

by EFF calculations.⁹ Experiments to extend these structures to create artificial receptors suitable for chiral discrimination between molecular substrates are in progress.

Experimental Section

General. ¹H NMR spectra were measured on the Bruker WH-270 spectrometer, or on the Varian FT-80 spectrometer, at concentrations of (1–2) × 10⁻² mol L⁻¹. Chemical shifts are reported in ppm on the δ scale relative to tetramethylsilane (TMS) as internal standard.

Infrared spectra were measured using the Nicolet-510 FTIR spectrometer at concentrations of (1–2) × 10⁻² mol L⁻¹. Absorption frequencies are given in cm⁻¹. UV-vis and circular dichroism (CD) spectra were measured using a Hewlett-Packard diode array spectrophotometer Model 8450A and a JASCO J-500C spectropolarimeter, respectively.

Chromatographic purifications were performed by column chromatography, using aluminum oxide, silica gel 60 (70–230-mesh ASTM), or flash chromatography using silica gel 60 (230–400-mesh ASTM). The homogeneity of the compounds was examined by thin-layer chromatography (mostly silica-coated plates, Merck), using at least two different solvent systems and two visualization methods (i.e. fluorescence quenching, iodine, ninhydrine). Solvents and commercially available reagents were of analytical grade. Protected amino acids were purchased from Sigma.

Preparation of H₂NCH(*i*-Bu)CONH-*i*-Pr, 3a. *N,N*-Dicyclohexylcarbodiimide (2.56 g, 12.4 mmol), and 4-(dimethylamino)pyridine (50 mg) were added to a solution of Cbz-*L*-leucine (3 g, 11.3 mmol) and (1.302 g, 11.3 mmol) *N*-hydroxysuccinimide in dry THF (50 mL) at 0 °C. The reaction mixture was allowed to stand at 4 °C overnight. The formed dicyclohexylurea was filtered and washed with THF. Isopropylamine (0.974 mL, 11.3 mmol) was added to the combined active ester solutions, and the reaction mixture was stirred at room temperature for 2 days. The THF was then evaporated, and the crude mixture was chromatographed on neutral alumina (CHCl₃) to afford CbzNHCH(*i*-Bu)CONH-*i*-Pr in 63% yield as an oil. IR (nujol): 1686 (OCO-NH), 1643 cm⁻¹ (CONH). ¹H NMR (80 MHz, CDCl₃): 7.33 (m, 5 H, Ar H), 7.0 (d, 1 H, *J* = 5.8 Hz, CONH-*i*-Pr), 5.10 (s, 2 H, ArCH₂), 5.8 (m, 1 H, OCONH), 4.86–3.98 (m, 2 H, CH of Leu and CH of *i*-Pr), 1.71–1.32 (m, 3 H, CH₂ and CH of *i*-Bu), 1.11 (d, 6 H, *J* = 6.5 Hz, CH₃ of *i*-Pr), 0.92 ppm (d, 6 H, *J* = 5.4 Hz, CH₃ of *i*-Bu).

A solution of protected CbzNHCH(*i*-Bu)CONH-*i*-Pr (2.3 g, 7.53 mmol) in ethanol was added to a suspension of Pd/C (5%) (0.576 g) in ethanol (50 mL). The mixture was hydrogenated at atmospheric pressure for 1 h, filtered, and evaporated to dryness to provide 3a as an oil in 92% yield. IR (CDCl₃): 1657 cm⁻¹ (CONH). ¹H NMR (80 MHz, CDCl₃): 7.01 (bs, 1 H, CONH-*i*-Pr), 4.18–3.91 (m, 1 H, CH of *i*-Pr), 3.32 (dd, *J* = 3.6 and 10 Hz, 1 H, CH of Leu), 1.82–1.57 (m, 3 H, CH₂ and CH of *i*-Bu), 1.14 (d, 6 H, *J* = 6.4 Hz, CH₃ of *i*-Pr), 0.94 ppm (m signals, 6 H, CH₃ of *i*-Bu).

