THE REACTION OF ALKYL BENZYL ETHERS WITH DIMETHYLDIOXIRANE: KINETICS

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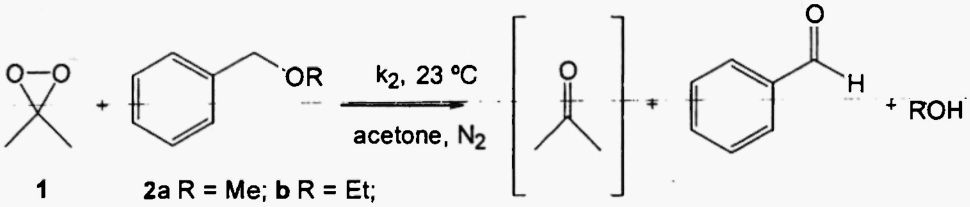
Abstract. The oxidation of a series of alkyl benzyl ethers, **2a-e**, by dimethyldioxirane, **1** (in excess), in dried acetone at 23 °C (under N_2) produced benzaldehyde and the corresponding alcohols in excellent yields. The reaction was found to be of the second order, yielding k_2 values on the order of 10^{-2} M^{-1} s^{-1}. A decrease in the k_2 values was observed with increased alkyl group size yielding a Taft ρ^* value of 0.98.

Introduction

Dimethyldioxirane (**1**) is a versatile reagent which can transfer oxygen-atoms rapidly and efficiently under mild conditions.[1] For example, dimethyldioxirane has been employed for the conversion of alkenes and related compounds to epoxides[2] and for heteroatom oxidations to the corresponding oxides.[3] Furthermore, oxidation by dimethyldioxirane generally produces high product yields with few side products. The C-H oxidation (oxygen-atom insertion reaction) of unactivated hydrocarbons by dioxiranes is of special interest.[4] Dimethyldioxirane is generally too unreactive for practical unactivated C-H oxygen-atom insertion reactions and most studies have employed the more reactive trifluoromethyl analog.[5] However, more reactive substrates do undergo formal C-H oxygen-atom insertion reactions with dimethyldioxirane. For example, the oxidations of substituted benzaldehydes,[6] secondary alcohols and ethers[7] by dimethyldioxirane have been reported. The mechanism of C-H oxygen-atom insertion reactions by dioxiranes continues to be a topic of research interest. Previous studies of the reaction of ethers with dimethyldioxirane have focused on systems that yielded ketones and alcohols as the primary products.[7] The use of dimethyldioxirane as a debenzylation reagent has been reported.[8] A recent, extensive study of the oxidation of ethers, in general, by dimethyldioxirane has explored structural and steric effects.[9] Herein, we report a kinetic and product study of the oxidation of a series of alkyl benzyl ethers by dimethyldioxirane in dried acetone and under nitrogen.

Results and Discussion

The oxidation of a series of alkyl benzyl ethers (**2a-e**) by dimethyldioxirane (**1**) in 5-fold excess and under N_2 atmosphere yielded benzaldehyde (and the corresponding alkyl alcohols) in excellent yields (Reaction 1). Substantial reductions in the yields of benzaldehyde were observed if reaction 1 was carried



(1)

1

2a R = Me; **b** R = Et;
c R = *n*-Pr; **d** R = *i*-Pr;
e R = *t*-Bu

out open to the atmosphere, with concomitant production of benzoic acid.[10] Progress of reaction 1 was monitored by GC/MS, with complete consumption of the substrate normally occurring within 2-4 hours. Under N_2, only trace amounts of benzoic acid were detected. Upon completion and quenching of the excess **1**, the isolated yields of benzaldehyde were 85-88%. The alcohol products were confirmed by GC analysis and were not isolated. Little or no benzyl alcohol was noted[11] as a product, indicating that oxygen-atom insertion was occurring at the benzyl position on the ethers even when the R group was *i*-Pr.

