaction between α-Peroxy Lactone 1 and Enol Ethers 2



of its ^{13}C NMR shift data with that of derivative **3e**, additional structural proof is provided by NOE experiments (Figure 1).

The cycloaddition was stereoselective in all cases and took place under retention of the olefin configuration. While the cyclic enol ethers **2c** (Table 1, entries 4 and 5) and **2e**−**h** (Table 1, entries 12−16) yielded exclusively the *cis* cycloadducts, only a small degree of inversion (ca. 10−20%) was found for the acyclic enol ethers **2b** (Table 1, entries 2 and 3) and **2d** (Table 1, entries 6−11).

The stereochemical course of the cycloaddition was established on the basis of NOE experiments and the

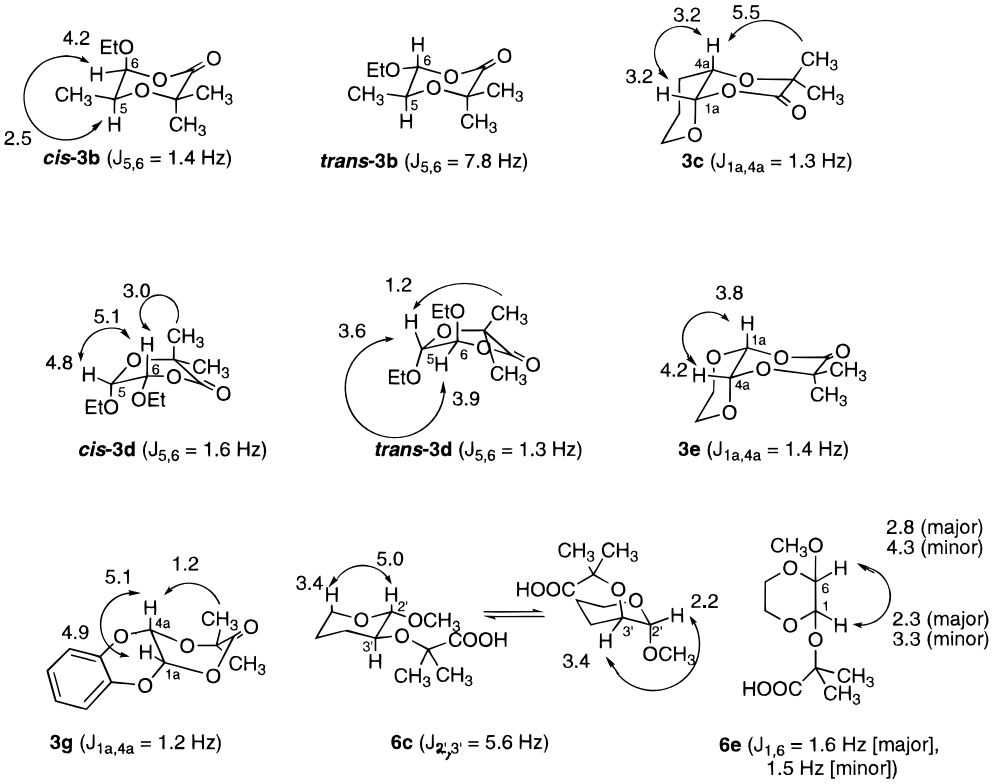


Figure 1. Structural assignments of the cycloadducts **3b,c,d,e,g** and the trapping products **6c,e** by NOE experiments (enhancements in percent; methyl group effects were not determined for ***cis***- and ***trans***-**3b**) and coupling constants.

coupling constants of the cycloadducts **3b**−**h** (Figure 1). For the ***cis***- and ***trans***-**3d** cycloadducts, the preferred conformation is dictated by the anomeric effect, such that the relative position of each of the acetal protons at the C-5 and C-6 positions is very similar in both diastereomers and similar NOE effects and $J_{5,6}$ coupling constants are observed. Fortunately, for the ***cis***-**3d** isomer, an appreciable NOE effect of 3.0% operates between the axial methyl substituent and the 6-H acetal proton, which allows us to identify the major diastereomer as ***cis***-**3d** in the cycloaddition with ***Z***-**2d**.