Preparation of EtC(CH₂OCH₂CONHCH(*i*-Bu)CONH-*i*-Pr)₃, 1a. The same procedure as used earlier for compound 1b⁹ was employed for synthesizing the derivative 1a using L-NH₂CH(*i*-Bu)CONH-*i*-Pr (3a) as amine. The crude mixture was purified by rapid chromatography on neutral aluminum oxide (CHCl₃-MeOH, 98:2 and 95:5) to remove pentachlorophenol and then by flash chromatography on silica gel (CHCl₃-MeOH, 98:2, 97:3, 95:5, and 90:10) to provide 1a in 17% yield as a solid, mp 73–76 °C. IR (10 mM, CDCl₃): 3427 and 3317 (NH), 1664 cm⁻¹ (CONH). ¹H NMR (270 MHz, CDCl₃): 7.20 (d, 3 H, *J* = 8.6 Hz, CONH-Leu), 6.35 (d, 3 H, *J* = 7.7 Hz, CONH-*i*-Pr), 4.44 (m, 3 H, CH of Leu), 4.02 (m, 3 H, CH of *i*-Pr), 3.98 (s, 6 H, CH₂CO), 3.45 (s, 6 H, CCH₂O), 1.69–1.48 (m, 9 H, CH₂ and CH of *i*-Bu), 1.15–1.10 (m, 18 H, CH₃ of *i*-Pr), 0.95–0.91 (m, 18 H, CH₃ of *i*-Bu), 0.87 ppm (t, 3 H, CH₃ of Et).

Preparation of EtC(CH₂OCH₂CONHCH(*i*-Bu)CONH-*i*-Pr)₃, 2a. The same procedure as employed earlier⁹ for compound 2b was employed for synthesizing compound 2a, using trisphenolate 2 and amine L-NH₂CH(*i*-Bu)CONH-*i*-Pr, 3a. The crude mixture was purified by rapid chromatography on neutral aluminum oxide (CHCl₃-MeOH, 98:2, 95:5, and 90:10) to remove

pentachlorophenol and then by chromatography on silica gel (CH₂Cl₂-MeOH, 98:2 and 95:5) and afforded a white glassy solid, 2a, in 57% yield, mp 203–5 °C (after precipitation from acetonitrile). FAB MS (3-nitrobenzyl alcohol): 813 (M + H)⁺. IR (10 mM, CDCl₃/CD₃CN): 3304 (NH), 1652 cm⁻¹ (CONH). ¹H NMR (270 MHz, CDCl₃): 7.70 (d, 3 H, *J* = 8.4 Hz, CONH-Leu), 6.68 (d, 3 H, *J* = 7.9 Hz, CONH-*i*-Pr), 4.45 (m, 3 H, CH-Leu), 4.01 (m, 3 H, CH-*i*-Pr), 3.63 (m, 6 H, OCH₂), 3.18 (AB q, 6 H, CCH₂O), 2.56 and 2.42 (2 m, 6 H, CH₂CO), 1.65 (m, 9 H, CH₂ and CH of *i*-Bu), 1.32 (q, 2 H, CH₂ of Et), 1.14 (m, 18 H, CH₃ of *i*-Pr), 0.93 (m, 18 H, CH₃ of *i*-Bu), 0.79 ppm (t, 3 H, *J* = 7.5 Hz, CH₃ of Et).

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Supplementary Material Available: ¹H NMR spectra of title compounds 3a and 4a (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Reactions of Molecules with Two Equivalent Functional Groups. 4. Selective Mono-oxidation in the Heterogeneous Reaction of Bis(hydroxymethyl)benzene Isomers with Manganese Dioxide

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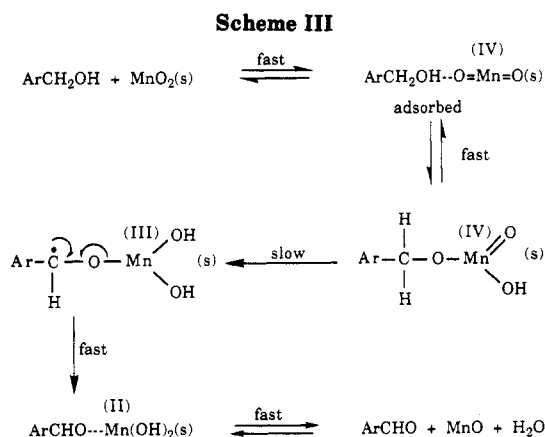
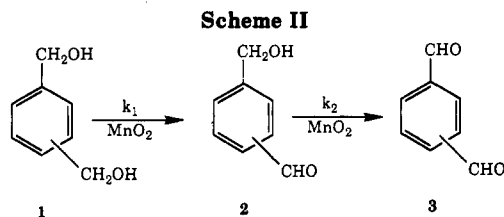
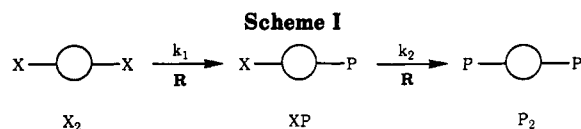
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Introduction

