EPOXIDATION OF α,β-UNSATURATED ESTERS BY DIMETHYLDIOXIRANE

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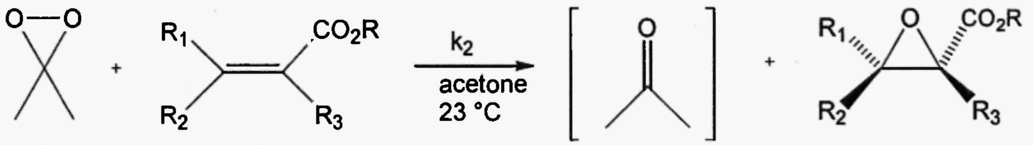
Abstract. Kinetic data for the epoxidation of a series of α,β-unsaturated esters, **2-10**, by dimethyldioxirane in dried acetone are reported. These epoxidations are less sensitive to steric effects and occur with lower k_2 values than those for simple alkenes. Relative reactivity could be modeled based on a spiro transition state mechanism. The density function calculations were in good agreement with the k_{rel} values except for those compounds with cis-β-substituents.

Introduction

Dimethyldioxirane (**1**) has been shown to be a powerful, selective oxygen atom transfer reagent for a wide variety of substrates.[1] The oxidations by **1** can readily be performed, *in situ*[2] or with isolated solutions[3] in acetone. Epoxidation by **1** normally is quantitative, stereospecific and occurs via an electrophilic process.[1] Epoxidation by **1** is strongly affected by steric factors and is generally accepted to proceed via a concerted "spiro" transition state mechanism.[4] Structural influences on epoxidation have been investigated extensively[5] for alkenes but limited data are available on α,β-unsaturated systems.[6] We report here the results of a kinetics study of the epoxidation of a series of α,β-unsaturated esters (**2-10**) by dimethyldioxirane in dried acetone.

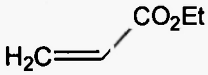
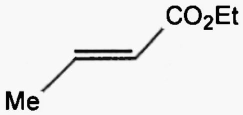
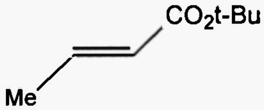
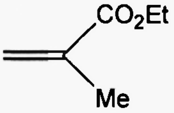
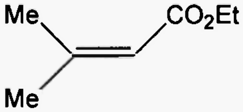
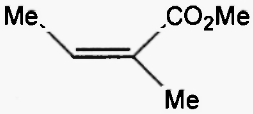
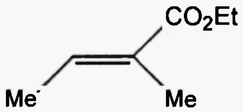
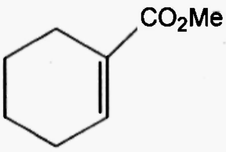
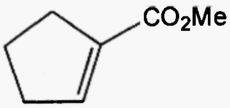
Results and Discussion

The reaction of dimethyldioxirane **1** with a series of α,β-unsaturated esters (**2** R_1=R_2=R_3=H, R=Et; **3** R_1=R_3=H, R_2=Me, R=Et; **4** R_1=R_3=H, R_2=Me, R=t-Bu; **5** R_1=R_2=H, R_3=Me, R=Et; **6** R_1=R_2=Me, R_3=H, R=Et; **7** R_1=R_3=Me, R_2=H, R=Me; **8** R_1=H, R_2=R_3=Me, R=Et; **9** R_1=H, R_2R_3=$(CH_2)_4$, R=Me; **10** R_1=H, R_2R_3=$(CH_2)_3$, R=Me) produced the corresponding epoxidations in essentially quantitative yields (rxn 1). The epoxides were isolated and characterized by comparison of spectral data with literature values[7] when available and with those of authentic samples. Kinetic studies were carried out by UV techniques in dried acetone at 23 °C. As expected, the stereospecific reactions were found to be of the first order with respect to both dioxirane and α,β-unsaturated ester. The k_2 values determined under pseudo first order conditions with 10:1 or 1:10 dioxirane to substrate ratios[8] were within experimental error of one another. The kinetics results are listed in Table 1.



