Steric and Stereoelectronic Control of the Mode Selectivity as a Function of Alkene Structure in the Reaction with Dimethyl α-Peroxy Lactone: Cycloadducts and Ene Products *versus* Epoxides

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Abstract: The oxidation of di-, tri-, and tetrasubstituted alkenes **2** by dimethyl α-peroxy lactone (**1**) affords the cycloaddition, ene, and epoxidation products **3**−**6**. In the presence of methanol, additionally the trapping products **7** are obtained. The observed dichotomy in the product distribution requires two different paths for this reaction, namely a path *via* an open, stretched 1,6 dipole and another path for epoxidation. Both paths arise from an S_N2 attack of the double bond of the alkene **2** on the peroxide bond of the α-peroxy lactone **1**, the first unsymmetrical (end-on attack), leading to the 1,6 dipole **A**, and the second symmetrical (central attack) with respect to the approach of the double bond, leading to epoxidation. The 1,6 dipole is postulated to afford the cycloadducts, of which the thermodynamically favored diastereomers are obtained, and the ene products. In the epoxidation, the α-lactone released after oxygen transfer oligomerizes to the polyester **8** or in the presence of methanol is trapped as α-methoxy acid **9**. The reaction is regioselective both with respect to the attacked oxygen atom of the α-peroxy lactone **1**, as revealed by the trapping products **7**, as well as with respect to the attacking carbon atom for unsymmetrical alkenes **2c**,**d**, as displayed by the ene products **5** and **6**. The former regioselectivity is dictated by the inherent polarization of the peroxide bond through the carbonyl group which makes the alkoxy oxygen the more electrophilic one toward nucleophilic attack, while for the latter the incipient positive charge of the open 1,6 dipole is better stabilized by the more substituted carbon atom of the end-on attacking unsymmetrical alkene. The preferred reaction mode has been found to be sensitive to the structure of the alkene and the difference in reactivity has been explained in terms of steric and stereoelectronic factors. Thus, for the sterically less hindered *cis*-di- and trisubstitued alkenes the path along the open 1,6 dipole is favored (stereoelectronic control), while the more sterically demanding *trans*-di- and tetrasubstituted alkenes react by the epoxidation mode (steric control).

Introduction

The oxidation of olefins by cyclic peroxides has been studied over the last decades[1] from both the synthetic and mechanistic point of view. The earliest mechanistic studies have been carried out with cyclic peroxides such as phthaloyl peroxide[1a] and more recently α-methylene β-peroxy lactones[1b] and 1,2-dioxetanes.[1c] During the last few years, the dioxiranes[1d] have acquired special importance because of their effective epoxidation of electron-rich as well as electron-poor olefins under mild conditions. The wide scope has rendered them an indispensable synthetic tool, as documented by the intensive use.

Of particular relevance for the present study are the 3,3-disubstituted 1,2-dioxetanes, which in contrast to their three-membered ring congeners, the dioxiranes, are ineffective epoxidizing agents of olefins. Instead, cycloaddition and ene-type products are mainly observed, for which a 1,6-dipolar intermediate was postulated as precursor, proposed to arise from an S_N2 attack of the olefin double bond on the peroxide bond of the dioxetane. The definitive evidence for this mechanism was provided by trapping the postulated intermediate in methanol. The reaction is controlled by steric factors, since the nucleophilic substitution takes place at the oxygen atom adjacent to the unsubstituted carbon. Thus, tetrasubstituted 1,2-dioxetanes are sterically too hindered and unreactive toward most nucleophiles, except triphenylphosphine[2] and hydride ions ($LiAlH_4$).[3]

Herein we have directed our attention to dimethyl α-peroxy lactone (**1**), a strained, thermally labile, cyclic peroxy ester, which was made available by us in earlier times.[4] In view of the inherent polarization of the peroxide bond due to the ester functionality in **1**, we expected the α-peroxy lactones to be more reactive toward nucleophiles than 1,2-dioxetanes, and the nucleophilic attack should take place at the more sterically hindered but more electrophilic alkoxy-type oxygen atom. We anticipated that the preferred reaction mode should be a sensitive function of the steric demand imposed by the attacking alkene nucleophile (Scheme 1). Therefore, we have chosen a series of structurally varied alkenes **2a**−**f** to explore the effects of the alkene structure on the preferred mode of nucleophilic attack in terms of the product distribution, *i.e.* cycloaddition, ene reaction, and epoxidation. The intervention of the expected 1,6-dipolar intermediate was to be established through trapping in

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(1) (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.; Andler, S.; Heil, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1365−1366. (d) Adam, W.; Hadjiarapoglou, L.; Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W., Ed.; John Wiley & Sons Ltd.: Chichester, 1992; pp 195−220.

(2) Bartlett, P. D.; Baumstark, A. L.; Landis, M. E.; Lerman, C. L. *J. Am. Chem. Soc.* **1974**, *96*, 5268−5269.

(3) Kopecky, K. R.; Filby, J. E.; Mumford, C.; Lockwood, P. A.; Ding, J.-Y. *Can. J. Chem.* **1975**, *53*, 1103−1122.

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

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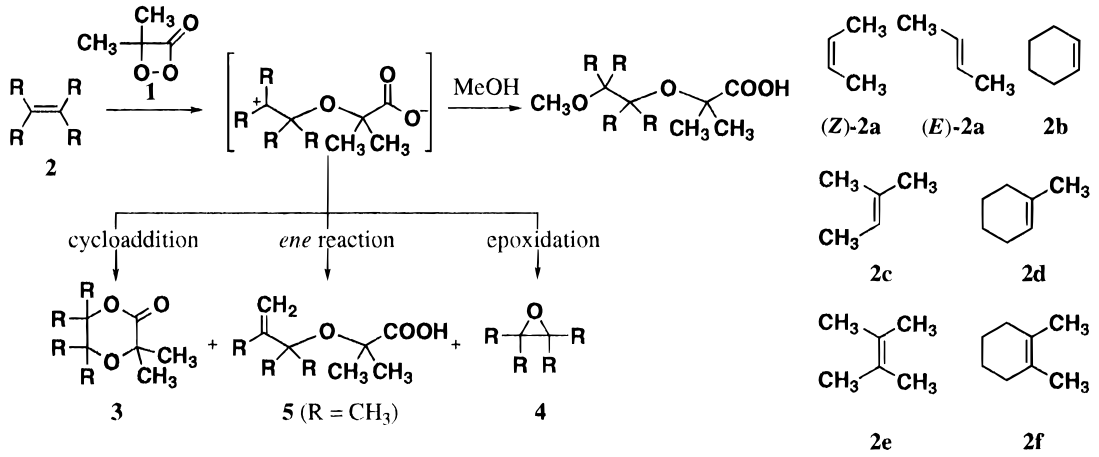
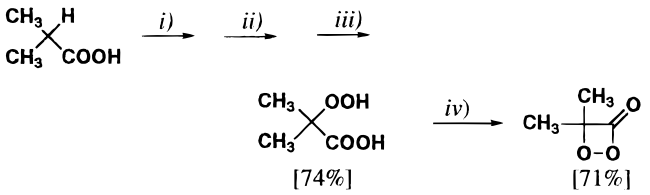
Scheme 1. Expected Products for the Reaction between α-Peroxy Lactone **1** and the Alkenes **2a**−**f**



Scheme 2



i) 2 LDA, - 40 °C, THF; *ii*) $^3O_2$, -70 to -100 °C, THF; *iii*) HCl (Et_2O), -80 °C, THF; *iv*) DCC, CH_3CCl_3, -20 °C

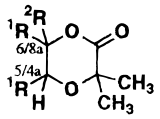
methanol. The general reactivity pattern as a function of steric demand was to be determined by the series of di-, tri-, and tetrasubstituted alkenes **2a**,**b**, **2c**,**d**, and **2e**,**f**, while the regioselectivity of the substitution from the point of view of the alkene nucleophile was to be tested with the unsymmetrical derivatives **2c**,**d**. The diastereomeric pair (***Z***,***E***)**-2a** was chosen to acquire information on the stereochemistry in the cyclization of the 1,6 dipole to the cycloadduct products. The series of cyclohexene derivatives **2b**,**d**,**f** was selected to assess the relative importance of cyclization *versus* ene reaction of the 1,6 dipole. Herein we present our results on the rather complex reaction of alkenes **2** with the α-peroxy lactone **1**. We demonstrate that the structure of the alkene nucleophile profoundly influences the preferred reaction mode, which is controlled by steric and stereoelectronic factors.

Results

α-Peroxy lactone **1** was synthesized according to the published procedure[4] (Scheme 2) and isolated by flash distillation (−10 °C/0.6 Torr). 1,1,1-Trichloroethane was the solvent of choice in view of its intermediate volatility (bp 74 °C) and good solubilizing properties. Since α-peroxy lactone **1** could not be isolated by selective distillation of the solvent, the oxidations of the alkenes were carried out by using directly the 1,1,1-trichloroethane solutions. The peroxide content was determined by iodometry. The trapping experiments with methanol had to be done in the presence of 1,1,1-trichloroethane as cosolvent.

