

POSSIBLE ROLE OF LEWIS ACID CATALYSIS IN THE OXIDATION OF ALKENES AND  $\alpha, \beta$ -UNSATURATED  
KETONES USING BLEOMYCIN-Zn(II) AND BLEOMYCIN-Fe(III)-IODOSYLBENZENE IN AQUEOUS METHANOL

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**Summary.**  $C_6H_5IO$  in  $CH_3OH-H_2O$  is activated towards electrophilic attack upon various alkenes by  $Fe(ClO_4) \cdot 9H_2O$ , Fe(III) bleomycin and Zn(II) bleomycin. The results imply that direct transfer of oxygen from an  $Fe(V)=O$  intermediate is not required in the mechanism of oxygenation by iron-containing species, and that much earlier work is questionable as models for biological oxygenation.

Iodosylbenzene may be converted into the electrophile  $C_6H_5I^+OH$  by protonation<sup>1</sup> or by  $BF_3-Et_2O$ .<sup>2,3</sup>  $C_6H_5I(OH)OTs$  is a crystalline, partially ionic compound<sup>4</sup> which serves as a source of the electrophile  $C_6H_5I^+OH$ .<sup>5</sup>

We report now that the Lewis acid  $Fe(ClO_4)_3 \cdot 9H_2O$  either alone<sup>6</sup> or as a bleomycin complex, BLM-Fe(III),<sup>7,8</sup> in the anaerobic system  $C_6H_5IO-CH_3OH-H_2O$ , causes epoxidation of alkenes and also catalyses solvent addition and rearrangement of the primary products. Valentine *et al.* have already reported epoxidation of olefins using ferric triflate- $C_6H_5IO-CH_3CN$ .<sup>6</sup> They ruled out Lewis acidity of the metal ions as playing a role. However, Zn(II)-BLM<sup>9</sup> (Table 1, entries 5,9) epoxidizes both E and Z-stilbene in yields comparable to BLM-Fe(III) and better than  $Fe(ClO_4)_3 \cdot 9H_2O-C_6H_5IO$  itself. In fact, the data in Table 1 indicate that coordination of Fe(III) as in BLM-Fe(III) or with chloro(tetraphenylporphyrinato)-Fe(III)<sup>10</sup> affords more effective catalysts for those oxidations and yield closely similar products, viz, epoxides Table 1, entries 2,4,7,8,12,15, as well as the same rearrangement products, entries 12 and 15 relative to entries 11 and 14. Others have studied BLM- $A_2$ -Fe(III)- $C_6H_5IO-CH_3OH-H_2O$  oxidations of stilbenes and styrene, i.e. entries 2, 7, 8 and 12 (Table 1, parenthesized percentages)<sup>11</sup>. Similar results were obtained in the present study relative to those in ref 11. In the cases of E and Z- stilbene, entries 2 and 7 respectively, the principal difference is that we observe substantial amounts of ring-opening. Since we demonstrated separately that this is a secondary reaction product derived from either Z or E- oxide under the reaction conditions, the product yields between the present study and ref. 11 are not strictly comparable.

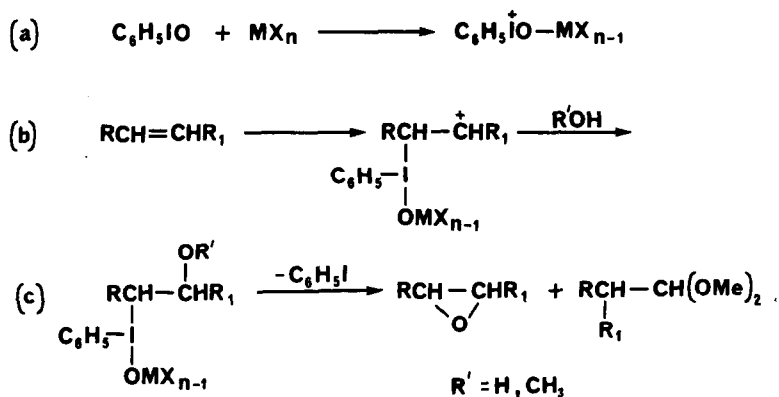
The same overall pattern of epoxide formation has been discussed in terms of "oxygen transfer" presumably *via* a metal-oxo intermediate.<sup>11</sup> This interpretation cannot apply to BLM-Zn(II) since formation of a metal-oxo,  $M=O$ , of redox behavior comparable to  $Fe(V)=O$  is unlikely.<sup>12</sup> Accordingly, entries 5 and 9 (Table 1) in which the products correspond in a formal sense to oxygen transfer, must be interpreted on a basis other than metal-oxo intermediates, and Lewis acid activity appears to be a reasonable alternative.

A further point which illustrates the importance of Lewis acid behavior in these systems is the formation of  $C_6H_5CH_2CH(OCH_3)_2$  from styrene, entries 11 and 13, in the oxidation

catalysed by  $\text{Fe}(\text{ClO}_4)_3 \cdot 9\text{H}_2\text{O}$ , 36%, and BLM-Zn(II) in the remarkably high 84% yield, respectively. These products are mechanistically significant in the sense that similar behavior has been observed in the reaction of styrene with  $\text{C}_6\text{H}_5\text{I}(\text{OH})\text{OTs}$ <sup>5</sup> and  $\text{C}_6\text{H}_5\text{IO}-\text{CF}_3\text{SO}_3\text{H}-\text{CH}_3\text{OH}$ .<sup>13</sup>

In the case of chalcone, rearrangement predominates in the  $\text{Fe}(\text{ClO}_4)_3$  system, entry 14, while the oxide is formed in the BLM-Fe(III) case, entry 15.

