Pergamon

Tetrahedron Letters 39 (1998) 1095–1098

TETRAHEDRON
LETTERS

Mechanisms for the Oxidation of *para*-Substituted Benzyl Alcohols and Benzyl Ethers by Permanganate

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Received 29 September 1997; accepted 25 November 1997

Key Words: oxidation, permanganate, benzyl alcohol, benzyl methyl ether, benzaldehyde, methyl benzoate

Abstract: Permanganate, solubilized in methylene chloride with the aid of a phase transfer agent, oxidizes benzyl alcohol to benzaldehyde and benzyl ethers to benzoate esters. Although the rate of oxidation of the ether is about an order of magnitude slower than alcohol oxidation, both respond in an identical way to the unique effects caused by introduction of substituents into the ring. In addition, primary kinetic isotope effects are observed for both reactions. Because of these similarities, it is proposed that benzyl alcohols and benzyl ethers are oxidized by similar mechanisms, the difference in rate being ascribed to steric effects.

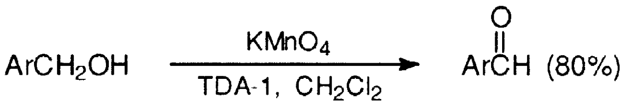
The mechanism of the reaction between alcohols and permanganate is of considerable interest, partly because of the synthetic value of this reaction[1] and partly because of the recent interest in the mechanism by which permanganate cleaves carbon-hydrogen bonds[2]. In particular, it is of interest to determine if the reaction is initiated by O-H or C-H cleavage, as has been done for other oxidants such as chromic acid. In the latter case Westheimer[3] has shown that the rate of oxidation of 2-propanol is about 1500 times greater than the oxidation of diisopropyl ether. From this he concluded that the initial reaction between the alcohol and the oxidant required participation of the O-H bond; *i.e.*, chromate ester formation. A great deal of subsequent research has proven to be consistent with this view.[4]

Oxidants, such as ruthenium tetroxide, which react with alcohols and ethers at comparable rates are assumed to proceed by initial cleavage of the α-C-H bond without prior involvement of the hydroxyl group.[5] Since the α-hydrogens in alcohols and ethers are electronically similar (each is attached to a carbon atom that is attached to an oxygen and other carbons or hydrogens), it is expected that they would react at similar rates with oxidants whose mode of reaction is C-H cleavage.

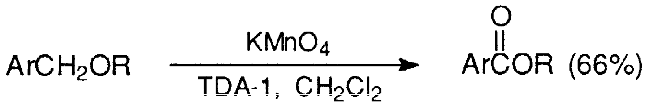
The only similar study of permanganate oxidations was limited to the use of water soluble compounds; Littler[6] reported that permanganate in 1 *M* H_2SO_4 reacts with isopropyl alcohol at a rate that is only 1.3 times greater than its rate of reaction with diisopropyl ether. With the assistance of phase transfer agents it is now possible to compare the rates of oxidation of a much wider range of alcohols and ethers. In the work that is reported here, solutions of permanganate in dichloromethane were prepared with the aid of the phase transfer

PII: S0040-4039(97)10788-2

agent, tris[2-methoxyethoxy)ethyl]amine, TDA-1, as described in the literature[7], and used to compare the rates of oxidation of substituted benzyl alcohols and the corresponding benzyl methyl ethers. The products of these reactions are substituted benzaldehydes and the corresponding benzoate esters as in Equations 1 and 2.



$$ArCH_2OH \xrightarrow[\text{TDA-1, } CH_2Cl_2]{KMnO_4} ArCH(=O) \ (80\%) \qquad (1)$$



$$ArCH_2OR \xrightarrow[\text{TDA-1, } CH_2Cl_2]{KMnO_4} ArC(=O)OR \ (66\%) \qquad (2)$$

Initial rates were determined by monitoring the decrease in absorbance at 528 nm while the reactions proceeded in cuvettes thermostated in the cell compartment of a Hewlett-Packard 8450A diode array spectrophotometer. Each rate constant was determined in at least triplicate; the results are summarized in Table 1.

Table 1. Rate Constants for the Oxidation of Substituted Benzyl Alcohols and Benzyl Methyl Ethers by Permanganate in Dichloromethane Solutions.