We have recently reported studies^{1–3} on reactions of molecules with two equivalent functional groups (X), where reagent R converts X to product functional group P as depicted in Scheme I. We demonstrated that when the functional groups in X₂, XP, and P₂ operate independently, and the reactions are irreversible, the fraction of each compound in the final product mixture can be accurately predicted by a system of simple equations.^{1,2} One important consequence of the independence of the groups is that X₂ is exactly twice as reactive as XP (i.e., $k_2/k_1 \equiv \kappa = 0.5$). Deviations from this behavior ($k_2/k_1 \neq 0.5$) give a quantitative measure of intramolecular interactions between the functional groups in X₂ and XP. Such deviations have been detected in several reactions such as acetylation of the ortho isomer of bis(hydroxymethyl)benzene ($\kappa = 0.61$),^{2a} substitution reaction of several α,ω -dibromoalkanes with KCN ($\kappa = 0.61$ to 1.15),³ and nucleophilic addition reaction of 1,10-cyclooctadecanedione with several nucleophiles.⁴ By contrast, the acetylation of *m*- and *p*-bis(hydroxymethyl)benzene^{2a} as well as of 1,6-hexanediol^{2b} gave results in complete agreement with the independent group model ($k_2/k_1 \approx 0.5$).

The new results reported herein demonstrate other important aspects of this study, including their applicability

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to organic synthesis and to heterogeneous reactions. Chemists often face the problem of carrying out a reaction at just one of two similar groups in a substrate molecule. In many cases the solution to this problem requires sophisticated strategies for deactivation (protection) of one of the groups, as well as extreme experimental care. Thus, there is always an interest in the development of improved and simplified methodologies to accomplish the desired selectivity.⁵ We show below that kinetic studies on the reaction of the three isomers of bis(hydroxymethyl)benzene (1) with solid manganese dioxide (Scheme II) indicate that in certain cases this reagent can be used for selective mono-oxidation of symmetrical unsaturated diols.

Results

It is well-known that solid manganese dioxide oxidizes unsaturated alcohols to the corresponding unsaturated aldehyde or ketone.⁶ The reaction can be performed in a variety of solvents, and over-oxidation to carboxylic acid is generally not observed. The elucidation of the mechanism of this reaction has proven difficult because of its heterogeneous nature. However, a large α -C-H isotope effect has been observed. Specifically, undeuterated benzyl alcohol reacted 18 times faster than α,α -dideuteriobenzyl alcohol, and α -deuteriobenzyl alcohol gave predominantly deuterated oxidation product.⁷ These results are consistent with the mechanism shown in Scheme III, with rate-limiting α -C-H bond cleavage and transfer of the hydrogen atom from the alcohol to the oxidant.⁷ The rate of the reaction is known to be influenced by many factors,

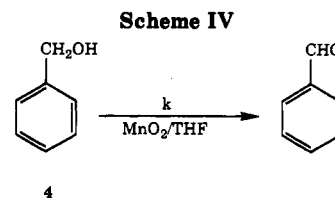


Table I. Reaction of 4 with MnO_2 in THF at 45 °C

run	[4] ₀ , M	quantity of MnO_2^a	reaction performed under	k^b
1	0.10	0.08	argon	1.13
2	0.20	0.18	argon	0.50
3 ^c	0.08	0.08	argon	0.09
4 ^c	0.08	0.08	oxygen	0.16
5	0.11	0.08	oxygen	0.25

^aQuantity of MnO_2 expressed in moles of MnO_2 added/L of original reaction mixture. ^bRate constants are in units of 10^{-4} L mol⁻¹ s⁻¹. ^cRuns 3 and 4 were performed in parallel using the same batch of MnO_2 .

including the activity of the oxidant, impurities that are present, the solvent and temperature, the structure of the substrate, and the relative amounts of the reactants.^{6b}

Pratt and Van de Castle^{8a} compared the rates of oxidation of different alcohols with MnO_2 . The results imply the presence of radical intermediates, as initially suggested by Henbest.^{8b} The decreased rates observed in benzyl alcohols possessing large α -substituents were ascribed to less efficient adsorption on the reagent surface due to steric effects.

