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STEREOSELECTIVE EPOXIDATION OF ALLYLIC AND HOMOALLYLIC ALCOHOLS WITH 30% HYDROGEN PEROXIDE CATALYZED BY TUNGSTIC ACID IN BUFFERED MEDIA

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Abstract : The aqueous tungstic acid-catalyzed hydrogen peroxide epoxidation of allylic alcohols affords the same major diastereoisomer as the $VO(acac)_2/tBuOOH$ system with quite comparable stereoselectivities. In contrast, epoxidation of homoallylic alcohols appears to be much less stereoselective.

In the preceeding paper (1), we showed that the tungstic acid-catalyzed hydrogen peroxide epoxidation of olefinic alcohols is a convenient and efficient method, using quite cheap and safe reagents, in buffered protic media at pH 4.5. Epoxidation of the olefinic bond occurs with complete retention of configuration for both *cis* and *trans* alkenes. Moreover, the reaction is chemoselective, depending on the nucleophilic character of the olefin. The increase in the epoxidation rate with the hydroxyl group-olefinic bond proximity, as well as other structural features, show that the olefinic alcohol is most likely coordinated to the catalytic species via the hydroxyl group, although the reaction occurs in water-methanol or other protic media (1).

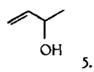
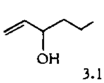
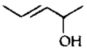
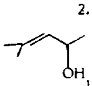
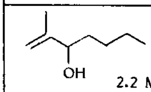
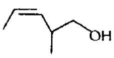
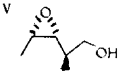
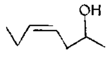
Therefore, we were encouraged to examine the stereoselectivity of this epoxidation for several allylic and homoallylic alcohols in order to get a better insight into the scope and the synthetic usefulness of the tungsten-catalyzed aqueous procedure with respect to other methods (2-9).

ACYCLIC ALLYLIC AND HOMOALLYLIC ALCOHOLS (Table I)

These substrates were selected in order to compare the stereoselectivities with those obtained by previous methods, either for the olefinic alcohol (3-6), or the corresponding trimethyl silyl ether (7). In contrast with other epoxidation reactions such as with peracids, catalytic Mo^{VI}/ tBuOOH or stoechiometric molybdenum peroxo complex, $Al(OtBu)_3/tBuOOH$, the major diastereoisomer in all examples is the same as the one obtained with the $VO(acac)_2/tBuOOH$ system.

Stereoselectivities compare well to those obtained with the vanadium-catalyzed t-butyl hydroperoxide reaction for the present allylic alcohols, but are significantly lower for the homoallylic alcohols.

TABLE I : Epoxidation of acyclic allylic and homoallylic alcohols

Alcohol (M)	Réaction Conditions			Yield	threo/erythro	Previous methods	
	buffer	temp °C	time (h)			T/E	$\neq$
 5.8 M	AcONa	r.tp	40	⊕	15/85	MCPBA V Mo Al	60/40 20/80 44/56 42/58
 3.1 M	AcONa	r.tp	40	22 % (24 % s.m)	25/75	V	+ 25/75
2.3 M  2.2 M	Me_3NO AcONa	r.tp 0° r.tp	4 5 4	65 % 94 % 93 %	40/60 40/60 40/60	MCPBA V Mo Al Si/V	64/36 29/71 62/38 64/36 46/54
2.2 M  1.6 M	Me_3NO	r.tp 0°	1.5 2	83 % 85 % (9 % s.m)	90/10 90/10	MCPBA V Mo Al Si/V	95/5 86/14 95/5 > 99.5 90/10
 2.2 M	Me_3NO	r.tp	8	95 % (2 % s.m)	5/95	MCPBA V Mo Al Si/V	41/59 2/98 16/84 13/87 35/65
 3.4 M	Me_3NO	r.tp	20	57 % (19 % s.m)	20/80 *	V  only	
 3.2 M	Me_3NO	r.tp	18	48 % (31 % s.m)	50/50	V Si/V	1/12 13/87

1.5 eq H_2O_2 30%; 1% mol H_2WO_4; 3% mol AcONa or Me_3NO; molarity M in H_2O_2 30%/CH_3OH

$\neq$ reported Selectivities : ref 3, 4b. 6, 7 ; s.m = Starting Material; + this work ; ⊕ not isolated ;
* we checked that the major diastereoisomer is the same obtained with $VO(acac)_2$ / tBuOOH

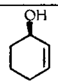
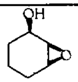
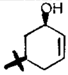
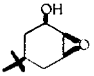
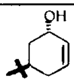
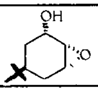
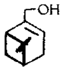
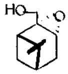
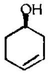
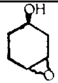
Stereoselectivity, when observed, is particularly noteworthy since the reaction solvent is water-methanol, thus showing the efficiency of the intramolecular epoxidation process by the catalytic species with respect to an intermolecular one, at least in some allylic examples.

Concerning the scope of the reaction, results are reported in Table I only for allylic and homoallylic alcohols since, as a matter of fact, *trans*-homoallylic or bis-homoallylic alcohols are much less reactive in the same conditions, at room temperature, consistently with the results we discussed in the preceeding paper (1).