To determine the yields by NMR analysis directly on the crude product mixtures, especially the yields of the volatile epoxides **4**, the reactions were carried out in deuteriochloroform, for which purpose the flash distillation of the α-peroxy lactone was performed in this solvent. The oxidation products are summarized in Scheme 3 and the product data are given in Table 1. The mass balances (fifth column in Table 1) are quite high (82−97%), except entries 1, 5, and 8. For entries 1 and 5, due to the long reaction times substantial decarboxylation of the α-peroxy lactone **1** into acetone was unavoidable even at −20 °C. However, the use of excess alkene **2** led to no substantial variation of the product composition nor better yields. Also an appreciable amount of undefined higher-molecular-weight material was found, presumably a polyester between the alkene and α-peroxy lactone **1**, as suggested by broad aliphatic C−H bands between 3000 and 2800 cm^{-1} and broad carbonyl bands at 1750 cm^{-1} in the IR spectrum of the nonvolatile residue. In the case of entry 8, the mass balance is ca. 94% if polyester **8** (the known oligomerization product of dimethyl α-lactone)[5] is considered (cf. footnote *l*, Table 1).

An overall view at the product distributions presented in Table 1 shows a clear dependence on the substitution pattern of the alkene. The *cis*-disubstituted alkenes (***Z***)**-2a** (entry 1) and **2b** (entry 5) gave the cycloadducts **3a** and **3b** together with



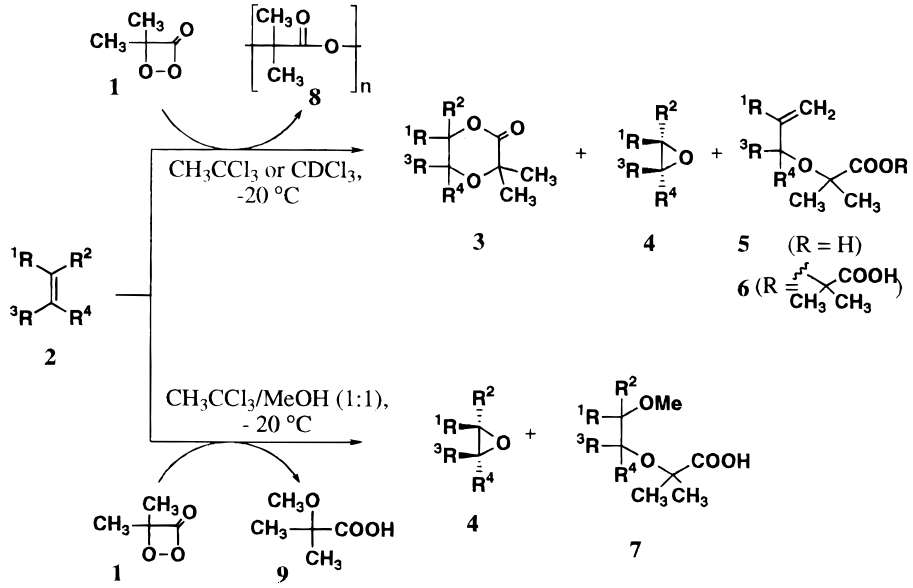
3a (R^1 =CH_3, R^2 = H): δ_{C5} = 69.4 (d), δ_{C6} = 81.6 (d)
3b [R^1 = $(CH_2)_2$, R^2 = H]: δ_{C4a}= 72.3 (d), δ_{C8a}= 82.6 (d)
3c (R^1 = R^2 =CH_3): δ_{C5} = 71.3 (d), δ_{C6} = 85.3 (s)
3d [R^1 = $(CH_2)_2$, R^2 = CH_3]: δ_{C4a}= 70.0 (d), δ_{C8a}= 84.1 (s)

substantial amounts of an unidentified, nonvolatile material as residue. In both cases only one of two possible cycloadduct diastereomers was isolated, namely the *trans* cycloadduct. Although it is possible that traces (ca. <5%) of the corresponding *cis* diastereomers are present in the nonvolatile residue, they were actually not detected by NMR analysis of the crude reaction mixture.

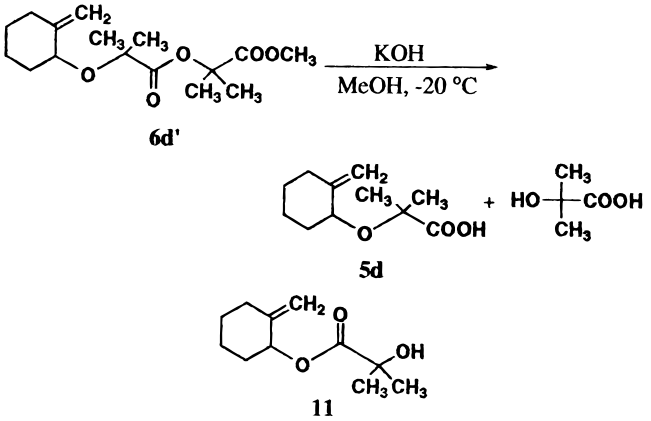
In contrast to the *cis*-alkenes, the *trans*-disubstituted (***E***)**-2a** (entry 3) led to the epoxide **4a** in high yield. The trisubstituted alkenes **2c** (entry 6) and **2d** (entry 7) afforded the epoxides **4c** and **4d**, the cycloadducts **3c** and **3d**, and the ene adducts **5c**,**d** and **6c**,**d**. Finally, the tetrasubstitued alkenes **2e** (entry 8) and **2f** (entry 10) gave exclusively the corresponding epoxides **4e** and **4f**. Formation of the epoxides **4** was accompanied by the polyester **8**. In the reaction with alkene **2e**, the polyester **8** was isolated and by mass spectroscopy its number of α-lactone units was determined as approximately nine (M^+ = 759). Furthermore, in methanol as a cosolvent, the trapping products **7** were observed (entries 2, 4, and 9) and the α-methoxy acid **9** (derived from the intermediary α-lactone).

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

Scheme 3. Conditions and Products for the Reaction between α-Peroxy Lactone **1** and Alkenes **2**

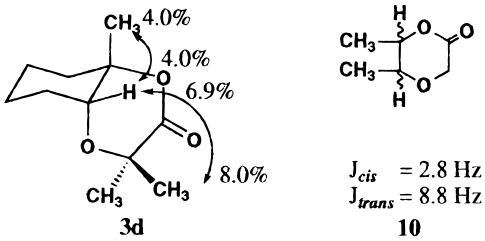


Scheme 4. Saponification of the Alkoxy Acid Derivative **6d′** and Structure of the Alternative Regioisomeric Hydroxy Ester **11**



The structures of the cycloadducts **3** were established on the basis of their spectral data. These 1,4-dioxan-2-ones show the characteristic ester band at 1705−1720 cm^{-1} in the IR spectrum and the ester carbonyl ^{13}C NMR shift at δ 174. The chemical shifts of the dioxane carbon atoms of the original alkene moiety in the cycloadducts **3** were helpful in determining the regiochemistry of the cycloaddition. Thus, for cycloadducts **3a** and **3b** two doublets appear respectively at δ ca. 70 (alkoxy substitution, C5 for **3a** and C4a for **3b**) and δ ca. 80 (carboxy substitution, C6 for **3a** and C8a for **3b**). For the derivatives **3c** and **3d**, the signals at high field (δ ca. 70) are also doublets, while the low-field shifts (δ ca. 85) appear here as singlets, which establishes that the additional methyl group is located at the carboxy-subsituted atom (C6 for **3c** and C8a for **3d**). Consequently, for the unsymmetric alkenes **2c**,**d** only one cycloadduct is obtained with the same regiochemistry.

The stereochemistry of the cycloadducts was assessed by means of the H−H coupling constants between the protons at C5 and C6 for cycloadduct **3a** and at C4a and C8a for **3b**. The values J_{3a} = 8.9 Hz and J_{3b} = 8.8 Hz for the cycloadducts **3a**,**b** correspond to an axial−axial arrangement of the protons, *i.e. trans* arrangement of the substituents. This assignment is in analogy to the known *cis* and *trans* diastereomers of 5,6-dimethyl-1,4-dioxan-2-one (**10**),[6] for which the coupling constants are J_{trans} = 8.8 Hz and J_{cis} = 2.8 Hz. Furthermore, the *trans* stereochemistry is also supported by NOE experiments since no effects were found between the methinyl ring protons for both *trans* stereoisomers **3a**,**b**.

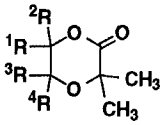
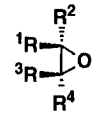
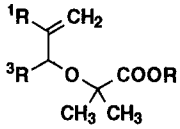
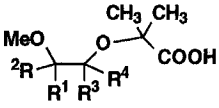
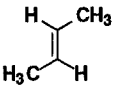
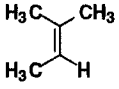
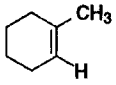
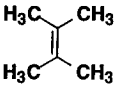
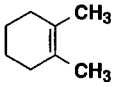


For the *cis* cycloadduct **3d**, a large (ca. 4%) NOE enhancement was observed between the bridgehead proton and the angular methyl group (cf. structure **3d**), which speaks for the *cis* configuration. The broad signal of the bridgehead proton is characteristic for equatorial protons in a six-membered ring and supports the indicated conformer. AM1 calculations showed that the enthalpy of formation is ΔH_f = −145.8 kcal/mol for both the *cis* and *trans* configurations, a fact that is well-known for decalins with methyl substitution at the bridgehead.[7] For comparison, the AM1 calculations for cycloadducts **3a**,**b** gave a lower ΔH_f value for the *trans* isomer ($\Delta H_{f,cis-3a}$ = −137.2 kcal/mol, $\Delta H_{f,trans-3a}$ = −137.7 kcal/mol; $\Delta H_{f,cis-3b}$ = −144.8 kcal/mol, $\Delta H_{f,trans-3b}$ = −145.4 kcal/mol); however, the differences are small (ca. 0.5 kcal/mol).