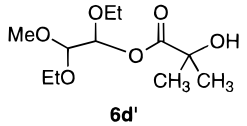
As far as the cycloadducts **3f** and **3h** are concerned, the assignment of the configurations was encumbered by the fact that the ^{1}H NMR chemical shifts of the methyl bridgehead substituents overlap severely with the methyl groups of the lactone ring. Furthermore, all attempts failed to grow suitable crystals for an X-ray structure determination. However, the fact that in all other cycloadditions the olefin geometry is conserved prompts us to assume that retention also applies for the derivatives **2f** and **2h**.

In the cases for which epoxidation took place, namely, for the enol ethers **2d** (Table 1, entries 6−11), **2g** (Table 1, entry 15), and **2h** (Table 1, entry 16), the corresponding oligomeric ester **8** derived from the α-lactone of **1**[8] was observed and quantified for olefins **2g** and **2h**. In the case of **2g**, the yield of epoxide **4g** matched the yield of oligomeric ester **8**, which establishes that both products are formed, as expected, in the same amounts. For the *Z*,*E*-diastereomeric enol ethers **2d**, formation of the oligomeric ester **8** could not be confirmed due to the overlap of its ^{1}H NMR signals with those corresponding to the cycloadduct **3d**; nevertheless, its presence is inferred from the fact that the epoxides **4d** are observed.

Additionally, a third type of product was obtained only in the case of enol ether **2c**, namely, the *ene* product **5c** (Table 1, entry 4, footnote *e*). While the presence of the acid functionality is evidenced both by the IR bands at 3600−2300 and 1700 cm^{-1} and the ^{13}C NMR resonance at δ 177.4, the dioxy-substituted double bond displays characteristic resonances at δ 6.47 (^{1}H NMR) and δ 133.2 and 137.6 (^{13}C NMR).

When the reaction of α-peroxy lactone **1** with the enol ethers ***Z***- and ***E***-**2d** was carried out in deuterioacetonitrile as cosolvent (Table 1, entries 7 and 10), the change in the polarity of the medium had only a moderate influence on the product distribution. Thus, the epoxide yield decreased, while more acetone was formed due to catalytic decomposition, whereas the stereoselectivity of the cycloaddition decreased slightly.

The trapping experiments were run in methanol as cosolvent (Scheme 2 and Table 1, entries 5, 8, 11 and 13). The trapping products **6** were identified on the basis of their spectral data, for which especially the IR bands at 3500−2500 and 1730 cm^{-1}, as well as the ^{13}C NMR resonances at δ 176, were definitive. This allows us to exclude the alternative hydroxy ester structure **6d′**.



Furthermore, additional proof was provided in favor of the regioisomer **6d** by esterification with diazomethane. In these methanol trapping experiments the cycloaddition remained stereoselective; in fact, for the acyclic enol ethers ***Z***- and ***E***-**2d** (Table 1, entries 8 and 11) even a higher degree of diastereoselectivity was found. Additionally, an acceleration of the reaction was observed; in the case of dihydropyran **2c** (Table 1, entries 4 and 5)

(8) Chapman, O. L.; Wojtowski, P. W.; Adam, W.; Rodríguez, O.; Rucktäschel, R. *J. Am. Chem. Soc.* **1972**, *94*, 1365−1367.

the reaction times decreased from 15 to 5 min in methanol. Furthermore, in the presence of methanol, the α-lactone derived from the α-peroxy lactone **1** on deoxygenation was trapped as the α-methoxy acid **9** (Scheme 2).

In regard to the configurations of the trapping products **6**, the cyclic enol ether **2c** yielded the diastereomeric mixture **6c** in a ratio of 87:13 (Table 1, entry 5). The major diastereomer ***trans*-6c** could be isolated, while the minor ***cis*-6c** diastereomer was identified in the ^{1}H NMR spectrum of the crude product mixture by a doublet at δ 4.57 (J = 2.3 Hz) for the 2-H' acetal proton and a singlet at δ 3.46 for the methoxy group. The configuration of the diastereomers was determined by NMR spectroscopy. While the NOE effects measured for ***trans*-6c** were not conclusive, the definitive assignment was made on the basis of the coupling constants between the protons of the alkoxy-substituted positions (Figure 1). Thus, the major diastereomer ***trans*-6c** has a coupling constant of 5.6 Hz, which is an average value of its two possible equilibrating conformers (ca. 10 Hz for the axial−axial and ca. 2 Hz for the equatorial−equatorial coupling constants).[9] For the minor isomer ***cis*-6c**, whose two conformers should show a small axial−equatorial coupling constant, a value of 2.3 Hz was measured, which confirms its *cis* configuration. Unfortunately, the configuration of the acyclic diastereomers **6d** (Table 1, entries 8 and 11) could not be assigned. Nevertheless, the spectra of the crude trapping mixtures for the individual *Z* and *E* isomers of the enol ether **2d** revealed that opposite ratios of diastereomers were obtained, which confirms that the intermediate precursor for the trapped products **6d** retains its initial configuration to a certain extent. As for the configuration of the 1,4-dioxene trapping product diastereomers **6e**, which were obtained in a ratio of 80:20 (Table 1, entry 13), an NOE experiment (Figure 1) allowed no distinction between the two isomers.