Alcohol	**k_2 (Ms^{-1} x 10^3)**	**Ether**	**k_2 (Ms^{-1} x 10^3)**
Benzyl	6.45 ± 0.63	Benzyl methyl	4.87 ± 0.46
4-Methylbenzyl	11.8 ± 0.8	4-Methylbenzyl methyl	7.42 ± 0.30
4-Methoxybenzyl	90.7 ± 5.1	4-Methoxybenzyl methyl	34.7 ± 1.6
4-Fluorobenzyl	38.4 ± 3.0	4-Fluorobenzyl methyl	23.1 ± 2.2
4-Nitrobenzyl	159 ± 8	4-Nitrobenzyl methyl	54.0 ± 6.0
α,α-d_2 Benzyl	0.53 ± 0.14	α,α-d_2 Benzyl methyl	0.90 ± 0.23
	(k_H/k_D = 12)		(k_H/k_D = 5.4)

The rate constants do not correlate well with any single set of published Hammett-type substituent constants. Despite the unique substituent effects demonstrated by the data in Table 1, the rate constants for ether oxidation correlate very well with those for alcohol oxidation, leading to the conclusion that the mechanisms must be similar. The slope of the plot in Figure 1 (0.74 ± 0.02) indicates that the rate constants for ether oxidations are slightly less sensitive to substituent effects. Both reactions also exhibit a primary kinetic isotope effect, although not of equal magnitude.

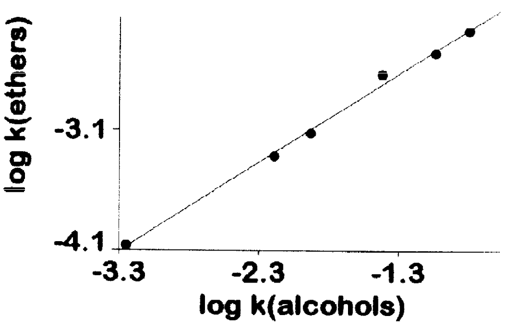
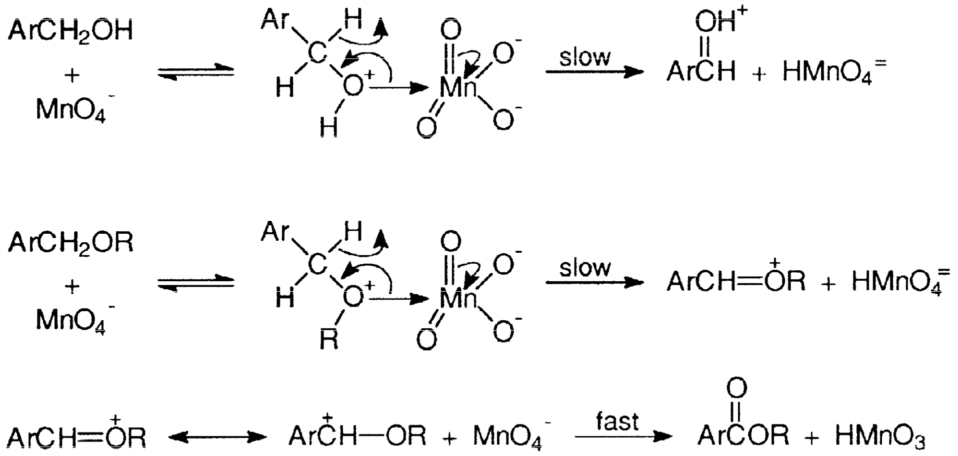


Figure 1. Correlation of the rate constants for the oxidation of alcohols and ethers. Slope = 0.74 ± 0.02, r = 0.998

The good correlation observed in Figure 1 indicates that the transition states for both alcohol and ether oxidation are likely very similar. The somewhat decreased reaction rates and the lower sensitivity to substituent effects demonstrated by ether oxidations suggests a somewhat looser transition state, which may be related to the greater steric effects expected for ethers. The lower isotope effect observed for ether oxidation is also consistent with a less symmetric transition state.[8]

A likely mechanism consistent with these results is one guided by a consideration of frontier molecular orbital theory. According to this approach the reaction would be initiated by an interaction of the highest occupied molecular orbital (HOMO) of the reductant with the lowest unoccupied molecular orbital (LUMO) of the oxidant.[9] For alcohols and ethers, the HOMO would be an oxygen 2*p* orbital containing a lone pair of electrons. For permanganate the LUMO would be a 2*e* antibonding molecular orbital located primarily on manganese.[10] This initial interaction would be followed by a rate limiting hydrogen transfer as indicated in Scheme 1.



Scheme 1. Proposed Mechanisms for the Oxidation of Alcohols and Ethers

Manganese(V), the product produced in the reactions depicted in Scheme 1, would be a very active oxidant under neutral conditions. It is known to be stable only under very basic conditions in aqueous solutions.[11] In methylene chloride solutions it would be expected to undergo a rapid one-electron reduction to give manganese(IV), the experimentally observed product.[12]

The reactions depicted in Scheme 1 are consistent with conclusions arrived at from attempts to theoretically model reactions in which alcohols are oxidized by high valent transition metal oxo compounds.[13] Although the details of the reaction sequences proposed in Scheme 1 remain somewhat speculative, the results reported herein provide conclusive evidence that the oxidations of alcohols and ethers by permanganate are very similar mechanistically.

The authors gratefully acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada.

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