(2 H, dd, J = 7.1, 2.2 Hz). Calcd for $C_{16}H_{18}O_5$: 290.1154. Found: 290.1152.

2′*S*,2*R*,3*S* isomer: IR ($CHCl_3$) 3305, 1756 (br) cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 1.12 (3 H, d, J = 6.9 Hz), 1.90 (1 H, d, J = 2.4 Hz), 3.01 (1 H, qdd, J = 7.0, 4.6, 2.4 Hz), 3.47 (3 H, s), 3.74 (3 H, s), 4.93 (1 H, s), 5.14 (1 H, d, J = 4.8 Hz), 7.34 (3 H, m), 7.48 (2 H, dd, J = 7.4, 2 Hz). Calcd for $C_{16}H_{18}O_5$: 290.1154. Found: 290.1155.

Method 3. Of (1*R,2*S**,5*R**)-Bicyclo[3.3.0]oct-7-en-*endo*-2-ol.** (*S*)-*O*-Methylmandelic acid (1.00 g, 6.02 mmol) was added to a white suspension prepared by the slow addition of 0.578 mL (6.62 mmol) of oxalyl chloride to 0.698 mL (9.03 mmol) of DMF in 20 mL of acetonitrile at 0 °C. After 5 min, a solution of 821 mg (6.62 mmol) of the title alcohol in 1.07 mL (13.2 mmol) of pyridine was added over a 5-min period and the resultant mixture stirred at 0 °C for 20 min. The pale yellow reaction mixture was diluted with 100 mL of ether, the organic phase washed twice with saturated aqueous cupric sulfate and dried over sodium sulfate, and the solvent removed in vacuo to give a yellow oil.

Purification by flash chromatography (3 cm, ether/hexanes, 1:4) gave 1.45 g (88%) of clear oil. A small amount of each diastereomer could be obtained pure utilizing a Waters analytical HPLC (10 Porasil radial-pak column, 1:9 ethyl acetate/hexanes, 2 mL/min flow rate), retention times 4.93 and 7.33 min. On a preparative scale, the following procedure was used for separation. The mixture of diastereomers obtained from the esterification above (1.45 g) was flash chromatographed (6 cm × 17.78 cm column, 1:19 ethyl acetate/hexanes, 50-mL fractions) to obtain the (*S*)-*O*-methylmandelate ester of (1*S*,2*R*,5*S*)-*cis*-bicyclo-[3.3.0]oct-7-en-*endo*-2-ol, a mixture of the two diastereomers, and the (*S*)-O-methylmandelate ester of (1*R*,2*S*,5*R*)-*cis*-bicyclo-[3.3.0]oct-7-en-*endo*-2-ol. The mixture obtained above was rechromatographed on the same column above under the same conditions to give that pure 1*S*,2*R*,5*S* isomer, (combined total 702 mg, 97% recovery), $[\alpha]^{26}_D$ +157° (*c* 4.44, methanol), and the pure 1*R*,2*S*,5*R* isomer (combined total 692 mg, 95% recovery), $[\alpha]^{26}_D$ −19.2° (*c* 2.54, methanol).

2′*S*,1*S*,2*R*,5*S* isomer: IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5 H), 5.68 (m, 1 H), 5.36 (m, 1 H), 5.15 (q, J = 8.2 Hz, 1 H), 4.73 (s, 1 H), 3.42 (s, 3 H), 3.40 (m, 1 H), 2.8–2.5 (m, 2 H), 2.05 (m, 1 H), 1.9–1.2 (m, 4 H).

Calcd for $C_{27}H_{30}O_3$: 272.1407. Found: 272.1415.

2′*S*,1*R*,2*S*,5*R* isomer: IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5 H), 5.40 (m, 1 H), 5.16 (q, J = 8.2 Hz, 1 H), 4.86 (m, 1 H), 4.71 (s, 1 H), 3.40 (s, 3 H), 3.23 (m, 1 H), 2.53 (m, 2 H), 2.1–1.2 (m, 5 H).

Calcd for $C_{27}H_{30}O_3$: 272.1407. Found: 272.1415.