Furthermore, to probe that the trapping products **6** did not arise from methanolysis of the cycloadducts **3**, a control experiment for **3d** in deuteriomethanol was carried out. Even after 1 d at room temperature, no reaction of the cycloadduct **3d** was observed, which confirms that the cycloadduct **3d** persists methanolysis under the reaction conditions for its formation from the α-peroxy lactone **1**.

Finally, the mass balances were satisfactory (>80%) in most of the cases. Although in the reaction of α-peroxy lactone **1** with the enol ether **2a** (Table 1, entry 1) the mass balance was only 74%, no additional products beside the cycloadduct **3a** and acetone could be detected. The low mass balance of identified products (71%) for the reaction with enol ether ***E*-2d** in deuterioacetonitrile as cosolvent (Table 1, entry 10) must be corrected for unknown products (13%), which were detected in the ^{1}H NMR spectrum of the crude reaction mixture. Finally, the low mass balance (60%) observed also in the trapping experiment for this enol ether (Table 1, entry 11) is tentatively attributed to catalytic decomposition of the α-peroxy lactone **1** to acetone.

Discussion

The present study on the reaction of α-peroxy lactone **1** with a series of mono- and dioxygen-substituted olefins **2** reveals two reaction modes, namely, formal cycloaddition to the 1,4-dioxanones **3** mainly with retention of initial configuration and oxidation of the enol ethers to the corresponding epoxides **4** (Table 1 and Scheme 2). The epoxidation mode only occurs with the 1,2-dioxy-substituted olefins ***Z*-** and ***E*-2d**, **2g**, and **2h** (Table 1, entries 6−11, 15, and 16). In the presence of methanol, the trapping products **6** are also observed, again mainly with retention of configuration.

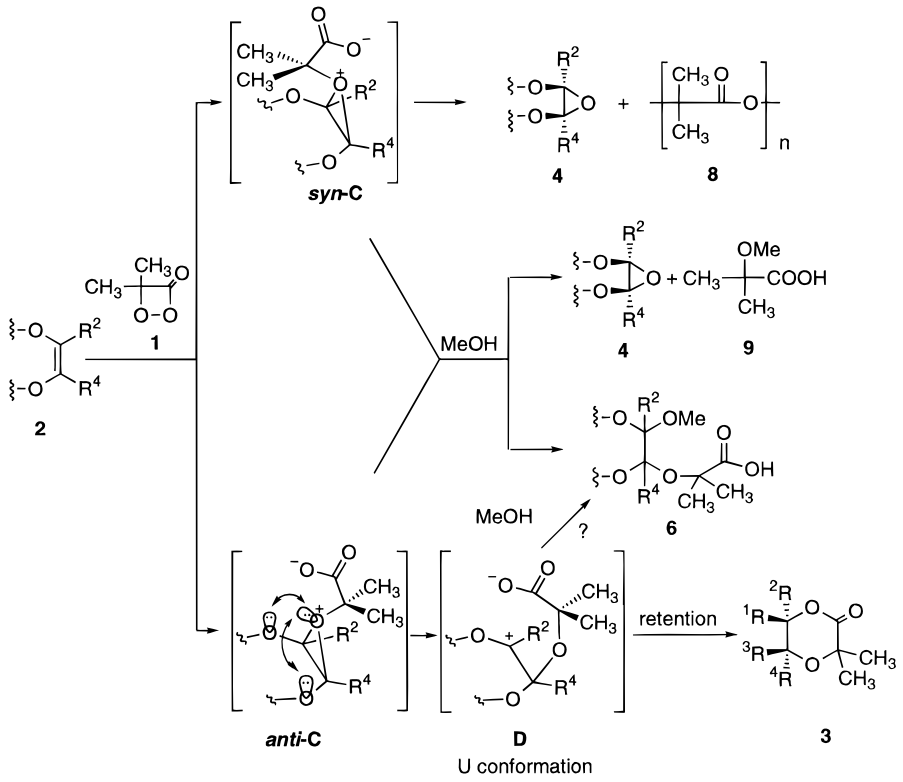
To rationalize this complex product distribution mechanistically, it is instructive to recall our previous results on the oxidation of alkenes with the α-peroxy lactone **1**.[1] For the latter case, two independent pathways were postulated for the formation of cycloadducts, the first *via* the formation of *ene* products and epoxides and the second by nucleophilic attack of the alkene double bond on the alkyl-substituted oxygen of the peroxide bond of the α-peroxy lactone **1** (Scheme 1). Mainly steric factors decide whether the end-on, unsymmetrical attack leads to the stretched 1,6-zwitterion **A** (W conformation) as the precursor to the cycloadducts **3** or the centered, symmetrical attack leads to the epoxide **4** through a concerted process with a "butterfly" transition state **B**. Beside cyclization under loss of the alkene configuration and formation of the *ene* products by intramolecular H transfer, the 1,6-zwitterion **A** could be trapped when the reaction was performed in methanol as cosolvent.