In order to establish optimal experimental conditions, the reaction between benzyl alcohol (4) and MnO_2 (Scheme IV) in THF solvent under an inert atmosphere was monitored by HPLC and ¹H-NMR spectroscopy. Commercially available MnO_2 (J.T. Baker, practical grade) was found to react very slowly with 4, especially in non-hydrocarbon solvents (diethyl ether, THF). Previous work on the activity of various forms of the oxidant suggests that γ - MnO_2 is the most efficient toward benzyl alcohol.⁹ Indeed, this dark-brown amorphous powder, prepared from MnSO_4 and KMnO_4 in water at 60 °C and then dried to a constant weight at the same temperature, gave conveniently fast oxidation.

Perhaps surprisingly, it was found that the reaction of 4 with γ - MnO_2 exhibits linear kinetics to at least 80% reaction (correlation coefficient of ≥ 0.989) according to the following phenomenological rate law:

$$\text{rate} = k[4](\text{mol of MnO}_2/\text{L of reaction mixture})$$

The number of moles of MnO_2 initially present was calculated as the mass of oxidant divided by its molecular weight (86.94). To confirm the purity (molar oxidizing capacity) of the MnO_2 , a limiting amount of the reagent was reacted with an excess of 4. The amount of benzaldehyde ultimately produced showed that the MnO_2 oxidized 0.95 ± 0.06 molar equiv of the alcohol.

Unfortunately, Table I shows that although the kinetic data for a given run are strictly linear, the derived rate constant varies significantly from run to run, not only when different initial concentrations are used but also with similar initial concentrations in different runs. This probably results from changes in the activity of MnO_2 as

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Table II. Kinetic Data for the Reaction of *p*-1 and *m*-1 with MnO₂/THF

compd	run no.	[1] ₀ , M	quantity of MnO ₂ ^a	k ₁ ^b	κ ^{c,d}	k ₂ ^b	temp, °C
<i>p</i> -1	6	0.01	0.02		1.4 ± 0.2 (1.5)		26
	7	0.05	0.10		1.6 ± 0.3 (1.5)		26
	8	0.05	0.10		1.4 ± 0.2 (1.4)		45
	9	0.15	0.26	0.75	1.3 ± 0.4 (1.1)	0.98	45
	10	0.16	0.26	0.18	1.7 ± 0.6 (1.6)	0.31	45
	av				1.5 ± 0.2		
<i>m</i> -1	11	0.10	0.15	1.15	0.10 ± 0.04 (0.10)	0.12	45
	12	0.10	0.14	0.68	0.09 ± 0.3 (0.14)	0.061	45
	13	0.15	0.25	0.62	0.18 ± 0.3 (0.20)	0.11	45
	av				0.12 ± 0.05		

^a Expressed in (moles of MnO₂ added/L of original reaction mixture). ^b Rate constants are in units of 10⁻⁴ L mol⁻¹ s⁻¹. ^c κ = k₂/k₁. Values in parentheses calculated with the method described in ref 11. ^d Error limits are standard deviations.

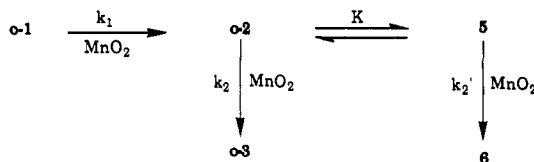
it ages. The same linear kinetic behavior was observed when the reaction was performed under oxygen. However, parallel runs (3 and 4, Table I) show a 75% increase in the rate constant in the presence of oxygen, although no change in the stoichiometry of the reaction was apparent, indicating that the reaction is not simply catalytic in MnO₂.

No over-oxidized carboxylic acid product was produced, regardless of whether the reaction was performed under an inert atmosphere or under oxygen. However, a small amount of 1,4-butanediol was detected by GC/MS in the final reaction mixture. Control experiments showed that THF is slowly oxidized by MnO₂ to give this product.