The isolation of the ene product **6d** required the methylation of the carboxylic acid functionality with diazomethane, which led to ester product **6d′**. The methylenic double bond of the ene adducts **5c**, **5d**, **6c**, and **6d′** (Scheme 3) is evidenced by the characteristic olefinic proton (two broad unresolved multiplets between δ 4.7 and 5.0) and carbon shifts (triplet at δ ca. 110 and singlet at δ ca. 150). Saponification of the ene products **6c** and **6d′** led to the corresponding initial ene derivatives **5c** and **5d** (Scheme 4, only illustrated for derivative **6d′**), which confirms that the products **6c** and **6d** result from follow-up reaction of **5c** and **5d** with the α-lactone. The structures of the ene adducts **6c** and **6d′** (M^+_{6c} = 256 and $M^+_{6d'}$ = 298 by mass spectrometry) are based on NMR spectral data, which include

(6) Äyräs, P. *Org. Magn. Reson.* **1975**, *7*, 177−178.
(7) Hannack, M. *Conformation Theory; Organic Chemistry*; Academic Press: New York, 1965; Vol. 3.

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

					product distribution [%][b]			
								
			time	m.b.[c]	**3**	**4**	**5, 6**	**7**
entry	**2**	solvent	[h]	[%]	cycloaddition[d]	epoxidation	*ene* reaction	trapping[e]
1		$CDCl_3$	60	67[f]	43 (*trans*)	-	-	-
2		$CDCl_3/CD_3OD$	4	>95	-	-	-	96 (95:5)
	(**Z-2a**)							
3		$CDCl_3$	48	≥82[g]	-	82	-	-
4		$CDCl_3/CD_3OD$	16	90[h]	-	34	-	47 (86:14)
	(***E*-2a**)							
5		CH_3CCl_3	60	69[f]	30 (*trans*)	-	-	-
	(**2b**)							
6		CH_3CCl_3	40	95[i]	34	11[j]	21, 20	-
	(**2c**)							
7		CH_3CCl_3	24	97[i]	30 (*cis*)	[k]	39, 14	-
	(**2d**)							
8		$CDCl_3$	15	≥66[l]	-	57	-	-
9		$CDCl_3/CD_3OD$	15	>95[m]	-	27	-	46
	(**2e**)							
10		$CDCl_3$	15	86	-	86	-	-
	(**2f**)							

[a] At −20 °C, conversion 100% referred to **1**. [b] Product distribution in CH_3CCl_3 determined by ^1H NMR spectroscopy (in $CDCl_3$ with hexamethyldisiloxane as internal standard) of the crude product mixture after distillation of the solvent. [c] Mass balance (m.b.) refers to α-peroxy lactone **1**. [d] Stereochemistry of the cycloadducts indicated in brackets. [e] Diastereomeric ratio (d.r.) of the trapping product mixture indicated in brackets. [f] Includes nonvolatile unidentified material; the deficit is mainly acetone due to decomposition of α-peroxy lactone **1** during such prolonged reaction times. [g] The polyester **8** yield was ca. 95%. [h] Includes 9% acetone; also 50% α-methoxy ester **9** was observed. [i] Product **6** accounts for 2 equiv of α-peroxy lactone **1** in the mass balance (cf. footnote *c*). [j] Determined for the reaction carried out in $CDCl_3$. [k] Product **4d** detected by GC analysis, yield not determined. [l] Includes 9% acetone; the polyester **8** yield was ca. 85%. [m] Includes 24% acetone; 33% α-methoxy ester **9** was observed.

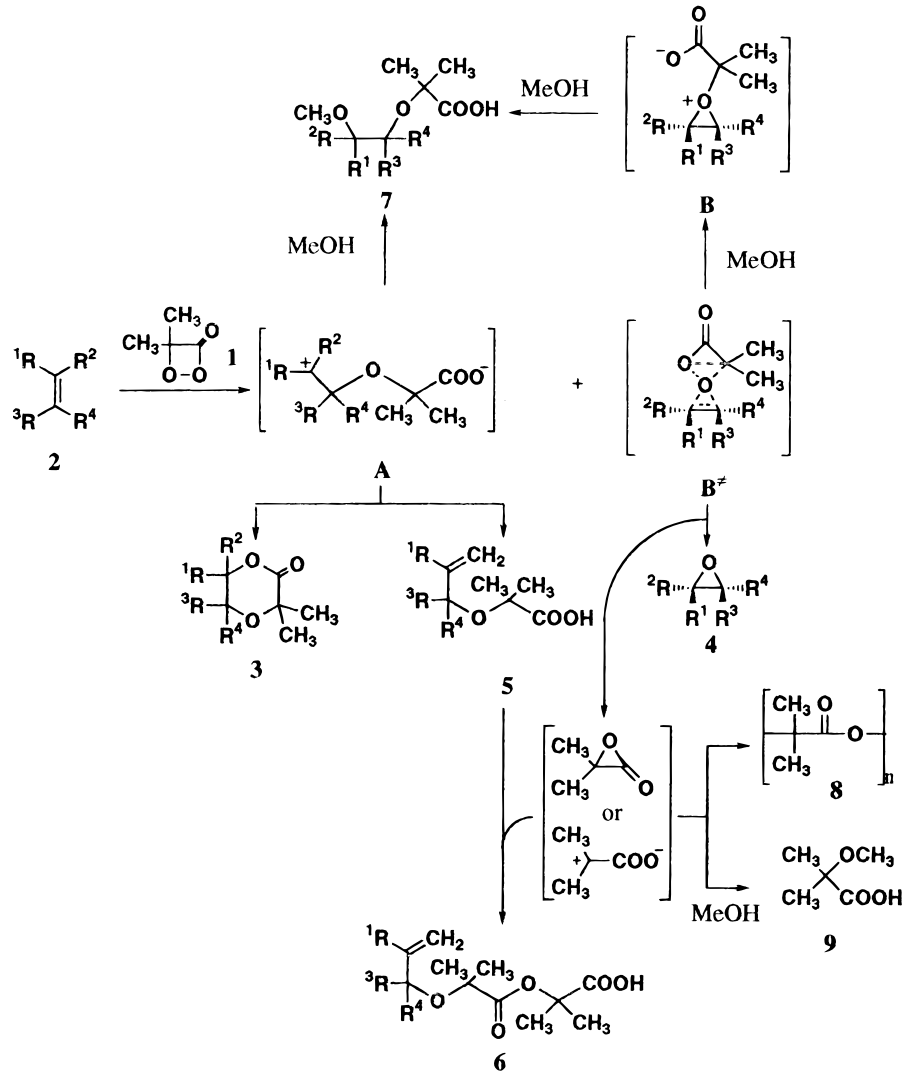
two carbonyl signals (δ_{6c} 174.3, 177.3 and $\delta_{6d'}$ 173.2, 174.1), two singlets for the α-alkoxy carbons C2 and C2′ (δ_{6c} 75.6, 78.5 and δ_{6d} 78.3, 78.5), and doublets for the alkoxy carbons derived from the olefin (δ_{6c} 75.5 and δ_{6d} 76.5). Furthermore, the fact that **5d** is the saponification product provides evidence for the alkoxy acid structure in favor of the alternative hydroxy ester **11** (Scheme 4). The same situation applies to derivative **5c**.

The structures of the trapping products **7a** and **7e** were assigned on the basis of their spectral data. The carboxylic acid functionality is evident through the IR bands at 3500−2200 and 1740 cm^{-1} and the carbon resonances at δ 177.2 for **7a** and δ 179.0 for **7e**. In the methanol trapping reaction both (***Z*)-2a** and (***E*)-2a** alkenes gave mixtures of the same diastereomeric trapping product **7a**. The major isomer was isolated by Kugelrohr distillation and exhibited the characteristic NMR resonance for the methoxy group at δ^1_H 3.47 and δ^{13}_C 56.8. The minor diastereomer was detected in the crude reaction mixture and possesses the corresponding resonances at δ^1_H 3.41 and δ^{13}_C 56.6. The α-lactone trapping product with methanol was identified as the α-methoxy acid **9**.

Discussion

The choice of the set of alkenes **2a**−**f** has been most instructive in gaining mechanistic insight into the complex product picture (Table 1) of oxidation by the α-peroxy lactone **1** in halogenated solvents (CH_3CCl_3, $CDCl_3$). It is the dichotomy in the product composition as a function of alkene

Scheme 5. Mechanism for the Reaction of α-Peroxy Lactone **1** with Alkenes **2** in the Absence and Presence of Methanol



structure which is impressive, namely the formation of the cycloadducts **3** from the *cis*-disubstituted alkenes (*Z*)-**2a** and **2b**, but epoxides **4** from the tetrasubstituted substrates **2e** and **2f**. Interestingly, the trisubstituted alkenes **2c** and **2d** afford both the cycloadducts **3** and epoxides **4**, but additionally the ene products **5** and **6**. Still more puzzling is the fact that the diastereomeric alkenes (*Z*)-**2a** and (*E*)-**2a** display this product dichotomy, in that (*Z*)-**2a** leads to the cycloadduct **3a** but (*E*)-**2a** leads to the epoxide **4a**.