X-ray Crystal Structure Analysis of 3. Large crystals of **3** ($C_{16}H_{17}NO_7S_3$) suitable for X-ray diffraction studies formed from ethanol with space group symmetry of $P2_12_12_1$ and cell constants of a = 10.740 (3) Å, b = 11.724 (4) Å, and c = 15.142 (3) Å for z = 4 and a calculated density of 1.503 g/cm^3. Of the 1492 reflections measured with an automatic four-circle diffractometer equipped with Cu radiation, 1444 were observed ($I \geq 3I$). The structure was solved with a multisolution tangent formula approach and difference Fourier analysis and refined by using full-matrix least-squares techniques.[11] Hydrogens were assigned isotropic temperature factors corresponding to their attached atoms. The function $\sum w(|F_o| - |F_c|)^2$ with $w = 1/(\sigma F_o)^2$ was minimized to give an unweighted residual of .064. Tables I–III containing the final fractional coordinates, temperature parameters, bond distances, and bond angles are available as supplementary material. Figure 1 is a computer-generated perspective drawing of **3** from the final X-ray coordinates showing the relative stereochemistry.

Acknowledgment. We thank the National Institutes of Health for their generous support of the programs at Wisconsin.

(11) The following library of crystallographic programs was used: Multan 80, P. Main et al., University of York, York, England, 1980; Ortep-II, C. K. Johnson, Oak Ridge National Laboratory, Oak Ridge, TN, 1970; SDP Plus V1.1, Y. Okaya et al., B. A. Frenz and Associates, College Station, TX, 1984.

Registry No. **3**(isomer 1), 101859-94-3; **3**(isomer 2), 101859-95-4; (±)-(5R*,6S*)-6-hydroxy-2,2,5-trimethyl-1,3-dioxepane, 59005-38-8; (*S*)-*O*-methylmandelic acid, 26164-26-1; 6-mandelate-2,2,5-trimethyl-1,3-dioxepane (isomer 1), 101859-92-1; 6-mandelate-2,2,5-trimethyl-1,3-dioxepane (isomer 2), 101976-97-0; (±)-methyl (2S*,3R*)-2-hydroxy-3-methyl-4-pentynoate, 82998-91-2; methyl 2-mandelate-3-methyl-4-pentynoate (isomer 1), 101859-93-2; methyl 2-mandelate-3-methyl-4-pentynoate (isomer 2), 101976-98-1; (±)-1R*,2S*,5R*)-bicyclo[3.3.0]oct-7-en-*endo*-2-ol, 68317-62-4; bicyclo[3.3.0]oct-7-en-2-ol(mandelate isomer 1), 86971-84-8; bicyclo[3.3.0]oct-7-en-2-ol(mandelate isomer 2), 86971-85-9; 2-mandelate-5-ethyl-cyclohex-3-en-1-carboxaldehyde (isomer 1), 101859-96-5; 2-mandelate-5-ethyl-cyclohex-3-en-1-carboxaldehyde (isomer 2), 101859-97-6; (*R*)-*O*-methylmandelic acid, 3966-32-3.

Supplementary Material Available: Tables of the atomic positional and thermal parameters, bond distances, and bond angles for **3** (4 pages). Ordering information is given on any current masthead page.

Opposite Regioselectivity in the Epoxidation of Geraniol and Linalool with Molybdenum and Tungsten Peroxo Complexes

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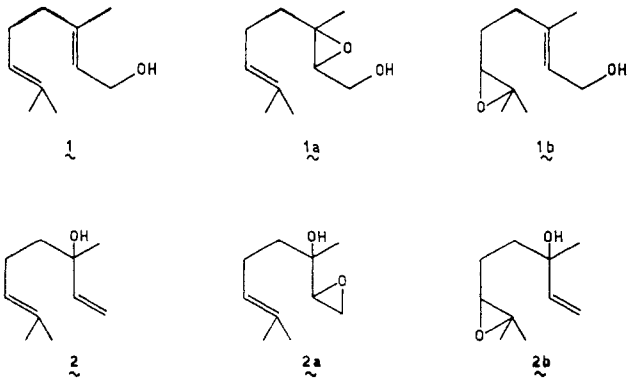
The epoxidation of geraniol (**1**) and linalool (**2**) with *tert*-butyl hydroperoxide and vanadium or titanium catalysts is remarkably faster than that of simple olefins and is regiospecific.[1,2] Only the monoepoxides 2,3-epoxygeraniol (**1a**) and 1,2-epoxylinalool (**2a**) are formed whereas no appreciable amounts of the 6,7-epoxides **1b** and **2b** are found.



1 **1a** **1b**

2 **2a** **2b**

It is also well-known that the Sharpless reagent, *t*-$BuO_2H/Ti(O\text{-}i\text{-}Pr)_4$/DET, enantiospecifically epoxidizes prochiral allylic alcohols.[3]

(1) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136.
(2) Sharpless, K. B.; Verhoven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.
(3) Sharpless, K. B.; Katsuki, T. *J. Am. Chem. Soc.* **1980**, *102*, 5976.