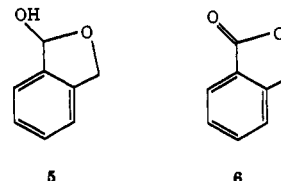
High performance liquid chromatography and 250-MHz ¹H-NMR spectroscopy were again used for kinetic analysis of the reactions of the isomers of diol 1 with MnO₂ (Table II). In order to extract rate constants k₁ and k₂, the relative amounts of 1, 2, and 3 were all monitored as a function of time in this competitive-consecutive reaction scheme. The method developed by Wideqvist^{2,3,10} was used to determine κ (=k₂/k₁) in the case of *p*-1 and *m*-1. These values of κ were compared with those determined independently by our recently reported computational method.¹¹ As shown in Table II, both methods give comparable results.

Generally, Wideqvist's method is able to determine the rate constant k₁. However, although the correlation coefficients for the appropriate graphs were excellent (≥0.995), identical runs gave significantly different k₁ values (runs 9, 10, and 11–13, Table II), just as was found in the case of 4. Nonetheless, the excellent reproducibility observed for the κ (=k₂/k₁) value for all data points throughout all runs demonstrates that both k₁ and k₂ are affected equally by the variable activity of the MnO₂. As a consequence, the κ values are believed to be accurate and can serve as the selectivity criterion for mono-oxidation. Values substantially lower than 0.5 demonstrate that the reaction is synthetically useful for mono-oxidation of unsaturated diols.

Scheme V



In the case of *o*-1 the reaction is less straightforward. In addition to *o*-2 and *o*-3, two cyclic products (5 and 6) were detected by ¹H NMR and GC/MS. The presence



of lactones such as 6 in this and similar reactions has been reported previously in the literature.¹² Hauptman and Blaskovits^{12a} rationalized the formation of 6 as resulting from oxidation of the postulated primary product 5, according to Scheme V. We have found that proton NMR studies not only provide evidence for the presence of 5 in the reaction mixture but also strongly suggest that there is a facile equilibrium involved between *o*-2 and 5, since the concentration ratio [5]/[*o*-2] (~2.7) was found to be constant throughout the reaction. This result is consistent with earlier findings by McClelland and co-workers.¹³ Although the equilibrium constant *K* was measured by NMR using acetone-*d*₆ as solvent (after filtration of the reaction mixture and evaporation of the THF), the formation of product 6 and the good reproducibility of the value of k₂/k₂' throughout each run together suggest that the change of the solvent (from THF to acetone-*d*₆) does not significantly alter this equilibrium.

By measuring the concentration of all the species involved (*o*-1, *o*-2, *o*-3, 5, and 6) as a function of time, rate and equilibrium constants k₁, k₂, k₂', and *K* (Table III) could be determined by the methods described above for *p*-1 and *m*-1. However, in this case κ is determined as (k₂ + k₂')/k₁. The values for the rate constants in Table III demonstrate that for *o*-1 k₁ is an order of magnitude larger than both k₂ and k₂'; the values of k₂ and k₂' are comparable.

Discussion

The present results, summarized below and in Tables I–III, show that the first oxidation of ortho and meta 1 with manganese dioxide is an order of magnitude faster than the second. Thus, from a synthetic standpoint, solid MnO₂ can be successfully used to mono-oxidize the ortho and meta diols. By contrast, in the case of the para isomer the second oxidation is 50% faster than the first.

It is clear that heterogeneous oxidations are controlled not only by the inherent oxidizability of the substrate but also by adsorption/desorption effects.^{8a,14} It has been