A reasonable mechanism for these reactions is outlined below. In step (a) the metal ion, either Fe(III) or BLM-Fe(III) or BLM-Zn(II), yields the coordinated electrophile; in step (b) an electrophilic attack upon the double bond of the alkene yields a carbonium ion intermediate which undergoes coordination with solvent ( $\text{H}_2\text{O}$  or  $\text{CH}_3\text{OH}$ ). In step (c) reductive elimination of  $\text{C}_6\text{H}_5\text{I}$  may yield the epoxide or rearrangement product:



As required by the above mechanism, the oxygen atom of the oxide must originate from solvent and this is the case. Entries 3 and 10.<sup>14</sup> The absence of any stereospecificity in these reactions also agrees with the suggested mechanism in terms of the likely existence of conformers in steps (b) and (c). The yields of products listed in Table 1 for Fe(III) catalysed reactions differ from system to system, be it  $\text{Fe}(\text{ClO}_4)_3$  alone, BLM-Fe(III), TPPCl Fe(III). In a Lewis-acid catalysed process it is not unreasonable that the environment of the Fe(III) will influence the product forming step. Finally this mechanism applies only to the  $\text{C}_6\text{H}_5\text{IO}-\text{CH}_3\text{OH}-\text{H}_2\text{O}$ -metal ion systems, and, accordingly, we consider this system to be an irrelevant model for oxygen atom transfer biomimesis.<sup>11</sup>  $\text{C}_6\text{H}_5\text{IO}-\text{CH}_3\text{CN}$ -metal ion systems, which do not contain a protic solvent, may yield epoxides by a different mechanism.<sup>10</sup> The role of Lewis acid catalysis in these latter systems is of interest.<sup>6</sup>

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Table 1. Reactions of cis and trans Stilbene, Styrene and Chalcone with  $C_6H_5IO-CH_3OH-H_2O$  in the Presence of Various Lewis Acids and BLM or TPP(Cl) <sup>a</sup>, <sup>e</sup>, <sup>f</sup>, <sup>g</sup>, <sup>h</sup>

Entry	Lewis Acid Oxidant	Olefin	Products					
			E-Stilbene Oxide%	Z-Stilbene Oxide%	$C_6H_5CHO$ %	$C_6H_5COCH_2C_6H_5$ %	$C_6H_5CH(OH)CH(OCH_3)C_6H_5$ %	
1	A: $Fe(ClO_4)_3 \cdot 9H_2O$ $CH_3OH-H_2O$	E-Stilbene	3	0	1	trace	4	b, c
2	B: BLM-Fe(III) $CH_3OH-H_2O$		8 (3)	0 (0)	6 (6)	1 (2)	14 (0)	b, c
3	C: BLM-Fe(III) $CH_3OH-H_2O$ (180)		8	85% 180 incorporation <sup>1</sup>				
4	D: TPP(Cl)-Fe(III) $CH_3OH-H_2O$		47	0	17		12	b, c
5	E: BLM-Zn(II) $CH_3OH-H_2O$		9	0	25	1		b, c
		Z-Stilbene						
6	A		2	trace	1	trace	2	b
7	B		18	9	62	6	20	
			(1)	(25, 22)	(5)	(7)	(0)	
8	D		23 (trace)	7	trace	37		
			(40)			(2)		
9	E		8	trace	17	1		b
10	E- $CH_3OH-H_2O$ (180)	Styrene	8	75% 180 incorporation				
		Styrene oxide						
11	A		12	36				b, d
12	B		42 (9, 21)	0 (0)		21 (0)		b
13	E	Chalcone	0	84				b
		Chalcone oxide						
14	A		3					b, d
15	B		17					

<sup>a</sup>Yields were determined by <sup>b</sup>HPLC, <sup>c</sup>GC and <sup>d</sup>NMR analysis and are based on amount of added isodosobenzene; quantitative conversion was assumed, <sup>e</sup> Percentages in parentheses are those found in ref. 11, <sup>f</sup> The Fe(III) complex of bleomycin (blenoxane, 60% BLM-A2) was formed in aqueous solution using  $Fe(ClO_4)_3 \cdot 9H_2O$  and the characteristic U.V. and visible spectra were observed (ref 8). All reactions run under N<sub>2</sub> in  $CH_3OH-H_2O$  solution using 0.44 mmol of alkene, 60  $\mu$ mol of  $C_6H_5IO$  and 2.1  $\mu$ mol of BLM-Fe(III) or BLM-Zn(II) or PFT-Fe(III), <sup>g</sup>A solution of  $C_6H_5IO$  (0.01 mole) in 20 ml  $CH_3OH$  was added to a solution of alkene (0.01 mole) and  $Fe(ClO_4)_3 \cdot 9H_2O$  (0.01 mole) in  $CH_3OH$  (30 ml) under N<sub>2</sub>. The products were isolated by <sup>h</sup>CHCl<sub>3</sub> extraction and analyzed by HPLC or n.m.r. and <sup>h</sup>All quantitation was done by comparison with known samples. <sup>i</sup> by high resolution mass spectrometry.

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