CYCLIC ALLYLIC AND HOMOALLYLIC ALCOHOLS (Table II)

The cyclohexenols were selected in order to get a better knowledge of the geometrical factors which may control the epoxidation rate and stereoselectivity, as in previous studies with other reagents (3, 5-6, 8-9). Quite surprisingly, whereas at most traces of conjugated enone are formed in acyclic compounds with the tungsten-catalyzed hydrogen peroxide reaction in our conditions, its formation is a largely competitive side-reaction for the 2-cyclohexen-1 ols.

Table II : Epoxidation of cyclic allylic and homoallylic alcohols

Olefinic alcohol (M)	Reaction Conditions buffer	temp °C	time (h)	epoxide yield (cis/trans)	major isomer	by-products
 2.1 M	Me_3NO AcONa	r.tp r.tp	19 17	38 % (95/5) 44 % (95/5)		43 % enone 10 % s.m 35 % enone 15 % s.m
 0.7 M	Me_3NO	r.tp	40	23 % (90/10)		50 % enone 3 % enone epoxide
 0.7 M	Me_3NO	r.tp	15	19 % (96/4)		66 % s.m 10 % enone
 1.2 M	Me_3NO	r.tp	6	85 %	 only	
 2.1 M	Me_3NO	r.tp	20	77 % (50/50)		9 % s.m

1.5 eq H_2O_2 30%; 1% mol H_2WO_4; 3 % mol AcONa or Me_3NO; Molarity (M) in H_2O_2 30%-CH_3OH
s.m = starting material

Several points are however worth some comment :

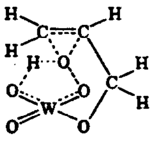
- Epoxidation is highly stereoselective, *cis* to the hydroxyl group, in 2-cyclohexen-1-ol and both *cis* and *trans* 5-t-butyl-2-cyclohexen-1-ols, but less than with some other transition metal-catalyzed epoxidations (3, 5, 6, 9),
- With respect to epoxidation, more enone is formed with the *cis* (OH pseudo equatorial) than with the *trans* 5-t-butyl-2-cyclohexen-1-ol (OH pseudo axial), as with the $VO(acac)_2$/tBuOOH system; however, by using the vanadium procedure, there is much more oxidation into the enone with the *cis* compound (91% enone, 9% epoxy-alcohol) and much less with the *trans* (8% enone, 92% epoxy alcohol), (9 b).

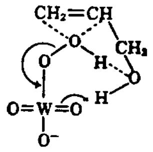
The myrtenol epoxide (10) is obtained in good yield, with no rearrangement or oxidation by-product. The epoxidation may be favoured here, with respect to the 2-cyclohexen-1-ols, either by a conformational effect or by the different nature of the allylic hydroxyl group.

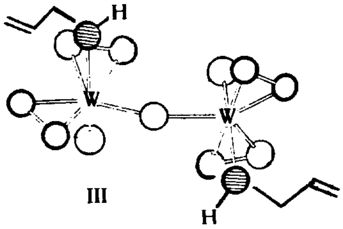
The quite different results obtained with acyclic and cyclic allylic alcohols, concerning the relative rates of epoxidation and enone formation, may reflect the fact that the optimal geometry, favourable for the epoxidation is not achieved in the 2-cyclohexen-1-ols, whereas it can be in the acyclic compounds.

In contrast with other transition metal-catalyzed epoxidations which are almost stereospecific to afford the *cis* 3-cyclohexen-1-ol epoxide (3, 5, 6, 9), no stereoselectivity is observed in the tungsten-catalyzed aqueous reaction as with peracids (11).

Concerning the mechanism of these tungsten-catalyzed reactions, more experimental results are still needed to discuss the early assumptions of H.C. STEVENS and A.J. KAMAN, that is either an allylic pertungstate ester (I) or a concerted delivery of the peroxy oxygen with coordination of the hydroxyl hydrogen by one of the W = O bonds (II) (12). An other possible mechanism might also involve a coordination of the olefinic alcohol via the oxygen to a pertungstate species (III). Such an intermediate would have a structure similar to that of $[K_2W_2O_{11}, 4H_2O]$ which has been determined by X-Ray (13), consistently with molecular weight measurements, infrared and Raman studies of solid samples and aqueous solutions (14) : the olefinic alcohol would just replace a water molecule as an axial ligand in the pentagonal bipyramidal structure.


I


II


III

Work is now in progress with some other ananchomeric cyclic compounds in order to determine more precisely the factors which may influence the rates of epoxidation and enone formation. Conversely, a better knowledge of the pertungstate solutions is also necessary for discussing the mechanism of these reactions. Nevertheless, the present preliminary results clearly show that the tungstic acid-catalyzed epoxidation of olefinic alcohols can be quite an efficient and synthetic useful reaction, in aqueous or protic conditions with 30% hydrogen peroxide. For allylic alcohols, the reaction is stereoselective and results nicely parallel those obtained with the VO(acac)$_2$/tBuOOH system, affording the same major diastereosisomer in all the examples reported herein.

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