The present methanol trapping experiments for the enol ethers **2** (Table 1, entries 5, 8, 11, and 13) exclude, despite the observed retention of configuration, concerted cycloaddition and suggest the intervention of a zwitterionic intermediate. The charge separation which accompanies the peroxide bond breakage to generate this zwitterionic intermediate is in part alleviated by the polar methanol, as exemplified by the rate acceleration for the dihydropyran **2c** (Table 1, entries 4 and 5). The question of mechanistic relevance is the structural nature of this intermediate, which exercises extensive stereomemory but can be trapped! It certainly cannot be the stretched 1,6-dipole **A** (W conformation) proposed in the reaction of the α-peroxy lactone **1** with alkenes (Scheme 1), because the trappable dipole **A** does not preserve its configuration. Moreover, to propose that the cycloaddition is concerted in nonpolar ($CDCl_3$, CH_3CCl_3) but stepwise in polar (CH_3CN, MeOH) solvents is not justified because the configuration of the cycloadducts is largely retained also in acetonitrile (Table 1, entries 7 and 10) and methanol (Table 1, entries 8 and 11) as cosolvents compared to chloroform (Table 1, entries 6 and 9). Consequently, the results in Table 1 demand a cycloaddition intermediate which largely retains its configuration and can be trapped, *i.e.*, different from the stretched 1,6-dipole **A** for the alkene oxidation (Scheme 1). Furthermore, a satisfactory mechanistic interpretation must account for the fact that *all* enol ethers **2** afford cycloadducts **3**, but only for certain ones, namely, the olefins ***Z*,*E*-2d**, **2g**, and **2h**, epoxides **4** are also obtained.

We propose that the reaction proceeds through the epoxonium 1,4-dipole (Scheme 3), whose structure is side-differentiated in terms of the two diastereomeric *spiro* configurations ***syn*-** and ***anti*-C**. The stereolabels refer to the location of the onium substituent with respect to the dioxy-substituted side of the substrate. Both structures arise from nucleophilic attack of the enol ether **2** on the peroxide bond of the α-peroxy lactone **1** in a central and symmetric approach. Thus, in contrast to the alkene nucleophiles, the two lateral sides of the π bond are electronically differentiated, with the sole exception of the centrosymmetric substrate ***E*-2d**. In addition we

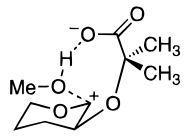
(9) Sweet, F.; Brown, R. K. *Can. J. Chem.* **1966**, *44*, 1571−1576.

Scheme 3. Mechanism for the Reaction of α-Peroxy Lactone 1 with Enol Ethers 2 and Methanol Trapping Illustrated for the *cis*-Dioxy-Substituted Cases