Despite the perplexing complexity in this reactivity pattern, fortunately some common chemical traits are observed when this reaction is run in methanol as cosolvent. Informative again is the diastereomeric 2-butene pair (*Z*)-**2a** and (*E*)-**2a**, for which the trapping product **7a** completely replaces the cycloaddition mode with (*Z*)-**2a** and partially replaces the epoxidation mode with (*E*)-**2a**, as exhibited in Table 1. The latter situation, *i.e.* trapping in competition with epoxidation, also applies to tetramethylethylene (**2e**) as alkene substrate. Such trapping products **7** clearly implicate dipolar intermediates in the reaction of α-peroxy lactone **1** with the alkenes **2**.

In this context, we recall our previous studies on the reaction of 3,3-disubstituted 1,2-dioxetanes with electron-rich olefins, which as π-type nucleophiles react by S_N2 attack on the sterically less hindered oxygen atom of the peroxide bond in the four-membered ring peroxide to afford mainly cycloadducts and ene products, while the epoxidation reaction was hardly significant.[1c] Methanol trapping experiments definitively showed that 1,6-dipolar intermediates intervened. In analogy, we propose that the 1,6 dipole **A** (Scheme 5) is an intermediate in some cases of the α-peroxy lactone/alkene oxidation. However, the open 1,6 dipole is not sufficient to explain all the product data in Table 1, because unlike the reaction of dioxetanes with olefins, α-peroxy lactone **1** epoxidation takes place in substantial amounts for the alkenes (*E*)-**2a**, **2e**, and **2f**. In earlier work we and others[8] showed that epoxidation is the exclusive reaction with dioxiranes irrespective of alkene structure, and a concerted oxygen transfer process with the *spiro*-type "butterfly" transition state has been proposed since trapping products are not observed in methanol.[9] We propose that the reaction proceeds by two major paths: one involves the 1,6 dipole **A** and the other concerted epoxidation.

In nonprotic solvents the open 1,6 dipole **A** may coil up and cyclize by charge annihilation to the cycloadducts **3** or oligomerize to a polyester composed of alternate alkene and α-peroxy lactone units. The oligomerization mode explains the significant amount of undefined high-molecular-weight material, while the low mass balances observed for alkenes (*Z*)-**2a** and **2b** may be attributed to the thermal decomposition of α-peroxy lactone **1** during the long reaction times (Table 1, entries 1 and 5, footnote

(8) For a recent review see: Adam, W.; Hadjiarapoglou, L. *Top. Curr. Chem.* **1993**, *164*, 45−62.

(9) (a) Baumstark, A. L.; McCloskey, C. J. *Tetrahedron Lett.* **1987**, *28*, 3311−3314. (b) Murray, R. W.; Gu, D. *J. Chem. Soc., Perkin Trans. 2* **1993**, 2203−2207.

f). However, Grob-type fragmentation of the intermediate **A** into CO_2, acetone, and alkene is unlikely since a control experiment established that no isomerization of (***Z***)-**2a** occurred.

While the occurrence of the cycloaddition and ene reaction through the 1,6 dipole **A** is well established by the products and the trapping of the intermediate **A** in the presence of methanol, for the epoxidation path we postulate a concerted mechanism through the *butterfly*-type transition state $\mathbf{B}^{\neq}$. However, in view of the trapping experiments for (***E***)-**2a** (Table 1, entry 4) and **2e** (entry 9), it is tempting to postulate the participation of the epoxonium intermediate **B** rather than the concerted epoxidation path. Nevertheless, it is hard to believe that **A** and **B** do not interconvert to give a mixture of cycloadducts and epoxides instead of the dichotomy in the product data. Therefore, we favor the concerted mechanism through transition state $\mathbf{B}^{\neq}$ for the epoxidation and not the epoxonium intermediate **B**! As to the formation of trapping products in methanol, a polar solvent effect may operate by which the reaction proceeds through the dipolar epoxonium intermediate **B** and possibly the 1,6 dipole **A**. In view of the dependence of the product distribution on subtle structural changes, it appears that a flat potential surface applies for this oxygen transfer process, and the differentiation between the concerted (transition state $\mathbf{B}^{\neq}$) and stepwise (epoxonium intermediate **B**) mechanisms for the epoxidation is expectedly difficult.

We must now scrutinize the electronic and steric factors prevalent in the encounter between the α-peroxy lactone **1** and the structurally varied alkene **2**, which guide the reaction either to cycloaddition or to epoxidation. This reaction, like other olefin oxidations by peroxides, particularly the epoxidation by peracids,[10] for which much mechanistic information is avalaible,[11] entails an S_N2 attack of the alkene as π-type nucleophile on the peroxide bond of α-peroxy lactone. The fact that the ene products possess the alkoxy acid **5** structure rather than the alternative hydroxy ester **11** structure (Scheme 4) clearly demonstrates nucleophilic attack at the alkoxy oxygen atom of the peroxide bond with concomitant displacement of the carboxy oxygen atom in the α-peroxy lactone. Optimal overlap between the π orbital of the alkene and the σ^* orbital of the peroxide bond is given in a perpendicular approach in line with the peroxide bond. Recent calculations for the reaction of ethylene with performic acid make this geometrical arrangement plausible in terms of the energetics of the process.[11d]

The direct generation of the 1,6 dipole **A** requires an unsymmetrical, end-on attack by the π nucleophile with preferred bonding of the less substituted alkenic carbon atom with the alkoxy-type peroxide atom. The mixed cases, namely the unsymmetrical alkenes **2c**,**d**, which display both the cycloaddition as well as the epoxidation modes (Table 1), support this end-on attack at the less substituted alkenic site through the regiochemistry of the cycloadducts **3** and the ene products **5** and **6**. In contrast, for the epoxidation a symmetrical, central approach applies, with simultaneous bonding at both alkenic carbon atoms.

For 1,2-dioxetanes, *i.e.* the related four-membered ring cyclic peroxides, steric factors dramatically control the regioselectivity toward nucleophiles. Thus, in the S_N2 reaction for the 3,3-disubstituted derivatives the more sterically exposed unsubstituted oxygen atom is attacked by the nucleophile, while the tetrasubstituted derivatives are esentially unreactive.[1c] The situation, however, is impressively inverted in the case of α-peroxy lactones, for which the inherent polarization of the peroxide bond makes the alkoxy-type oxygen atom more electrophilic and prone to nucleophilic attack, as is clearly exhibited in the regioselectivity of the cycloadducts and ene products (Scheme 5). Thus, electronic control applies for the S_N2 reaction with the α-peroxy lactone **1** and it is the more sterically encumbered oxygen atom, namely the one adjacent to the dimethyl-substituted site, that is attacked by the π nucleophile. This aspect of the reaction is in good accordance with the known nucleophilic substitutions at *tert*-butyl peroxy benzoate, which also take place at the sterically more hindered alkoxy-type oxygen.[12]

It is now instructive to examine the structurally varied alkene **2** substrates in terms of nucleophilicity, steric demand, and stabilization of the resulting dipole with the purpose of classifying them with respect to which route (1,6 dipole **A** or epoxidation) is preferred. In regard to the nucleophilicity, the trend for this set of alkenes follows the increasing order **2a**,**b** < **2c**,**d** < **2e**,**f**, which would be in line with the observed reactivity in that the tetrasubstituted substrates **2e**,**f** are the fastest. However, the temptation to argue that this nucleophilicity order of the alkene partner favors the symmetric, central approach to afford an epoxide does not explain the product dichotomy displayed by the equally nucleophilic diastereomeric 2-butenes (***Z***)-**2a** and (***E***)-**2a**. In this context, arguments in terms of carbocation stabilization of the open 1,6 dipole **A** are also not productive, because the (***Z***,***E***)-**2a** diastereomeric pair should lead to the same intermediate, which cannot be the case in view of the distinct product picture. Besides, the most stabilized carbocation sites would be the tertiary ones in the intermediate **A** derived from tetrasubstituted alkenes **2e**,**f** and trisubstituted **2c**,**d**, but these are precisely the substrates for which epoxidation is observed.

Unlike the regioselectivity of the nucleophilic attack, which is governed by the electronic factors discussed above, the reaction mode and product distribution appear to be decisively dictated by steric interactions between the π nucleophile **2** and the α-peroxy lactone **1**. Clearly, severe steric interactions are encountered during the *spiro*-type approach between the substituents of the alkene **2** substrate and the *gem*-dimethyl group in the α-peroxy lactone **1**. The steric hindrance is more serious for the unsymmetrical end-on attack to generate the open 1,6 dipole **A** than for the symmetrical central one leading to the epoxide. This is manifested by the product dichotomy (Table 1), since the sterically less encumbered *cis*-disubstituted substrates (***Z***)-**2a** and **2b** afford exclusively cycloadducts **3** (dipole **A**) and the sterically congested tetrasubstituted alkenes **2e**,**f** exclusively epoxides **4**.