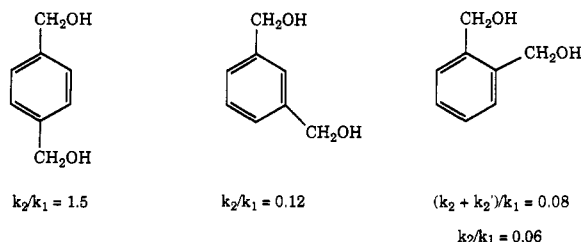
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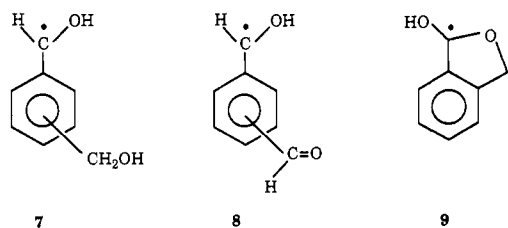
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previously suggested that, in general, electron-donating substituents on aromatic rings stabilize (while electron-withdrawing groups destabilize) benzylic radicals.¹⁵ Recently, a σ^* scale was developed by Arnold¹⁶ to describe quantitatively the effects of meta and para substituents in homogeneous radical substitution reactions at benzylic positions. The σ^* values most relevant to the present study are 4-COMe, 0.060; 4-Me, 0.015; 3-Me, 0.002; 3-CO₂Me, -0.014. These values lead to the prediction that, provided the reaction is controlled mainly by the ease of benzylic C-H oxidation (i.e., homolytic cleavage), the MnO₂ oxidation of *p*-2 should proceed faster than that of *p*-1 by a factor of $\sim 10^{0.045}$ (=1.11), while *m*-2 should undergo oxidation slower than *m*-1 by $\sim 10^{-0.016}$ (=0.96). Our results (Table II) are in the correct direction but of larger magnitude, suggesting a ρ value substantially greater than 1 for this reaction.

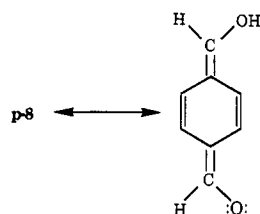
Our results are also qualitatively consistent with the results of extended Hückel calculations¹⁷ on these structures (1, 2, 5, and the corresponding benzyl radicals 7, 8, and 9). The atomic coordinates for the energy-minimized



structures were obtained from molecular mechanics calculations.¹⁸ The calculated bond dissociation energies of the benzylic C-H bonds of the appropriate structures were derived by the equation below and are given in Table IV.

$$\text{BDE} = \text{calcd energy of radical species} + \text{energy of formation of H}^* - \text{calcd energy of precursor}$$

It can be seen from this table that the calculated BDE of the benzylic C-H bond of *p*-1 (5.31 eV) is larger than the value for *p*-2 (5.02 eV). By contrast, the BDE of the same C-H bond of *m*-1 (5.18 eV) is less than that of *m*-2 (5.31 eV). These values seem to be largely controlled by whether or not the C=O in 2 is positioned to engage in through-resonance with the unpaired electron. The situation is more complicated in the case of the ortho isomer. Extended Hückel calculations (Table IV) suggest it should be easier to cleave the benzylic C-H bond in *o*-1 (4.33 eV)



than those in *o*-2 (4.94) and 5 (5.98). Although this is consistent with our findings that $k_2/k_1 = 0.06$ and $k_2' < k_2$ (Scheme V), the BDE for 5 seems too large to account for the more modest differences between k_2' and k_1 ($k_2'/k_1 = 0.038$) as well as k_2' and k_2 ($k_2'/k_2 = 0.61$). This may reflect the limitation of representing the chemisorbed radical intermediate (cf. Scheme III) as an isolated free radical.

Conclusions

The oxidation of the ortho and meta isomers of 1 with γ -MnO₂ in THF gives predominantly products of mono-oxidation (*o*-2, 5, and *m*-2). By contrast, dialdehyde *p*-3 is the major product of the reaction of *p*-1, even when just 1 equiv of the oxidant is used. The differences in behavior between the three isomers are well correlated with the calculated homolytic bond dissociation energies of the benzylic C-H bonds, indicating that adsorption/desorption effects are probably of only minor importance.

Experimental Section

General. The instruments used included the following: Bruker AC 250 (NMR); Hewlett Packard Model 5995 (MS); Spectra-Physics SP 8800 with Spectra 100 variable wavelength UV detector and Hewlett Packard 3394 integrator (HPLC). The HPLC analyses were performed with a 235 \times 4.70 (i.d.) mm Whatman P/5 ODS 3 reversed phase column. The response factors for each aldehyde product (P) relative to the starting alcohol (A) were determined by HPLC analysis of standard solutions and application of the equation $R_{fp} = (\text{moles of P}/\text{moles of A})/(\text{signal area for A}/\text{signal area for P})$. Standard solutions were prepared from pure materials or reaction mixtures quantitatively analyzed by ¹H NMR. The response factors are given below. The numbers in parentheses represent the wavelength setting of the HPLC detector. Benzaldehyde, 0.011 ($\lambda = 252$ nm); *p*-2, 0.013 ($\lambda = 261$ nm); *p*-3, 0.011 ($\lambda = 261$ nm); *m*-2, 0.019 ($\lambda = 261$ nm); *m*-3, 0.020 ($\lambda = 261$ nm).