propose that the ***syn*-C** intermediate is sufficiently long-lived to release the epoxide **4** by intramolecular nucleophilic substitution of the carboxylate ion on the α carbon atom of the incipient α-lactone. In contrast, the ***anti*-C** intermediate opens up to the coiled 1,6-zwitterion **D** (U conformation), which due to the proximity of the carboxylate and the carbocation centers is too short-lived to stereorandomize and cyclizes to the cycloadducts **3** with retention of the enol ether configuration. In fact, an analogous, U-shaped intermediate has been postulated in the reaction of tetracyanoethylene with enol ethers,[10] for which cycloaddition under stereoretention and stereoselective trapping of the intermediate are observed. Furthermore, interconversion of the diastereomeric ***syn*-** and ***anti*-C** can be excluded on the basis of computational results for analogous perepoxide intermediates.[11] Thus, MINDO/3 calculations on the addition of singlet oxygen to 1,3-butadiene[11a] give an activation barrier of 24 kcal/mol for the interconversion of the perepoxide diastereomers, while in a multiconfiguration CASSCF calculation with a double-ξ basis set on the singlet oxygen addition to ethylene[11b] the inversion barrier was estimated to be as high as 78 kcal/mol.

1,4-Dipoles ***syn*-** and ***anti*-C**, as well as the coiled 1,6-zwitterion **D**, may be trapped stereoselectively by methanol to afford the adduct **6**. Thus, for dihydropyran **2c** S_N2 attack takes place at the epoxonium **C** preferentially to afford ***trans*-6c** as the major trapping product. The small (13%) amount of the ***cis*-6c** diastereomer may derive from the methanol aggregate **D** (MeOH), analogous to the one proposed for the trapping of a zwitterionic intermediate in the reaction of tetracyanoethylene with ethyl *cis*-propenyl ether.[10b] Also for the open diastereomeric pair, ***Z,E*-2d** diastereomeric mixtures of the trapping products **6** are obtained with opposite diastereomeric ratios, which shows that the trapped intermediate exercises a certain degree of stereomemory.



Conformation **D** (MeOH)

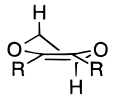
The driving forces for the ring opening of the ***anti*-C** epoxonium dipole are the electronic repulsion between the lone pair electrons of the onium center and the enol ether oxygen substituents, which are located on the same side of the intermediate ***anti*-C**, and the stabilization of the incipient carbocation by the adjacent O-substituent. The possibility as to whether the proposed **D** species, instead of a *bona fide* intermediate, may be a transition state on the way to the cycloadducts **3** is unlikely in view of the partial stereoisomerization observed for the cycloadducts **3** and the trapping products **6** (Table 1, entries 6−11). Additionally, the formation of the cycloadducts **3** directly from the 1,4-dipoles ***syn*-** or ***anti*-C** through S_N2 attack at the epoxonium function can be excluded for geometric reasons.

The observed epoxidation for the 1,2-dioxy-substituted substrates ***Z*-** and ***E*-2d**, **2g**, and **2h** is accounted for by their nucleophilic attack on the α-peroxy lactone **1** to afford the ***syn*-C** epoxonium intermediate (Scheme 3). The electronic repulsion argued for ***anti*-C** species is absent in ***syn*-C**, so that the ***syn*-C** epoxonium structure does not open but leads to the epoxide by intramolecular S_N2 attack. In contrast, for the analogous **2e** and **2f** derivatives, which give no epoxides (Table 1, entries 12−14), their central, symmetric approach to generate a ***syn*-C** intermediate is sterically blocked by the 5,6-

(10) (a) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117−124. (b) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 199−206.

(11) (a) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 2338−2339. (b) Hotokka, M.; Roos, B.; Siegbahn, P. *J. Am. Chem. Soc.* **1983**, *105*, 5263−5269.

substituents in view of their puckered conformations; thus, only cycloaddition through the ***anti*-C** route instead of epoxidation occurs.



Conformations **2e,f**

For the *cis*-configurated olefins ***Z*-2d**, **2g**, and **2h**, the dioxy-substituted side is accessible for the α-peroxy lactone **1** electrophile, because in the acyclic substrate ***Z*-2d** the ethoxy groups are conformationally free to rotate out of the way, while for the benzo-substituted derivatives **2g,h** the flat benzene ring presents no steric obstacles. Indeed, the electron-rich arene moiety may provide through charge transfer complexation an additional incentive for the ***syn*-C** attack of the electrophilic oxidant in analogy to the effect proposed for electrophilic additions to aryl-substituted benzobicyclo[2.2.2]octadienes and 11-isopropylidenedibenzonorbornadienes,[12] where the electrophile approaches the double bond from its benzo-substituted face in those cases in which other effects do not intervene.