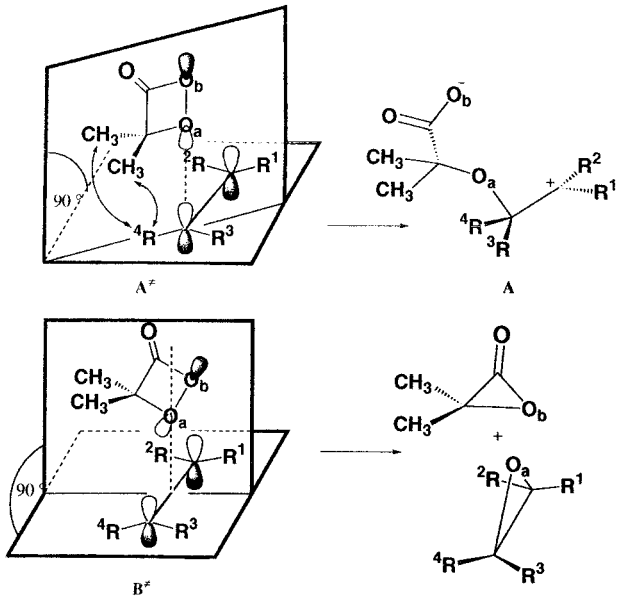
We envisage the two transition states $\mathbf{A}^{\neq}$ and $\mathbf{B}^{\neq}$ for the encounter between α-peroxy lactone **1** and alkene **2** (Scheme 6), of which the unsymmetrical, end-on attack $\mathbf{A}^{\neq}$ leads to the open 1,6 dipole **A** and the symmetrical, central attack $\mathbf{B}^{\neq}$ to the epoxide. A compromise between stereoelectronic and steric factors decides whether the encounter $\mathbf{A}^{\neq}$ or $\mathbf{B}^{\neq}$ prevails. As already mentioned, recent theoretical studies[11d] on the peracid oxidation of olefins suggest a linear arrangement of the alkene π orbital and the σ^* orbital of the peroxide bond. This situation is realized in transition state $\mathbf{A}^{\neq}$ for α-peroxy lactones, but comes at the expense of serious steric repulsion between the R^4 substituent and the *gem*-dimethyl groups; this approach is

(10) Plesničar, B. In *The Chemistry of Peroxides*; Patai, S., Ed.; John Wiley and Sons: New York, 1983; pp 521−584.

(11) (a) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5231−5233. (b) Plesničar, B.; Tasevski, M.; Ažman, A. *J. Am. Chem. Soc.* **1978**, *100*, 743−746. (c) Bach, R. D.; Owensby, A. L.; González, C.; Schlegel, H. B. *J. Am. Chem. Soc.* **1991**, *113*, 2338−2339. (d) Bach, R. D. Personal communication.

(12) (a) Lawesson, S.-O.; Yang, N. C. *J. Am. Chem. Soc.* **1959**, *81*, 4231. (b) Meesters, A. C. M.; Benn, M. H. *Synthesis* **1978**, 679−680.

Scheme 6. Conformation of the In-Line, End-On Unsymmetrical ($\mathbf{A}^{\neq}$) and Tilted, Central Symmetrical ($\mathbf{B}^{\neq}$) Nucleophilic Attack of the Alkene π Double Bond on the α-Peroxy Lactone O_a Peroxide Atom

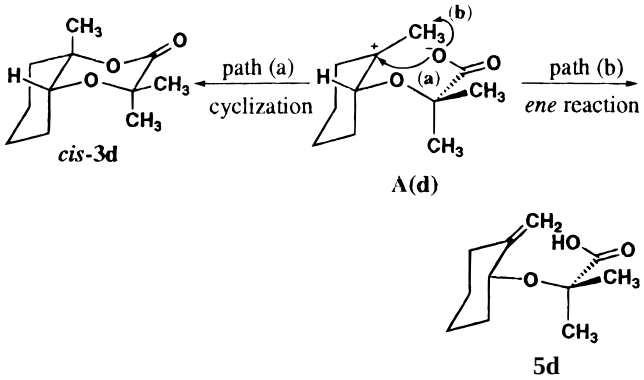


only feasible when R^4 = H. This particularly applies to the *cis*-disubstitued substrates (*Z*)-**2a** and **2b**, which afford the open 1,6 dipole **A** with the stretched zigzag conformation, *i.e.* the cycloaddition mode.

When the end-on attack to the more stable 1,6 dipole **A** is sterically encumbered, as appears to be the case for the tetrasubstituted alkenes **2e**,**f**, the way out is to engage the *spiro* attack $\mathbf{B}^{\neq}$, the epoxidation mode. Although steric repulsions are reduced, they are by no means eliminated. Due to the inherent structural features of the four-membered ring, the *gem*-dimethyl groups protrude in the direction of the incoming π nucleophile and encumber the attack on the O_a atom. This alone will tend to tilt the α-peroxy lactone away from the ideal stereoelectronic linear arrangement (indicated in Scheme 6 by the vertical dashed line in transition state $\mathbf{B}^{\neq}$). Additionally, as drawn, the R^2 and R^4 substituents will tend to minimize steric repulsions with the *gem*-dimethyl groups and promote the degree of tilting. As the O_a atom penetrates the π cloud, charge transfer from the alkene to the α-peroxy lactone ensues with rupture of the peroxide bond by displacement of the O_b atom. The developing positive charge on the alkene is rescued in this symmetrical, central approach by bonding with the O_a lone pair and epoxidation is the preferred reaction mode.

As far as the trisubstituted alkenes **2c**,**d** are concerned, these are intermediate cases in which, in addition to steric effects, the stabilization of the 1,6 dipole **A** also plays an important role. Since the R^1 substituent exercises a minimal steric effect in transition state $\mathbf{A}^{\neq}$, both substrates possess similar steric demand, which is considerably greater than that for the *cis*-disubstituted substrates (*Z*)-**2a** and **2b** (R^2 = alkyl *versus* R^2 = H). Consequently, for the trisubstituted alkenes **2c**,**d**, the tendency will be to proceed along the epoxidation pathway (transition state $\mathbf{B}^{\neq}$), but the effective stabilization of the 1,6 dipole **A** (R^1 and R^2 both alkyl) promotes some unsymmetrical attack along the cycloaddition route and both types of products are observed. Finally, the striking difference in the reaction mode between the diastereomeric 2-butene pair (*Z*,*E*)-**2a** is explained by the greater steric hindrance in the diastereomer (*E*)-**2a** due to the secondary steric interactions caused by the substituent R^2 of the alkene (R^2 = alkyl for (*E*)-**2a** *versus*

Scheme 7. Ring Closure to Cycloadduct **3d** (a) and Proton Abstraction to Ene Product **5d** (b) as Alternative Pathways for Intermediate **A**(**d**)



R^2 = H for (*Z*)-**2a**), and therefore epoxidation through the transition state $\mathbf{B}^{\neq}$ occurs preferentially.

The two pathways ($\mathbf{A}^{\neq}$ and $\mathbf{B}^{\neq}$) are necessary not only to rationalize the product dichotomy but also to explain the observed diastereoselectivity in the cycloaddition process and the fact that ene products **5** and **6** are obtained for the trisubstituted alkenes **2c**,**d**, in addition to the cycloadducts **3** and the epoxides **4**. The unsymmetrical attack in transition state $\mathbf{A}^{\neq}$ obliges that initially the stretched, zigzag (W-shaped) open 1,6 dipole **A** is formed (Schemes 5 and 6). In the process of coiling up to bring the charges into proximity for cyclization, the 1,6 dipole **A** possesses, as shown above, sufficient lifetime to select the thermodynamically preferred *trans* isomer, as observed for the alkenes (*Z*)-**2a** and **2b**. AM1 calculations ascribe to the *trans* cycloadducts a slightly lower (ca. 0.5 kcal/mol) formation enthalpy (ΔH_f). However, for the alkene **2d**, only the cycloadduct ***cis*-3d** was observed, with large amounts of ene products **5d** and **6d**. The AM1 calculations suggest the same ΔH_f values and, in fact, in bridgehead-substituted decalins the *cis* and *trans* diastereomers are nearly of the same energy.[7] However, we suspect that in the favored coiled-up conformation of the intermediate **A**(**d**), it is easier to abstract an H atom to produce the ene product **5d** than to push the carboxylate ion past the methyl group at the tertiary carbocationic site to afford the *trans* cycloadduct through back-side attack; front-side collapse affords the ***cis*-3d** cycloadduct (Scheme 7). The **A** intermediate derived from substrate **2b**, lacking the methyl group of **A(d)**, cyclizes to afford the thermodynamically preferred ***trans*-2b** cycloadduct.

Conclusion

Our detailed mechanistic analysis has provided a rationale consistent with the complex product picture observed in the oxidation of alkenes **2** by the α-peroxy lactone **1**, particularly the astounding product dichotomy. The latter reflects the unprecedented reactivity of α-peroxy lactone **1** toward alkenes, which combines the characteristic features of other known strained cyclic peroxides, namely the dioxiranes (epoxidation) and 1,2-dioxetanes (addition). Thus, controlled by the alkene structure, either the epoxidation or the cycloaddition/ene reaction mode prevails. Compared with the 1,2-dioxetanes,[1c] the regioselectivity as to which oxygen atom of the peroxide bond is attacked is not controlled by steric factors but by the inherent polarization of the peroxide bond in the α-peroxy lactone. Nevertheless, in analogy to our findings for α-peroxy lactone **1**, epoxidation by 1,2-dioxetanes takes place, although in small yields, exclusively when the reaction is sterically encumbered, *i.e.* for tetrasubstituted alkenes. The present results are intended

to encourage further experimental and theoretical studies on this complex but interesting mechanistic subject.