Materials. The three isomers of 1 and 3 were supplied by Aldrich Chemical Company. *p*-1 was recrystallized from chloroform and *o*-1 was sublimed prior to use. Benzyl alcohol and benzaldehyde were distilled under N₂. THF was freshly distilled over potassium. Manganese sulfate (MnSO₄·H₂O) was supplied by Fisher Scientific.

Preparation of Active γ -MnO₂.¹⁹ To a 2.0-L round-bottomed flask containing 75 g of MnSO₄·H₂O in 1.4 L of water immersed in an oil bath at 60 °C was added slowly 0.5 L of an aqueous solution containing 50 g of KMnO₄. After the solution was stirred for 90 min, the precipitate was filtered and washed thoroughly with water. The solid material was oven-dried at 60 °C for several days to give 49.6 g (77% yield) of a dark-brown amorphous powder, which was kept in a dessicator.

Kinetic Method. After argon was bubbled for several minutes through a mixture of the desired amount of MnO₂ in 10.0 mL of THF in a two-neck 25-mL round-bottomed flask inserted in an oil bath at 45 \pm 0.1 °C, a balloon was fitted on one neck and a stopcock with a septum on top of the other neck. More argon was added until the balloon was inflated, and then a 10.0-mL solution of THF containing the desired amount of the diol (or benzyl alcohol) was added via syringe. Aliquot portions (0.1–2 mL) of the continuously stirred heterogeneous mixture were

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Table III. Kinetic Data for the Reaction of *o*-1 with MnO₂/THF at 45 °C

run	[<i>o</i> -1] ₀ , M	quantity of MnO ₂ ^a	k ₁ ^b	κ ^{c,d}	(k ₂ + k ₂ ') ^{e,f}	K ^{c,g}	(k ₂ /k ₂ ') ^{c,i}	k ₂ ^{b,h}	(k ₂ ') ^{b,h}
14	0.040	0.13	2.2	0.10 (0.09)	0.22	2.6	1.6	0.135	0.084
15	0.026	0.15		0.08 (0.05)		2.7	1.4		
16	0.090	0.15		0.07 (0.07)		2.8	1.2		
av				0.08 ± 0.02		2.7 ± 0.1	1.4 ± 0.2		

^a Expressed in (moles of MnO₂ added/L of original reaction mixture). ^b Rate constants k₁, k₂, and k₂' are in units of 10⁻⁴ M⁻¹ s⁻¹. ^c Error limits are standard deviations. ^d Values in parentheses calculated with the method in ref 11. ^e Mean of a point-by-point κ. ^f Calculated from k₂ + k₂' = κk₁. ^g Mean of a point-by-point K (= [5]/[*o*-2]). ^h Calculated from k₂ + k₂' and k₂/k₂'. ⁱ Mean of a point-by-point k₂/k₂' (= [o-3]/[6]).

Table IV. Bond Dissociation Energies of Benzylic C-H Bonds from Extended Hückel Calculations

compd	BDE, eV	compd	BDE, eV
<i>o</i> -1	4.33	<i>m</i> -2	5.31
<i>o</i> -2	4.94	<i>p</i> -1	5.31
5	5.98	<i>p</i> -2	5.02
<i>m</i> -1	5.18		

withdrawn every 2-6 h, filtered, diluted with water, and analyzed by HPLC (or filtered, evaporated, dissolved in acetone-*d*₆/TMS and analyzed by ¹H-NMR spectroscopy). Absolute concentrations of 1 (or 4), 2, and 3 (or benzaldehyde) were determined from HPLC or ¹H-NMR integrations (corrected for response factors) and the known initial concentration of the alcohol. The unreacted amount of MnO₂ at each analysis time was calculated from its known initial amount less the total amount of aldehyde product(s) formed. Thus in the reaction of benzyl alcohol (moles of MnO₂/L of original reaction mixture) = (initial moles of MnO₂/L of original reaction mixture) - [benzaldehyde] and in the reaction of the diols (moles of MnO₂/L of original reaction mixture) = (initial moles of MnO₂/L of original reaction mixture) - [2] - 2[3].