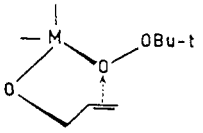
0022-3263/86/1951-2374$01.50/0

Table I. Rates of Oxidation of Geraniol (1), Linalool (2), and 2,4,4-Trimethyl-2-pentene (3) to the Corresponding Epoxides with MO_5HMPT in DCE[a]

substrate	conc, M	oxidant	t, °C	product	10^3k(obsd), s^{-1} [b]	10^2k_2, M^{-1} s^{-1} [c]
1	0.09	WO_5HMPT	20	**1a**	4.2	4.7
1	0.67			**1a**	27.5	4.1
1	0.89			**1a**	36.9	4.2
1	0.44	MoO_5HMPT		**1a**	7.9	1.8
1	0.67			**1a**	10.9	1.6
1	0.89			**1a**	13.0	1.5
2	0.1	WO_5HMPT		**2b**	0.61	0.61
2	0.28			**2b**	1.6	0.57
2	0.09	MoO_5HMPT		**2b**	0.05	0.055
2	0.38			**2b**	0.22	0.058
2	0.76			**2b**	0.48	0.063
3	0.09	WO_5HMPT	40	**4**	0.34	0.37
3	0.45	MoO_5HMPT	40	**4**	0.14	0.031

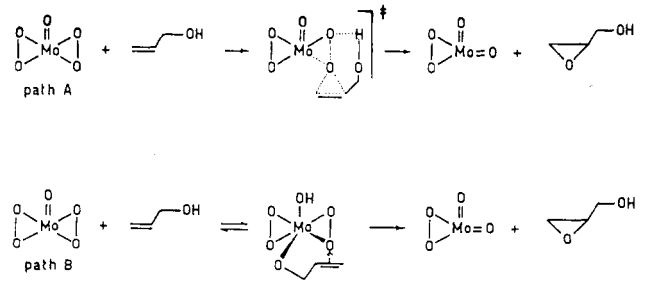
[a] In all experiments $[O]_{Act}$ = 2 MO_5HMPT = 0.02 M. [b] Obtained from the slopes of plots of ln $[O]_{Act}$ vs. time, linear up to 80% (MoO_5) and to 50% (WO_5). [c] Obtained as k(obsd)/[substrate].

All these features, i.e., regio- and enantioselectivity and rate acceleration, are explained by the same general mechanism which requires the equilibrium formation of a ground-state ternary complex, an alkoxohydroperoxometal compound.[2] In the case of titanium catalyst, this intermediate is likely a dimeric or polymeric species.[4] In such a complex, an intramolecular transfer of the peroxide oxygen to the double bond proximate to the alkoxo function is assumed to be easily accomplished.[1,2]



A kinetic evidence of this mechanistic proposal is the zero-order dependence of epoxidation rates on substrate concentration observed when the excess of the allylic alcohol over the metal leads to saturation of the hydroperoxometal complex.[5]

We recently reported that also the molybdenum-catalyzed epoxidation of 1 with hydrogen peroxide, in alcoholic solvents, is regiospecific and faster than that of simple olefins of comparable nucleophilicity, affording only **1a**.[6,7] However, in our system, where the oxidizing species is a side-bonded oxodiperoxomolybdenum(VI) complex, $MoO(O_2)_2(ROH)_n$, no saturation of the metal was observed even at very high excess of 1.[7] Moreover, the activation parameters of the reaction, particularly the entropic one, were much more consistent with an intermolecular rather than an intramolecular oxygen transfer.[6] Therefore, we suggested that the epoxidation of 1 with MoO_5 was more likely to proceed according to path A than B.[6]



In our proposal, both directing and accelerating effect of the hydroxo function should be related to the intramolecular hydrogen bonding in the transition state of an intermolecular oxygen-transfer process.

In order to provide further evidence on the mechanism depicted in path A, we have examined the stoichiometric epoxidation of **1** and **2** with the isolated peroxo complexes MO_5HMPT (M = Mo(VI), W(VI)) in DCE.[8] As reported below, we found that the reactions are in all cases fast and regiospecific. However, to our surprise, an opposite regiochemistry is observed in the product epoxides, which are respectively **1a** and **2b**. Therefore, an unprecedented regiospecific epoxidation of the double bond of linalool further removed from the hydroxo function is taking place. We also observed that such a process is still faster than the epoxidation of a simple, trialkyl-substituted olefin. The interpretation of these results supports the hypothesis that the role played by the hydroxo group of the allylic alcohol is mainly related to its hydrogen bonding ability.