Experimental Section

General Aspects. Melting points were taken on a Reichert Thermovar Kofler apparatus and are uncorrected. ^{1}H NMR spectra: Bruker AC 200 (200 MHz), $CDCl_3$ as internal standard. ^{13}C NMR spectra: Bruker AC 200 (50 MHz), $CDCl_3$ as internal standard. Infrared spectra: Perkin-Elmer 1420 ratio recording infrared spectrophotometer. Mass spectra: Finnigan MAT 8200 and Finnigan MAT 90. Combustion analyses (±0.5%) were carried out by the Microanalytical Division of the Institute of Inorganic Chemistry, University of Würzburg. Column chromatography: silica gel (63−200 μm) from Woelm or florisil (100−200 mesh) from Acros with an adsorbant/substrate ratio of ca. 100:1. Thin-layer chromatography (TLC): Polygram SIL G/UV_{254} (40 × 80 mm) from Machery and Nagel. Peroxides were detected with 10% aqueous KI solution, other compounds with a 5% ethanolic solution of molybdophosphoric acid. The product data in the individual experiments represent absolute *yields of isolated material*, while in Table 1 (for mechanistic convenience) the yields of the products were determined by NMR analysis directly on the crude product mixture before workup.

2-Hydroperoxy-2-methylpropanoic Acid. A solution of lithium diisopropylamide (LDA) in THF/hexane was prepared in the usual manner in a 500-mL, round-bottomed flask under an argon gas atmosphere by starting with 145 mL (ca. 0.130 mol) of a 0.91 N solution of *n*-BuLi in hexane, 150 mL of dry THF (freshly distilled from potassium metal), and 18.6 mL (0.132 mol) of diisopropylamine (freshly distilled from CaH_2). The solution was titrated with menthol in dry THF by using phenanthroline as indicator[13] and a solution of 0.0510 mol (4.71 mL) of 2-methylpropanoic acid (0.5 equiv) in 10 mL of dry THF was added dropwise at −78 °C. The solution was allowed to warm up to room temperature and the solvent removed by distillation (20 °C, 0.1 Torr). The residue was redissolved in 200 mL of freshly distilled, dry THF and the solution transfered to a 250-mL addition funnel, attached to a 500-mL, three-necked, round-bottomed flask, which contained a cooled, O_2-saturated solution of 150 mL of THF. The addition funnel should possess a long tip to allow the addition of the dianion solution below the surface of the O_2-saturated solution. The addition was performed slowly by keeping the temperature of the cooling bath between −70 and −90 °C, while a slow stream of O_2 was passed continually through the solution. After 4 h, the addition was complete and the resulting solution was acidified with a solution of HCl gas in dry ether. The solvent was distilled (20 °C, 0.1 Torr) and the residue dissolved in CH_2Cl_2 and then filtered over Celite. The crude product was chromatographically purified by eluting with a 2:1 mixture of CH_2Cl_2/diethyl ether at −40 °C to afford 4.54 g (74%) of 2-hydroperoxy-2-methylpropionic acid.

General Procedure for the Synthesis of Dimethyl α-Peroxy Lactone (1). A solution of 2-hydroperoxy-2-methylpropanoic acid (1.0 equiv) in the corresponding solvent was placed into a 100-mL, two-necked, round-bottomed flask attached to a distillation apparatus and a high-capacity pump (Leybold SV 16), cooled to −30 °C, and a solution of 1.0 equiv of dicyclohexylcarbodiimide (DCC) in the corresponding solvent was added dropwise. The volatile materials of the resulting suspension were flash distilled (0.6 Torr) and the distillate collected in a liquid nitrogen trap. Portions of about 1.5 mL of new solvent batches were added to resuspend the solid residue and the mixture was flash-distilled as above until the residue showed only a weak peroxide test (almost complete recovery of α-peroxy lactone **1**). The peroxide titer was determined iodometrically (KI/AcOH).

Synthesis of Dimethyl α-Peroxy Lactone (1) in 1,1,1-Trichloroethane. The above general procedure was followed, except the temperature of the cooling bath was held between −20 and −10 °C to avoid freezing of the solvent. In a typical run, 124 mg (1.03 mmol) of 2-hydroperoxy-2-methylpropanoic acid and 213 mg (1.03 mmol) of DCC afforded a solution of 75.0 mg (71%) of **1** in 32.5 mL of CH_3CCl_3.

Synthesis of Dimethyl α-Peroxy Lactone (1) in Deuteriochloroform. The above general procedure was followed, except the temperature of the cooling bath was held between −25 and −20 °C. In a typical run, 98.0 mg (0.820 mmol) of 2-hydroperoxy-2-methylpropanoic acid and 168 mg (0.820 mmol) of DCC afforded a solution of 16.0 mg (20%) of **1** in 8 mL of $CDCl_3$.

General Procedure for the Reaction of Dimethyl α-Peroxy Lactone (1) with Alkenes 2. Alkene **2** was added to an equimolar amount of dimethyl α-peroxy lactone (**1**) solution in CH_3CCl_3 or $CDCl_3$ at −20 °C. The reaction was run at −20 °C until a negative peroxide test (KI/AcOH) indicated complete conversion of **1**. At the preparative scale (reaction run in CH_3CCl_3), the product solution was dried over $MgSO_4$, the latter removed by filtration, and the solvent distilled at 20 °C/20 Torr. The product mixture was purified by column chromatography on silica gel or florisil and/or by distillation on a Kugelrohr distillation apparatus.

(*Z*)-2-Butene ((*Z*)-2a). According to the general procedure, ca. 30 μL (0.3 mmol) of (*Z*)-2-butene ((***Z*)-2a**) was added to 27.0 mg (0.260 mmol) of α-peroxy lactone **1** in 10 mL of CH_3CCl_3 at −20 °C. After 60 h, the reaction mixture was worked up as described and 9.0 mg (22%) of the cycloadduct **3a** was isolated by Kugelrohr distillation at 50−60 °C/20 Torr as a colorless oil. The results are given in Table 1.

3,3,5,6-Tetramethyl-1,4-dioxan-2-one (3a): IR ($CDCl_3$) 2980, 2930, 2860, 1720, 1375, 1350, 1300, 1265, 1200, 1185, 1175, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (d, J = 6.3 Hz, 3H, CH_3), 1.29 (d, J = 6.4 Hz, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 3.63 (dq, J_d = 8.9 Hz, J_q = 6.2 Hz, 1H, H-5), 4.30 (dq, J_d = 8.9 Hz, J_q = 6.4 Hz, 1H, H-6); ^{13}C NMR ($CDCl_3$) δ 16.9 (q, CH_3), 17.6 (q, CH_3), 24.8 (q, CH_3), 27.7 (q, CH_3), 69.4 (d, C-5), 76.2 (s, C-3), 81.6 (d, C-6), 173.4 (s, C-2). Anal. Calcd for $C_8H_{14}O_3$ (158.1): C, 60.73; H, 8.93. Found: C, 60.44; H, 8.80.

(*E*)-2-Butene ((*E*)-2a). According to the general procedure, ca. 10 μL (0.1 mmol) of (*E*)-2-butene ((***E*)-2a**) was added to ca. 5 mg (0.05 mmol) of α-peroxy lactone **1** in 0.8 mL of $CDCl_3$ at −20 °C. After 72 h, the ^{1}H NMR spectrum of the sample revealed the epoxide *trans*-**4a** and the oligomer **8**, which were identified by their characteristic signals and the yields determined by using hexamethyldisiloxane (HMDSO) as internal standard. The results are given in Table 1.

Cyclohexene (2b). According to the general procedure, 48.0 μL (0.470 mmol) of alkene **2b** was added to 48.0 mg (0.470 mmol) of α-peroxy lactone **1** in 14.5 mL of CH_3CCl_3 at −20 °C. After 60 h, the reaction mixture was worked up as described and 30.0 mg (30%) of the cycloadduct **3b** was isolated by Kugelrohr distillation at 65−75 °C/0.2 Torr as a white solid. The results are given in Table 1.

3,3-Dimethyl-1,4-dioxabicyclo[4.4.0]decan-2-one (3b): mp 59−60 °C; IR ($CDCl_3$) 2920, 2840, 1710, 1440, 1365, 1310, 1260, 1205, 1190, 1170, 1130, 1060, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19−1.29 (complex signal, 3H), 1.36 (m, 1H), 1.45 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.73 (cs, 2H), 1.92 (cs, 2H), 3.40 (m, J_{4a-5eq} = 4.6 Hz, J_{4a-5ax} = 10.7 Hz, J_{4a-8a} = 8.8 Hz, 1H, H-4a), 4.05 (ddd, J_{8a-8eq} = 4.5 Hz, J_{8a-8ax} = 11.4 Hz, J_{8a-4a} = 8.8 Hz, 1H, H-8a); ^{13}C NMR ($CDCl_3$) δ 23.3 (t), 23.7 (t), 25.4 (q, CH_3), 27.9 (q, CH_3), 29.9 (t), 30.2 (t), 72.3 (d, C-4a), 77.2 (s, C-3), 82.6 (d, C-8a), 173.3 (s, C-2). Anal. Calcd for $C_{10}H_{16}O_3$ (184.2): C, 65.19; H, 8.75. Found: C, 64.71; H, 8.76.