Kinetic studies for the oxidation of **2a-e** by **1** were carried out in acetone at 23 °C by UV techniques. A kinetic study of the reaction of benzaldehyde (**3**) and **1** under argon was performed as a control experiment For all the kinetic experiments, excellent linear correlations (≥0.99) were obtained under pseudo-first order conditions with the dioxirane in at least 10-fold excess. Reproducibility between duplicate runs was excellent, generally between 2-3%. The k_2 values for **2a**-e were of the order of 10^{-2} $M^{-1}s^{-1}$ and varied by only a factor of 2 with variation of the R groups. Surprisingly, the k_2 value for **2a** was substantially greater (roughly an order of magnitude) than those reported[7a] in the literature for 1-methoxy-1-phenylethane. The k_2 values of **2a-e** are generally one or two orders of magnitude greater than those reported[9] for the oxidation of aliphatic ethers by dimethyldioxirane. The reaction of **3** with **1** yielded a k_2 value of 1.1×10^{-4} $M^{-1}s^{-1}$. This shows that the direct secondary oxidation under N_2 by **1** is at least two orders of magnitude slower than that of the ether oxidation by **1**.[10] Thus, the formation of benzoic acid noted when rxn. 1 was carried out in the presence of oxygen can not be due to direct reaction and is most likely due to secondary, free-radical competing chain processes. The results are summarized in Table 1.

Table-1: Second order rate constants (k_2) for oxidation of ethers **2a**-e and benzaldehyde **3** by dimethyldioxirane in dried acetone at 23 °C.

Entry	Compound	k_2 ($M^{-1}s^{-1}$)	Relative reactivity
2a	benzyl methyl ether	$1.85 \pm 0.02 \times 10^{-2}$	1.00
2b	benzyl ethyl ether	$1.50 \pm 0.02 \times 10^{-2}$	0.81
2c	benzyl *n*-propyl ether	$1.38 \pm 0.02 \times 10^{-2}$	0.75
2d	benzyl *i*-propyl ether	$1.19 \pm 0.02 \times 10^{-2}$	0.64
2e	benzyl *t*-butyl ether	$9.45 \pm 0.05 \times 10^{-3}$	0.51
3	benzaldehyde*	$1.1 \pm 0.1 \times 10^{-4}$	0.006

*under N_2

The data show that only one process is leading to the aldehyde product when the reaction is carried out under nitrogen; either a direct insertion or a radical cage abstraction mechanism. Dimethyldioxirane is relatively stable at 23 °C but does undergo decomposition leading to radical products after a lag period. In the presence of oxygen, free radical chain oxidations can occur and other oxidizing species can be formed due to dioxirane decomposition. An earlier study of benzaldehyde oxidation by **1** noted[6] marked increases in side product formation in the presence of oxygen. For relatively unreactive substrates like ethers, free-radical chain (indirect) competing reactions, due to dioxirane decomposition, can be the major route under certain conditions. This type of crossover has led to mechanistic confusion and often conflicting mechanistic explanations.

An excellent linear relationship (r = 0.998) was obtained for the plot of log k_2 vs. Taft σ^* yielding a Taft ρ^* value of 0.98 ± 0.01 for compounds **2a-2e** (Figure 1). The Taft ρ^* value obtained for variation of the alkyl group in series **2a-e** is smaller than that of 1.7[7b] obtained for the reaction of **1** with a series of secondary alcohols with variation of the alkyl group directly attached to a benzylic position and that of 3.2 for the analogous methyl ether series.[7b] The lower sensitivity observed in the present case appears to be due to the greater distance of the size variation of the alkyl groups from the benzylic hydrogen atoms.

