EPOXIDATION BY DIMETHYLDIOXIRANE: KINETICS FOR *cis*-ALKENES

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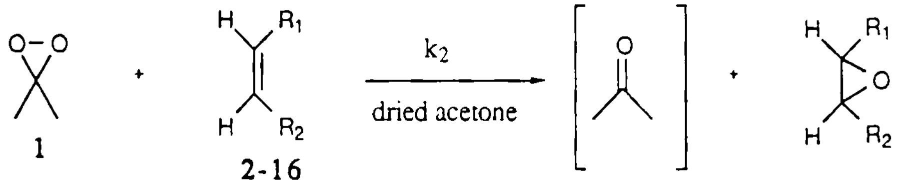
Abstract. Kinetic data for epoxidation of a series of *cis*-alkenes and cycloalkenes by dimethyldioxirane in dried acetone are reported; the results are consistent with a concerted, electrophilic process with a spiro-transition state.

Introduction

Dioxiranes, powerful, new oxidants, have been employed to carry out synthetically useful transformations, efficiently transferring oxygen atoms to a wide variety of organic substrates.[1] In particular, dimethyldioxirane (1) has been shown to be an important and versatile oxidizing agent.[1] The epoxidation of double bonds has been a major area of application of dimethyldioxirane methodology. A wide range of alkenes have been effectively converted to epoxides by **1**. The epoxidation of double bonds by **1** is stereospecific and quantitative for most compounds. Previous studies have shown that the reaction is electrophilic and that increased alkyl substitution on the double bond enhances reactivity.[2] The relative reactivity of *cis*/*trans* alkenes has been interpreted in terms of a "spiro" transition state[2d] for the concerted oxygen-atom transfer process. We report here the results of a study of the epoxidation of a series of cis-alkenes and cycloalkenes by dimethyldioxirane in dried acetone.

Results and Discussion

Kinetic studies of the epoxidation of a series of *cis*-alkenes (**2-7**) and cycloalkenes (**8-16**) by dimethyldioxirane[3,4] (**1**) in dried acetone were carried out employing UV techniques at 23 °C (rxn 1). The oxygen-atom transfer reactions were



shown to be of the first order in both dioxirane and alkene. Pseudo first order conditions with 1:10 and [illegible] alkene/dioxirane ratios gave essentially identical k_2 values for epoxidation of the various *cis*-alkenes. The kinetic data are summarized in Table 1. Product studies showed the stereospecific formation of the corresponding epoxide as the sole

Table 1. Second Order Rate Constants for the Epoxidation of cis-Alkenes and Cycloalkenes by Dimethyldioxirane in Dried Acetone at 23°C.

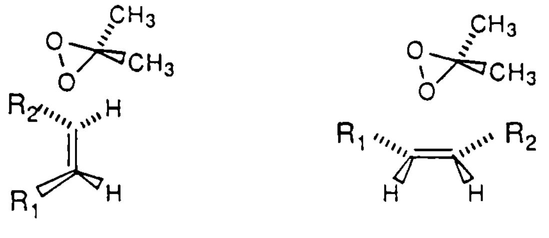
Entry	Alkene	k_2 $M^{-1}s^{-1}$	Rel. React.	k_{rel}(exp)^{c}	k_{rel} (calc)^{c,d}
2	*cis*-2-Pentene	0.46 ± 0.04	0.94	≡1.00	≡1.00
3	*cis*-3-Hexene	0.46 ± 0.03 (0.47 ± 0.03)^{a}	0.94	1.00	1.00
4	*cis*-2-Methyl-3-hexene	0.46 ± 0.01	0.94	1.00	0.89
5	*cis*-2,2-Dimethyl-3-hexene	0.26 ± 0.02	0.53	0.56	0.70
6	*cis*-2,5-Dimethyl-3-hexene	(0.39 ± 0.02)^{a}	0.80	0.85	0.68
7	*cis*-4,4-Dimethyl-2-Pentene	(0.33 ± 0.02)^{a}	0.67	0.72	0.47
8	Cyclopentene	0.49 ± 0.03	≡1.00	≡1.00	≡1.00
9	Cyclohexene	0.48 ± 0.02 (0.48 ± 0.03)^{a}	0.98	0.98	0.87
10	Cycloheptene	0.45 ± 0.02	0.92	0.92	0.70
11	Cyclooctene	0.43 ± 0.03	0.88	0.88	-
12	3,3,5,5-Tetramethylcyclopentene	0.20 ± 0.01	0.41	0.41	0.36
13	1,4-Cyclohexadiene	0.48 ± 0.02^{b}	0.98	0.98	0.81
14	4-Methylcyclohexene	0.35 ± 0.01	0.71	0.71	0.85
15	Bicyclo[2.2.1]hept-2-ene	0.33 ± 0.02	0.67	≡1.00	≡1.00^{e}
16	Bicyclo[2.2.2]oct-2-ene	0.047 ± 0.005	0.096	0.14	0.16