2-Methyl-2-butene (2c). According to the general procedure, 109 μL (1.09 mmol) of alkene **2c** was added to 111 mg (1.09 mmol) of α-peroxy lactone **1** in 60 mL of CH_3CCl_3 at −20 °C. After 24 h, the reaction mixture was worked up as described. Kugelrohr distillation at 75−85 °C/20 Torr of the residue afforded 28.0 mg of a mixture of cycloadduct **3c** and ene product **5c** as determined by ^{1}H NMR. The mixture was separated by column chromatography (florisil) with a 3:1 mixture of petroleum ether (30−50 °C)/diethyl ether, which afforded 8.0 mg (4%) of **3c** as a colorless oil. The column was washed with methanol and 14.0 mg (7%) of **5c** was collected as a colorless oil. The distillation residue was further distilled (Kugelrohr) at 50 °C/0.4 Torr and finally at 160 °C/0.4 Torr. The final fraction afforded 21.0 mg (11%) of ene product **6c** as a colorless oil. The results are given in Table 1.

3,3,5,6,6-Pentamethyl-1,4-dioxan-2-one (3c): IR ($CDCl_3$) 2970, 2920, 2850, 1705, 1450, 1370, 1300, 1195, 1140, 1095, 960 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.17 (d, J = 6.4 Hz, 3H, CH_3-5), 1.26 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 3.78 (q, J = 6.4 Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$) δ 16.1 (q, CH_3), 20.7 (q, CH_3), 24.7 (q, CH_3), 25.3 (q, CH_3), 27.5 (q, CH_3), 71.3 (d, C-5), 76.2 (s,

(13) Vedejs, E.; Larsen, S. *Org. Synth.* **1986**, *64*, 127−137.

C-3), 85.3 (s, C-6), 173.8 (s, C-2). Exact mass calcd for $C_9H_{16}O_3$ 172.1099, found 172.1099.

2-Methyl-2-(1,2-dimethyl-2-propenoxy)propanoic acid (5c): IR ($CDCl_3$) 3300, 2960, 2910, 2840, 1760, 1695, 1450, 1350, 1175, 1075, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (d, J = 6.4 Hz, 3H, CH_3-1′), 1.44 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.74 (bs, 3H, CH_3-2′), 4.10 (q, J = 6.4 Hz, 1H, H-1′), 4.81 (bs, 1H, H-3′), 4.93 (bs, 1H, H-3′); ^{13}C NMR ($CDCl_3$) δ 17.5 (q, CH_3), 22.1 (q, CH_3), 23.6 (q, CH_3), 24.6 (q, CH_3), 74.4 (d, C-1′), 78.6 (s, C-2), 111.1 (t, C-3′), 147.5 (s, C-2′), 176.5 (s, C-1). Anal. Calcd for $C_9H_{16}O_3$ (172.2): C, 62.98; H, 9.77. Found: C, 62.76; H, 9.37.

2-Methyl-2-[(2-methyl-2-(1,2-dimethyl-2-propenoxy)propanoyl)-oxy]propanoic acid (6c): IR ($CDCl_3$) 3400−2300, 2980, 2920, 1730, 1710, 1460, 1450, 1365, 1290, 1190, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (d, J = 6.2 Hz, 3H, CH_3-1″), 1.38 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.72 (bs, 3H, CH_3-2″), 3.98 (q, J = 6.2 Hz, 1H, H-1″), 4.73 (bs, 1H, H-3″), 4.89 (bs, 1H, H-3″); ^{13}C NMR ($CDCl_3$) δ 17.7 (q, CH_3), 23.9 (q, CH_3), 24.1 (q, CH_3), 24.3 (q, CH_3), 24.6 (q, CH_3), 26.6 (q, CH_3), 75.5 (d, C-1″), 75.6 (s), 78.5 (s), 109.9 (t, C-3″), 148.9 (s, C-2″), 174.3 (s, C-1′), 177.3 (s, C-1). Exact mass calcd for $C_{13}H_{22}O_5$ 258.1467, found 258.147.

1-Methyl-1-cyclohexene (2d). According to the general procedure, 48.0 μL (0.470 mmol) of alkene **2d** was added to 48.0 mg (0.470 mmol) of α-peroxy lactone **1** in 14.5 mL of CH_3CCl_3 at −20 °C. After 24 h, the reaction mixture was worked up as described, by collecting the distillate in a liquid nitrogen trap. The product composition of the distillate was determined by gas-chromatographic analysis, for which a 30-m, OV-1701 column (film thickness 0.25 μm, injector temperature 80 °C, detector temperature 180 °C, oven temperature 25 °C) was used. The epoxide **4d**, which was independently synthesized by epoxidation of the olefin **2d** with dimethyldioxirane, was identified by co-injection with an authentic sample. Kugelrohr distillation at 75−85 °C/0.2 Torr of the residue afforded 30.0 mg (30%) of the cycloadduct **3d** as a colorless oil. The distillation residue was further distilled (Kugelrohr) at 140 °C/0.4 Torr and the distillate purified by column chromatography (florisil) with diethyl ether as eluent. The ene product **5d** was washed from the column with methanol, which afforded 21.0 mg (7%) of **5d** as a white solid. The distillation residue was dissolved in 5.0 mL of dichloromethane and an excess of diazomethane solution in diethyl ether was added at 20 °C. After 5 min, the excess of diazomethane and the solvent were distilled at reduced pressure (20 °C/14 Torr) and the residue purified by column chromatography (SiO_2) with a 7:1 mixture of petroleum ether (30−50 °C) and diethyl ether to afford 3.0 mg (2%) of **6d′** as a colorless oil. The results are given in Table 1.

3,3,8a-Trimethyl-1,4-dioxabicyclo[4.4.0]decan-2-one (3d): IR ($CDCl_3$) 2970, 2930, 2850, 1710, 1295, 1210, 1190, 1170, 1095, 1085, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.35−2.0 (cs, 8H), 3.75 (bs, 1H, H-8a); ^{13}C NMR ($CDCl_3$) δ 19.0 (t), 22.9 (q, CH_3), 23.2 (t), 24.6 (q, CH_3), 27.6 (q, CH_3), 28.5 (t), 33.9 (t), 70.0 (d, C-4a), 75.3 (s, C-3), 84.1 (s, C-8a), 173.7 (s, C-2). Anal. Calcd for $C_{11}H_{18}O_3$ (198.3): C, 66.64; H, 9.16. Found: C, 66.38; H, 9.40.

2-Methyl-2-((2-methylenecyclohexyl)oxy)propanoic acid (5d): mp 42−44 °C; IR ($CDCl_3$) 3300, 2990, 2920, 2840, 1760, 1695, 1350, 1220, 1180, 1070, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.32−2.12 (m, 7H, cyclohexyl), 2.32−2.48 (m, 1H, H-3′), 3.96 (m, 1H, H-1′), 4.77 (bs, 1H, exomethylene), 4.88 (bs, 1H, exomethylene); ^{13}C NMR ($CDCl_3$) δ 23.6 (q, CH_3), 23.8 (t), 24.5 (t), 27.8 (q, CH_3), 33.7 (t), 36.1 (t), 75.2 (d, C-1′), 78.3 (s, C-2), 107.1 (t, exomethylene), 150.0 (s, C-2′), 177.9 (s, C-1). Exact mass calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.125.

Methyl 2-methyl-2-[(2-methyl-((2-methylenecyclohexyl)oxy)propanoyl)oxy]propanoate (6d′): IR ($CDCl_3$) 2960, 2910, 2830, 1720, 1650, 1435, 1365, 1355, 1280, 1185, 1165, 1115, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28−1.61 (cs, 3H), 1.40 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 1.61−2.12 (cs, 4H), 2.40 (m, 1H, H-3″), 3.72 (s, 3H, CH_3O), 3.76 (m, 1H, H-1″), 4.74 (bs, 1H, exomethylene), 4.94 (bs, 1H, exomethylene); ^{13}C NMR ($CDCl_3$) δ 24.3 (q, 2 × CH_3), 24.4 (t), 24.6 (q, CH_3), 26.3 (q, CH_3), 28.1 (t), 34.3 (t), 36.4 (t), 52.3 (q, CH_3O), 76.5 (d, C-1″), 78.3 (s), 78.5 (s), 106.3 (t, exomethylene), 150.7 (s, C-2″), 173.2 (s), 174.1 (s). Exact mass calcd for $C_{16}H_{26}O_5$ 298.1780, found 298.178.

2,3-Dimethyl-2-butene (2e) in 1,1,1-Trichloroethane. According to the general procedure, 169 μL (1.40 mmol) of alkene **2e** was added to 143 mg (1.40 mmol) of α-peroxy lactone **1** in 48 mL of CH_3CCl_3 at −20 °C. After 17 h, the reaction mixture was worked up as described, by collecting the distillate in a liquid nitrogen trap. The residue was dried at 80 °C/40 Torr to afford 102 mg (85%) of the oligoester **8**. A mass spectrum of **8** showed a M^+ peak of 759 (n = 8.8). The product composition of the distillate was determined by gas chromatography, for which a 30-m, OV-1701 column was used (film thickness 0.25 μm, injector temperature 170 °C, detector temperature 180 °C, oven temperature 25 °C). The epoxide **4e** was identified by co-injection with an authentic sample.[14] The results are given in Table 1.