1
2-10
(1)

Table 1. Second Order Rate Constants for the Epoxidation of α,β-Unsaturated Esters **2-10** by **1** in Dried Acetone at 23 °C

Cmp #	Structure	$k_2 (M^{-1}s^{-1})$	k_{rel}[a]	k_{calc}[b]
2		1.7×10^{-4}	≡1.0	≡1.0
3		3.5×10^{-4}[c]	2.1	1.5
4		2.7×10^{-4}	1.6	--
5		2.35×10^{-3}[c]	14	13
6		1.6×10^{-3}	9.4	NA
7		2.0×10^{-3}	12	NA
8		9.6×10^{-3}	57	43
9		6.7×10^{-3}	39 (≡1.0[d])	NA (≡1.0[d])
10		1.5×10^{-2}	88 (2.2[d])	NA (2.4[d])

a) Relative reactivity to that of **2**; b) Predicted relative rate constants from density function method relative to that of **2**; all calculations were done as methyl esters; c) The k_2 values for the methyl esters of **3** (3.9×10^{-4}) and **5** (2.3×10^{-3}) have been previously reported[6b] but were erroneously switched; d) Relative reactivity vs. **9**.

The kinetic data for α,β-unsaturated esters **2-10** showed the compounds to be several hundred times less reactive than similarly substituted simple alkenes. This is as expected due to the lower electron density of the carbon-carbon double bond. The effect of the R group on reactivity of the ester appeared to be minimal; the k_2 values seemed to decrease for compounds with bulkier R groups. Furthermore, these epoxidations were much less sensitive to increased substitution on the double bond and to steric effects than those for simple alkenes. For these α,β-unsaturated systems, formal addition of a β-alkyl substituent increased reactivity by only a factor of 2 to 4 while that for an α-alkyl group was larger. Unexpectedly, the presence of a cis-β-methyl substituent seemed to reduce reactivity. Compound **10** was roughly two-fold more reactive than **9**, which is slightly larger than the trend observed for simple cycloalkenes.[9] The results for **3** and **5** are in agreement with the reported results for the corresponding methyl esters[6b], noting that the previous values were erroneously switched. In addition the reported k_2 value[6b] for α-methylene y-lactone (2.0 x 10^{-3} $M^{-1}s^{-1}$) is quite similar to that for **5**.

The relative reactivities for these α,β-unsaturated esters were modeled by the density function (6-31G* basis set, Spartan '04) approach. Each structure was constrained to both an s-cis and an s-trans conformation and minimized (as a methyl ester). Transition state calculations were carried out. Regardless of the starting geometry, all cases yielded a spiro transition state after optimization. The calculations were carried out from both spiro geometries on each conformation of each compound. All the transition state calculations yielded a single imaginary frequency corresponding to the local minimum in energy along the reaction coordinate (see Fig. 1). Animation of the imaginary frequency (motion) correlated with the breaking and making of the appropriate bonds leading to the formation of the products. The differences in energies from the spiro transition state with the least steric hindrance (lowest) from that of the ground state energies of the esters and that of **1** were used to determine energies of activation. The calculated activation energies were used to predict relative reactivities (k_{calc} in Table 1).

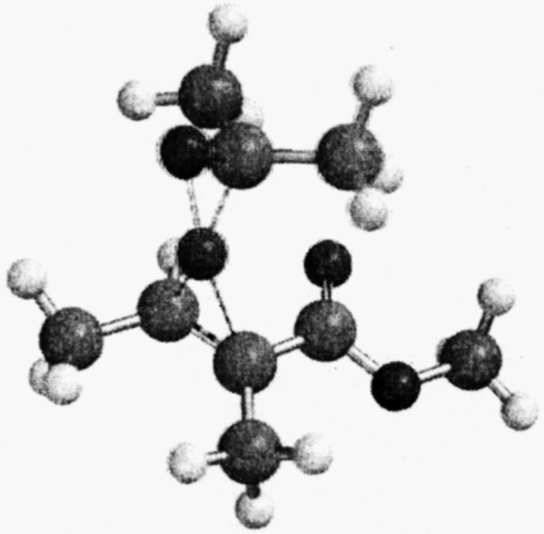


Figure 1. Optimized transition-state for the epoxidation of **8** by **1** showing spiro approach from least hindered side.

As expected, calculations based on a semi-empirical (AM-1) approach did not correlate for this series of compounds. Density function calculations, on the other hand, yielded reasonable relative reactivities (k_{calc} in Table 1) for all the compounds except **6** and **7**. It is unclear as to why the model did not work for the compounds with the cis-β-methyl groups. Previous studies on epoxidation of simple alkenes have shown that the reaction can be modeled based on a spiro transition state by AM-1 and density function methods. Calculational studies on epoxidation of α,β-unsaturated ketones[6b] by dimethyldioxirane found that AM-1 results did not correlate while those from density function approach were predictive in agreement with the current study.

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(8) Substrates were commercially available. Product studies were carried out with a three-fold excess of dioxirane. For convenience, 10:1 substrate to dioxirane ratios were normally employed for the kinetic studies since the substrate concentration could be readily calculated.

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