Results and Discussion

The epoxidation of geraniol (1) and linalool (2) with MO_5HMPT (M = Mo(VI), W(VI)) in dichloroethane is, under the experimental conditions adopted, highly selective, affording quantitative yields (~95%) of the corresponding monoepoxides. However an opposite regioselectivity is observed: geraniol affords the 2,3-epoxygeraniol (**1a**) whereas from linalool the 6,7-epoxy derivative (**2b**) is obtained.

The rates of epoxidation of 1 and 2 were measured in DCE under the pseudo-first-order condition of [substrate] $\gg$ $[O]_{Act}$ ($[O]_{Act}$ = 2[MO_5HMPT]) by following the disappearance of O_{Act}. For comparative purposes the rates of oxidation of 2,4,4-trimethyl-2-pentene (**3**) to the corresponding epoxide **4** have also been measured. In all cases, pseudo-first-order plots of ln $[O]_{Act}$ vs. time were linear up to 80–90% reaction for MoO_5HMPT, whereas, in the epoxidation with WO_5HMPT, such plots consist of two straight lines crossing at ca. 50% reaction. This feature, as discussed elsewhere,[9] may derive from a different reactivity of the two peroxo groups in the W(VI)–diperoxo complex, being the transfer of the first peroxidic oxygen faster than that of the second one.

Table I collects the values of the pseudo-first-order rate constants, k_{obsd} obtained from the slopes of plots of ln $[O]_{Act}$ vs. time taking, for WO_5HMPT, the slopes of the first straight line up to ca. 50% reaction. It is observed

(4) Williams, I. D.; Pedersen, S. F.; Sharpless, K. B.; Lippard, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 6430.
(5) Di Furia, F.; Modena, G.; Curci, R.; Edwards, J. O. *Gazz. Chim. Ital.* **1979**, *109*, 571.
(6) Bortolini, O.; Di Furia, F.; Modena, G. *J. Mol. Catal.* **1983**, *19*, 319.
(7) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *J. Mol. Catal.* **1983**, *19*, 331.
(8) Mimoun, H.; de Roch, I. S.; Sajus, L. *Tetrahedron* **1970**, *26*, 37.
(9) Amato, G.; Arcoria, A.; Ballistreri, F. P.; Tomaselli, G. A.; Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G.; Valle, G. *J. Mol. Catal.*, in press.

Table II. Rates of Epoxidation of 2,4,4-Trimethyl-2-pentene with WO_5HMPT in DCE (at 40 °C) in the Presence of Increasing Amounts of CH_3OH and CF_3CH_2OH[a]

added alcohol	conc, M	10^3k(obsd), s^{-1} [b]
		(0.34)
CH_3OH	0.5	0.42
	1.2	0.50
	2.5	0.50
	3.7	0.40
	5.0	0.37
CF_3CH_2OH	0.06	0.40
	0.1	0.50
	0.25	0.58
	0.36	0.41
	0.50	0.33
	0.64	0.29
	1.0	0.28

[a] In all experiments, [substrate] = 0.09 M, $[O]_{Act}$ = 0.02 M. [b] See note b, Table I.

that k_{obsd} values are linearly dependent on substrate initial concentration. Thus, the slopes of plots of k_{obsd} vs. $[substrate]_o$, having near zero intercept, provide the second-order rate constants k_2.

Both allylic alcohols are significantly more reactive than 2,4,4-trimethyl-2-pentene. Considering that the epoxidation of **1** and **2** is carried out at 20 °C whereas that of **3** is at 40 °C, one may estimate[6] that the rate enhancements are 40-fold for **1** and 6-fold for **2** in the case of WO_5HMPT and 200-fold and 8-fold, respectively, for MoO_5HMPT.

The experimental facts that need to be reconciled may be summarized as follows: (i) hydroperoxovanadium and -titanium complexes regiospecifically epoxidize **1** and **2** at the allylic double bond with a large rate acceleration in respect to simple olefins of comparable nucleophilicity;[1,2] (ii) peroxomolybdenum and -tungsten complexes epoxize the allylic double bond in **1** but the 6,7-double bond in **2**, both with a significant rate acceleration which is at any rate much larger for **1**; (iii) the kinetic order of the substrate in the epoxidation of allylic alcohols with V and Ti hydroperoxo complexes is almost zero[5] whereas with Mo and W peroxo complexes the order is one in a fairly large substrate concentration interval; (iv) there is a dramatic difference in the activation parameters for the epoxidations with the two kinds of oxidants.[6] In particular, the rate acceleration in the epoxidation with hydroperoxo complexes of V and Ti is mainly due to the entropic factor, whereas the enthalpic one plays the dominant role in the oxidation with peroxo complexes of Mo and W.[6] Clearly the first conclusion which may be drawn is that there must be some significant difference between the two classes of oxidants as far as their mode of reaction is concerned. The epoxidation with hydroperoxo V and Ti complexes occurs through the formation of an alkoxohydroperoxo complex in the group state.[1,2] The geometry of such a complex favors the oxygen transfer to the allylic double bond so that these processes become much faster than the epoxidation of an isolated double bond. By way of contrast the epoxidation with Mo and W peroxo complexes should not involve a coordinated substrate. This is confirmed by the kinetic order one in the substrate and by the lower rate enhancements particularly in the epoxidation of **2**. Thus, it is reasonable to propose the involvement of a transition-state effect, i.e. a hydrogen-bonding assistance in the oxygen transfer process. Further evidence on this point is given by the data reported in Table II.