2,3-Dimethyl-2-butene (2e) in Deuteriochloroform. According to the general procedure, ca. 10 μL (0.1 mmol) of alkene **2e** was allowed to react with 5.0 mg (0.050 mmol) of α-peroxy lactone **1** in 0.8 mL of $CDCl_3$ at −20 °C for 17 h. The ^1H NMR spectrum of the reaction mixture revealed the products epoxide **4e** and the oligomer **8**, which were identified spectrally by their characteristic signals, and the yields were determined by using HMDSO as internal standard. The results are given in Table 1.

1,2-Dimethylcyclohexene (2f). According to the general procedure, ca. 10 μL (0.1 mmol) of alkene **2f** was allowed to react with 5.0 mg (0.050 mmol) of α-peroxy lactone **1** in 0.8 mL of $CDCl_3$ at −20 °C for 17 h. The ^1H NMR spectrum revealed the products epoxide **4f** and the oligomer **8**, which were identified spectrally by their characteristic signals, and the yields were determined by using HMDSO as internal standard.

General Procedure for the Reaction of Dimethyl α-Peroxy Lactone (1) with Alkenes 2 in Methanol. Alkene **2** was added to an equimolar amount of dimethyl α-peroxy lactone (**1**) solution in a 1:1 mixture of CH_3CCl_3/CH_3OH or $CDCl_3/CD_3OD$ at −20 °C. The reaction was run at this temperature until a negative peroxide test (KI/AcOH) indicated complete consumption of **1**. At the preparative scale (reaction run in CH_3CCl_3/CH_3OH) the solvent was evaporated at 20 °C/20 Torr and the product mixture purified by column chromatography (silica gel) and/or distillation on a Kugelrohr apparatus.

(*Z*)-2-Butene ((*Z*)-2a) in a 1:1 Mixture of 1,1,1-Trichloroethane/Methanol. According to the general procedure, ca. 0.2 mL (2 mmol) of alkene (***Z*)-2a** was allowed to react with 117 mg (1.15 mmol) of α-peroxy lactone **1** in 40 mL of a 1:1 mixture of CH_3CCl_3/CH_3OH at −20 °C for 24 h. The reaction mixture was worked up as described and distilled on a Kugelrohr apparatus. After a first fraction (55−65 °C/1.0 Torr), 32.0 mg (43%) of trapping product **7a** was isolated at 95−105 °C/1.0 Torr as a colorless oil. Product **9** was identified in the ^1H NMR spectrum of the crude product mixture by its characteristic singlet at δ 3.32, while a second singlet at δ 3.41 was assigned to the second diastereomer of **7a**. The results are given in Table 1.

2-(2-Methoxy-1-methylpropoxy)-2-methylpropanoic acid (7a): IR ($CDCl_3$) 3500−2200, 2990, 2940, 1735, 1460, 1385, 1355, 1340, 1185, 1170, 1085 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (d, J = 6.0 Hz, 3H, CH_3), 1.16 (d, J = 6.0 Hz, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 3.25 (dq, J_d = 8.6 Hz, J_q = 6.2 Hz, 1H), 3.46 (dq, J_d = 8.6 Hz, J_q = 6.1 Hz, 1H), 3.47 (s, 3H, CH_3O); ^{13}C NMR ($CDCl_3$) δ 14.8 (q, CH_3), 19.3 (q, CH_3), 23.2 (q, CH_3), 28.7 (q, CH_3), 56.8 (q, CH_3O), 74.9 (d, C-3′), 79.5 (s, C-2), 81.6 (d, C-2′), 177.2 (s, C-1). Anal. Calcd for $C_9H_{18}O_4$ (190.2): C, 56.83; H, 9.52. Found: C, 56.61; H, 9.85.

(*Z*)-2-Butene ((*Z*)-2a) in a 1:1 Mixture of Deuteriochloroform/Deuteriomethanol. According to the general procedure, ca. 10 μL (0.1 mmol) of alkene (***Z*)-2a** was allowed to react with 5.0 mg (0.050 mmol) of α-peroxy lactone **1** in 1.0 mL of a 1:1 mixture of $CDCl_3/CD_3OD$ at −20 °C for 4 h. The ^1H NMR spectrum of the reaction mixture revealed the trapping product **7a**, which was identified spectrally by its characteristic signals, and the yield was determined by using HMDSO as internal standard. The results are given in Table 1.

(*E*)-2-Butene ((*Z*)-2a) in a 1:1 Mixture of 1,1,1-Trichloroethane/Methanol. According to the general procedure, ca. 0.1 mL (1 mmol) of alkene (***E*)-2a** was allowed to react with 40.0 mg (0.390 mmol) of α-peroxy lactone **1** in 28 mL of a 1:1 mixture of CH_3CCl_3/CH_3OH at

(14) Eliel, E.; Rerick, M. *J. Am. Chem. Soc.* **1960**, *82*, 1362−1367.

−20 °C for 24 h. The reaction mixture was worked up as described and the diastereomers of the trapping product **7a** and product **9** were identified by their characteristic signals in the ^{1}H NMR spectrum of the crude product mixture. The results are given in Table 1.

(*E*)-2-Butene ((*E*)-2a) in a 1:1 Mixture of Deuteriochloroform/Deuteriomethanol. According to the general procedure, ca. 10 μL (0.1 mmol) of alkene (***E*)-2a** was allowed to react with 5.0 mg (0.050 mmol) of α-peroxy lactone **1** in 1.0 mL of a 1:1 mixture of $CDCl_3$/CD_3OD at −20 °C for 4 h. The ^{1}H NMR spectrum of the reaction mixture revealed the trapping product **7a**, the epoxide **4a**, and the α-methoxy acid **9**, which were identified spectrally by their characteristic signals, and the yield was determined by using HMDSO as internal standard. The results are given in Table 1.

2,3-Dimethyl-2-butene (2e) in a 1:1 Mixture of 1,1,1-Trichloroethane/Methanol. According to the general procedure, 85 μL (0.71 mmol) of alkene **2e** was allowed to react with 73.0 mg (0.710 mmol) of α-peroxy lactone **1** in 54 mL of a 1:1 mixture of CH_3CCl_3/CH_3OH at −20 °C for 15 h. The reaction mixture was worked up as described and Kugelrohr distillation at 40 °C/0.2 Torr afforded 9.0 mg (11%) of product **9**, and at 60 °C/0.2 Torr 24.0 mg (15%) of the trapping product **7e** was isolated. The results are given in Table 1.

2-(2-Methoxy-1,1,2-trimethylpropoxy)-2-methylpropanoic acid (7e): IR ($CDCl_3$) 3500−2600, 2980, 2910, 1740, 1460, 1430, 1370, 1360, 1345, 1150, 1130, 1065; ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 6H, CH_3), 1.28 (s, 6H, CH_3), 1.50 (s, 6H, CH_3), 3.31 (s, 3H, CH_3O); ^{13}C NMR ($CDCl_3$) δ 18.7 (q, CH_3), 22.2 (br q, CH_3), 27.7 (br q, CH_3), 49.4 (q, CH_3O), 76.5 (s), 81.9 (s), 82.1 (s), 179.0 (s, C-1). Anal. Calcd for $C_{11}H_{22}O_4$ (218.2): C, 60.52; H, 10.16. Found: C, 60.27; H, 10.31.

2,3-Dimethyl-2-butene (2e) in a 1:1 Mixture of Deuteriochloroform/Deuteriomethanol. According to the general procedure, ca. 10 μL (0.1 mmol) of alkene **2e** was allowed to react with 5.0 mg (0.050 mmol) of α-peroxy lactone **1** in 1.0 mL of a 1:1 mixture of $CDCl_3$/CD_3OD at −20 °C for 4 h. The ^{1}H NMR spectrum of the reaction mixture revealed the trapping product **7e**, the epoxide **4e**, and the α-methoxy acid **9**, which were identified spectrally by their characteristic signals, and the yield was determined by using HMDSO as internal standard. The results are given in Table 1.

General Procedure for the Saponification of Ester 6. A sample of ester **6** was dissolved in 5.0 mL of a 0.1 N methanolic potassium hydroxide solution and agitated for 5 days. The solvent was distilled at reduced pressure (20 °C/14 Torr) and the residue dissolved in 10 mL of water. The water phase was acidifed with 10% aqueous HCl and extracted. The organic phase was dried over $MgSO_4$, the latter removed by filtration, and the solvent distilled at reduced pressure (20 °C/14 Torr).

Saponification of 2-Methyl-2-[(2-methyl-2-(1,2-dimethyl-2-propenoxy)propanoyl)oxy]propanoic Acid (6c). Approximately 2 mg (0.01 mmol) of the ene product **6c** yielded after saponification according to the general procedure and extraction of the acidified aqueous layer with 25 mL of diethyl ether approximately 1 mg (75%) of ene product **5c**, as confirmed by ^{1}H NMR spectroscopy.

Saponification of Methyl 2-Methyl-2-[(2-methyl-((2-methylenecyclohexyl)oxy)propanoyl)oxy]propanoate (6d′). A sample of 14 mg (0.047 mmol) of the ene product **6d′** afforded after saponification according to the general procedure and extraction of the acid aqueous layer with 25 mL of ethyl acetate 8 mg (54%) of a mixture (ca. 1:1) of ene product **5d** and α-hydroxyisobutyric acid (0.025 mmol), as confirmed by ^{1}H NMR spectroscopy.

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