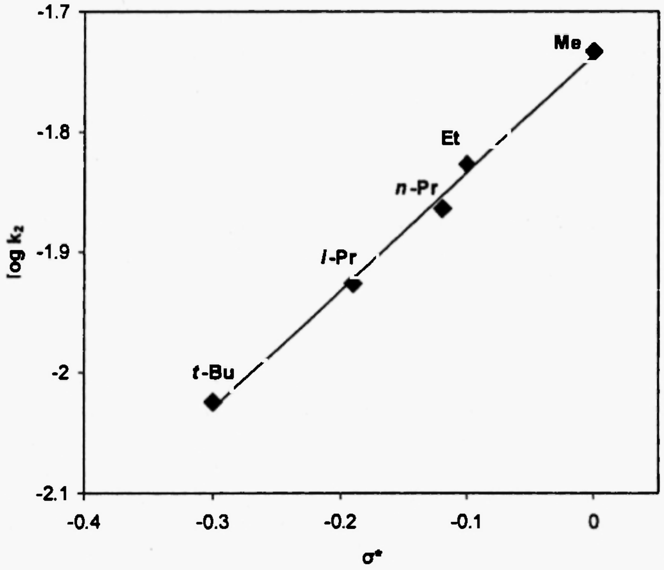
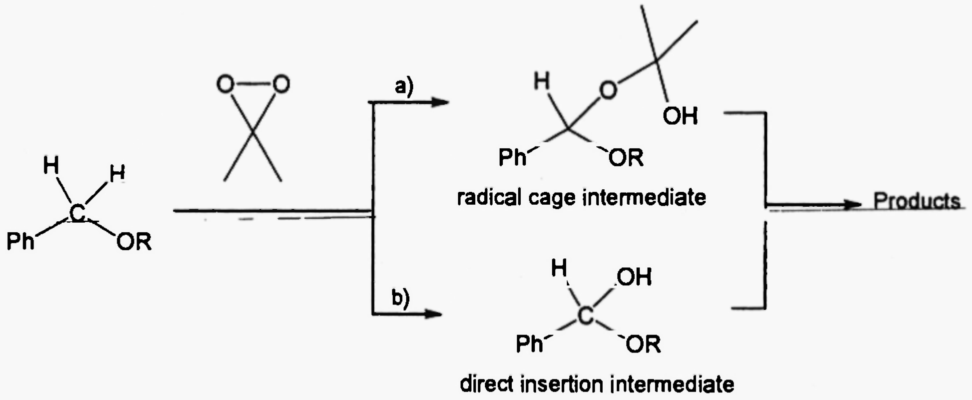


Figure-1: A plot of log k_2 values vs. Taft σ^* constants for the reaction of alkyl benzyl ethers (**2a-e**) with dimethyldioxirane (**1**).

The C-H insertion reactions by **1** have often been interpreted as either a direct insertion process or a radical cage process to give hemiacetal intermediates[7,9,11] (see Scheme 1). For hydrocarbon oxygen atom insertion most studies[1] favor the direct insertion mechanism. Our studies[7a,b,c,e] on secondary alcohol and ether oxidation by **1** have been interpreted to favor the radical cage process. A recent study[9] of aliphatic ether oxidation by **1** favored direct insertion and suggested competition from radical processes for ethers



Scheme-1: Intermediates for the two mechanistic extremes: a) radical cage and b) C-H insertion for direct oxidation of alkyl benzyl ethers by dimethyldioxirane.

with electron withdrawing groups. Given the relatively subtle differences between the two postulated extreme mechanisms, regardless of which process one favors, the other cannot be ruled out. It is likely that the mechanistic debate will continue unresolved until one can effectively explain all the data rather than only a selected set.

In conclusion, the results show the reactivity at the benzyl position of ethers is comparable to that of secondary alcohols and substantially greater than those of most ethers.[7,9] The reactivity decreases with increase in steric size of the other group (R) on the ether. The inherent reactivity at the benzyl position of ethers by **1** does not appear to be sufficient for efficient, selective debenzylation of protected oxygenated positions.

Acknowledgment

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10. The yield of benzoic acid obtained by reaction 1 carried out in the presence of oxygen was higher for the less reactive ethers, approaching 40% for the reaction with 2e
11. Preliminary results indicate that the k_2 value for the oxidation of benzyl alcohol by **1** is ~$1x10^{-2}$ $m^{-1}s^{-1}$ Thus, if formed, benzyl alcohol would be detectable before competitive oxidation since the concentration would be low, especially under conditions where substantial amounts of the ethers are still present.

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