In the case of the centrosymmetric, *trans*-configurated ***E*-2d** substrate only one epoxonium species is possible, which partitions between epoxidation and cycloaddition. Also some Grob-type fragmentation into acetone and presumably CO_2 with regeneration of olefin ***E*-2d** (entries 9 and 10) takes place. In the presence of methanol, significant amounts of trapping product **6d** (Table 1, entry 11) are observed with extensive loss of stereochemistry.

The mechanistic analysis in Scheme 3 also applies for the monooxy-substituted olefins **2a**−**c**. For these the sterically less hindered side is preferentially approached to afford the ***anti*-C** epoxonium intermediate. The latter opens up to the 1,6-dipole **D** and subsequently cyclizes stereoselectively to the cycloadducts **3** with predominant retention for the acyclic enol ethers ***Z*-** and ***E*-2b** (Table 1, entries 2 and 3) and exclusive *cis* cycloadduct **3c** for the dihydropyran **2c** (Table 1, entries 4 and 5). For the latter substrate also the methanol trapping to the adduct **6c** proceeds with a large degree of stereoselectivity, which implies that the methanol was added by a back-side attack directly to the epoxonium intermediate ***anti*-C** and/or to the transient U-shaped 1,6-dipole **D** to yield the *trans* diastereomer. That this dipole is sufficiently long-lived for trapping is substantiated by the observed H abstraction (in the dipolar intermediate **D** for **2c** R^4 = H, Scheme 3) to afford the *ene* product **5c** (Scheme 2).

At first glance, it may seem a contradiction to postulate for the α-peroxy lactone **1** oxidation of the enol ethers **2** a mechanism based on a 1,4-zwitterionic epoxonium intermediate **C** (Scheme 3) when in the alkene case concerted epoxidation (Scheme 1) was preferred. However, the higher nucleophilicity of the electron-rich enol ethers compared to alkenes seems to be decisive here. As an analogy, the addition of olefins to ketenes may be cited,[13] which is a concerted process for alkenes but a dipolar one for the more electron-rich enol ethers and enamines. Thus, the degree of charge transfer from the double bond to the peroxide bond is higher for the enol ethers than the alkenes, so that nucleophilic substitution occurs in which the carboxy oxygen of the peroxide bond in the α-peroxy lactone is displaced as a carboxylate ion and the epoxonium-type intermediate **C** is formed instead of concerted epoxidation. Moreover, although stepwise oxidation processes with peroxides in nonpolar solvents have been claimed to be disfavored by the high-energy barriers for the charge separation when the developing charge is not stabilized,[14] in the present case there is indeed a stabilization due to the fact that the formed oxyanion is a carboxylate. Furthermore, it has to be explained why no end-on attack leading to an open-chain 1,6-dipole of the **A** type occurs with the enol ethers. We consider this an additional consequence of the high degree of charge transfer in the early stage of the reaction, since the alkoxy-substituted oxygen becomes more nucleophilic and traps more effectively the incipient carbocation through back-donation to form the bridged dipole **C**.

In conclusion, the high degree of stereomemory for the enol ethers but extensive stereorandomization for the alkenes in the cycloadduct formation, yet with methanol trapping for both substrates, demands two distinct intermediates, namely, the epoxonium-type 1,4-dipole **C** (Scheme 3) and the stretched 1,6-dipole **A** (Scheme 1). While the epoxonium species **C** rearranges by way of the coiled 1,6-dipole **D** highly stereoselectively to the cycloadduct **3**, the stretched 1,6-dipole **A** suffers substantial stereochemical loss prior to cyclization. Moreover, for the enol ethers the epoxonium intermediate **C** serves as a precursor to the epoxide, while for the alkenes the concerted epoxidation through the concerted transition state **B** is reasonable. Attempts to provide some insight into this mechanistic dichotomy through semiempirical (AM1, PM3) and low-level (3-21G*) *ab initio* calculations unfortunately failed; however, detailed *ab initio* calculations[14] might be informative.

Acknowledgment. We thank Prof. G. Tóth (Budapest) for his valuable help in the structural assignment of adducts ***cis*-** and ***trans*-3d** and **6c** by NMR spectroscopy. We thank the Deutsche Forschungsgemeinschaft (Schwerpunktprogramm "Peroxidchemie: mechanistische und präparative Aspekte des Sauerstofftransfers") for generous financial support, and L.B. thanks the Deutscher Akademischer Austauschdienst (DAAD) for a doctoral fellowship (1992−1996).

Supporting Information Available: Experimental section on the synthesis and complete characterization of the products (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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