It is observed that added alcohols CH_3OH and CF_3CH_2OH in DCE, at low concentration, caused a detectable enhancement of the epoxidation rates of a simple olefin such as 2,4,4-trimethyl-2-pentene, thus confirming that an accelerating effect by a protic species, likely via hydrogen bonding of the peroxo oxygen in the transition state, is taking place. The rate enhancements observed, which are rather modest when compared with those usually found in the epoxidation of allylic alcohols may be, nevertheless, taken as a good evidence favoring the mechanism proposed. In fact, the data of Table II refer to an intermolecular hydrogen bonding, and, at any rate, they may result from the balance of various effects. Indeed, at higher concentration, added alcohol causes a decrease of the epoxidation rates. Accordingly, in alcohol solvent, the epoxidation of similar olefins with MO_5HMPT is much slower than in DCE.[7]

Along these lines, the directing effect of the OH group of the allylic alcohols, i.e., the regioselectivity of their epoxidation with MO_5HMPT species, should be directly connected with the effectiveness of the intramolecular hydrogen bonding. Therefore, it is resonable that in geraniol, owing to the scarce difference in reactivity between 2,3- and the 6,7-double bond, the attack of the peroxide oxygen occurs at the 2,3 one whereas in linalool, where the 6,7-double bond is significantly more nucleophilic than the 1,2 one, an opposite selectivity is observed. On the other hand, the rate acceleration observed in linalool epoxidation, though smaller than that of geraniol, indicates that a hydrogen bonding between the distal OH group and the peroxide oxygen is still possible.

Finally, it is worth pointing out that these results, particularly the regiospecific epoxidation of **2** to the 6,7-epoxide, not only shed light on the mechanism of epoxidation with peroxo species such as MO_5 but also provide a useful synthetic route for the preparation of 6,7-epoxylinalool avoiding the use of peroxocarboxylic acids.[1]

Experimental Section

Materials. Geraniol, linalool, and 2,4,4-trimethyl-2-pentene were commercially available, reagent grade (EGA Chemie) materials, purified by distillation before use. 2,3-Epoxygeraniol was obtained by epoxidation of the parent allylic alcohol with t-BuO_2H–$VO(acac)_2$, according to the original method described by Sharpless et al.[1] 6,7-Epoxylinalool was obtained by epoxidation of linalool with MCPBA. This procedure gives small amounts (~3%) of the 1,2-epoxide.[1] The oxodiperoxo(hexamethylphosphoroamido)aquo complexes, MO_5HMPT·H_2O (M = Mo(VI), W(VI)), were prepared following reported procedures.[8] The dehydrated complexes MO_5HMPT were obtained by keeping MO_5HMPT·H_2O in vacuo for 48 h. Dichloroethane, methyl alcohol, and trifluoroethyl alcohol were purified by standard procedures.

Procedures. The kinetic experiments were run under nitrogen atmosphere following the general technique reported in previous papers.[6,7] The direct quantitative determination of the products was carried out at the end of the reaction (complete consumption of the oxidant, revealed by absence of iodometric titer) by GLC analyses (internal standard) on a Varian 3700 instrument equipped with a Varian CDS 401 integrator using a 1-m, 15% Carbowax 20M on Chromosorb 80–100 column. Yields are in all cases ≥97%. The identity of the products was confirmed by isolation (low-pressure column chromatography, silica gel, 30:70 Et_2O–$CHCl_3$) of the epoxides which showed ^1H NMR and mass spectra identical with those of authentic samples.

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Registry No. 1, 106-24-1; **1a**, 50727-94-1; **2**, 78-70-6; **2b**, 15249-34-0; **3**, 107-40-4; **4**, 96-06-0; WO_5HMPT, 34110-41-3; MoO_5HMPT, 25377-12-2; CH_3OH, 67-56-1; CF_3CH_2OH, 75-89-8.