a) Ref. 4; b) k_2 for mono epoxidation; c) normalized for each series; d) calculated using AM1 approach; e) exo

product (quantitative yield) for all cases. The epoxides were isolated and the structures proven by comparison of spectral properties with those of authentic samples. For the cis-alkene series, compounds **2-4** showed similar relative reactivity; however, compounds **5-7** showed decreased relative reactivity presumably due to the presence of larger alkyl groups. The k_2 values for the epoxidation of the cycloalkene series **8-11** in dried acetone were found to be roughly identical, although there appears to be a slight dependence (decrease) on increasing ring size. The relative reactivities of compounds **12**, **14-16** were lower than those of the 5- and 6-ring parent compounds **8** and **9**. Compounds **8-9** and **13** minimize steric interactions to approach to the the double bond and yield k_2 values that are slightly larger than those of simple cis-alkenes **2-4**. The tetrasubstituted cyclopentene (**12**) showed a lower k_2 value (~2.5 fold) than that for the unsubstituted cyclopentene (**8**), presumably due to steric interactions from the presence of the four methyl groups. The bicyclic compounds (**15**,**16**) showed the largest difference in relative reactivity, with the k_2 for **15** ~7-fold faster than that for **16**.

Although there are potential liabilities in the application of semiempirical methods to calculation of activation energies, the considerable time savings relative to those of the *ab initio* approach[5] prompted an assessment. Semiempirical calculations (AM1)[6] were applied to the reaction of the alkenes and dimethyldioxirane. In all cases, a viable transition state was located only for the spiro approach (Scheme 1) in agreement with experimental data[2b,d, 4] and *ab initio* calculations.[5]. Setting the geometry initially to a planar (butterfly) approach was found to be unacceptable, resulting in reorganization to that of spiro approach. No structures meeting transition state requirements could be found for the butterfly arrangement even when dihedral angles or atomic positions were constrained. Transition state calculations were performed for two unique directions of approach (when demanded by alkene geometry). The approach shown in Scheme 1 for the spiro geometry was determined to be optimum.

Scheme 1



spiro

Butterfly (planar)

After determining that AM1-level calculations yielded reasonable results for transition state geometry, the origin of the observed rate differences was explored. Evaluation of the ground state geometries of the alkenes did not show any trends. Rate constants were calculated for each epoxidation based on the calculated difference between energies of the spiro transition state and the most stable alkene conformer or as weighted average of several conformers.[7] The calculated k_2 values were normalized for each group of alkenes to yield k_{rel} (calc) values (Table 1). These values show reasonable agreement with the experimental values of k_{rel} despite the obvious pitfalls associated with rationalization of small rate differences. Systems in which there are several conformations available yielded calculated k_{rel} values that showed larger deviations. However, despite this difficulty the trends in the calculated values parallel those shown in the experimental data. The values showed very good agreement for rigid systems (compare **15** and **16** or less flexible systems (compare **8** and **12**). The lower reactivity of alkenes **12** and **16** appears to be due to steric interactions of the lone pairs on the "top" oxygen atom on **1** and the methyl groups for **12** and the bridge positions 6 and 7 for 16.

Previous experimental data attributed[2,4] the lower reactivity of *trans* vs *cis*-alkenes to steric effects of the substituents on the alkene with a methyl group of the dioxirane resulting in the postulation of the spiro transition state mechanism.[2d] The present study clearly shows they are steric interactions of the substituents of *cis*-alkenes with the oxygen lone-pairs of the dioxirane. For simple acyclic *cis*-alkenes, the data show essentially no effect on k_2 values until the steric bulk of the substituents reaches a threshold. After that point, there seems to be a steady decrease in k_2 values. For cyclopentene, steric interactions are at a minimum, resulting in the largest value of k_2. As the cycloalkenes become more flexible (more conformers) steric interactions are increased. This is reflected in a small but consistent decrease in experimental k_2 values. AM1-type calculations are of value to estimate relative reactivity for epoxidation by dimethyldioxirane.

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(6) Calculations were performed on a Silicon Graphics Indigo 2 workstation using Spartan version 3.1 (Wavefunction, Inc.). Transition state determination was judged successful when the calculated structure possessed a single imaginary frequency that when animated illustrated that it was on the reaction coordinate.

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