The apparent rate constant *k* for the reaction of benzyl alcohol was determined by a usual second-order rate plot. The determination of the apparent rate constants for the consecutive-competitive reactions of *p*-1 and *m*-1 was performed as before^{2,3} by the graphical integration method of Wideqvist.¹⁰ For each data point the value of ln ([1]₀/[1]) and Θ (≡ ∫₀^t {unreacted moles of MnO₂/L of original reaction mixture} dt) were determined. The value of k₁ was found as the slope of a linear plot of ln ([1]₀/[1]) versus Θ. Then for each data point, the value of κ (=k₂/k₁) was determined from the equation

$$\frac{1}{\kappa - 1} \left[1 - \left(\frac{[1]}{[1]_0} \right)^{\kappa - 1} \right] - \frac{[2]}{[1]} = 0$$

The κ value for a given run was the mean of the point-by-point κ values. From this value, k₂ was calculated (k₂ = κk₁). The value of κ was determined also by a computational method, the details of which can be found in ref 11. For the kinetic analysis of the reaction of *o*-1 the concentrations of *o*-1, *o*-2, *o*-3, 5, and 6 were determined from ¹H-NMR integrations and the known initial amount of *o*-1. The unreacted amount of MnO₂ was calculated from the equation (moles of MnO₂/L of reaction mixture) = (moles of MnO₂ initially added/L of reaction mixture) - [*o*-2] - 2[*o*-3] - [5] - 2[6]. The value of k₁ was determined graphically as described above. The κ value in this reaction (Scheme IV) defined as κ = (k₂ + k₂')/k₁ was determined from the equation

$$\frac{1}{\kappa - 1} \left[1 - \left(\frac{[o-1]}{[o-1]_0} \right)^{\kappa - 1} \right] - \frac{[o-2] + [5]}{[1]} = 0$$

The κ value for a given run was again the mean of the point-by-point κ values.

Partial 250-MHz proton NMR and mass spectral data of the species involved in this reaction are given below. In each case these data were consistent with previously published lower resolution spectra. Spectra of pure material in acetone-*d*₆/TMS were obtained for *o*-1 and *o*-3, whereas the data for *o*-2, 5, and 6 were obtained by GC/MS and ¹H-NMR analysis of the reaction mixture after the appropriate treatment. Acetone-*d*₆/TMS was used for all NMR analyses; peaks marked with an asterisk are those used for determining relative amounts of reactants and products. Acetone or THF was used as a solvent for the GC/MS analyses.

The numbers in parentheses in the MS spectra are relative abundances.

o-1: ¹H NMR²⁰ δ 4.31* (t, *J* = 4.8 Hz, 2 H), 4.71 (d, *J* = 4.8 Hz, 4 H). For the MS spectrum, see ref 2a.

o-2: ¹H NMR²¹ δ 4.47 (t, *J* = 5 Hz, 1 H), 5.03* (d, *J* = 5 Hz, 2 H), 10.28* (s, 1 H); MS *m/z* 136 (10), 135 (13), 119 (13), 118 (97), 92 (11), 91 (21), 90 (82), 89 (100), 87 (8), 86 (9), 85 (5), 79 (15), 77 (28), 74 (7), 65 (7), 64 (13), 63 (65), 62 (34), 61 (14), 59 (13), 53 (7), 52 (7), 51 (25), 50 (24), 49 (7), 43 (5), 40 (8), 39 (48), 38 (17), 37 (12).

o-3: ¹H NMR²² δ 10.54* (s, 2 H); MS *m/z* 135 (3), 134 (26), 133 (15), 107 (3), 106 (36), 105 (100), 79 (2), 78 (19), 77 (99), 76 (13), 75 (8), 74 (18), 73 (4), 63 (6), 62 (6), 61 (4), 53 (5), 52 (14), 51 (72), 50 (50), 49 (7), 39 (16), 38 (11), 37 (9).

5: ¹H NMR²¹ δ 4.91 (d, *J* = 13 Hz, 1 H), 5.12* (dd, *J*₁ = 2 Hz, *J*₂ = 13 Hz, 1 H), 5.58 (d, *J* = 7.5 Hz, 1 H), 6.41 (dd, *J*₁ = 2 Hz, *J*₂ = 7.5 Hz, 1 H); MS *m/z* 119 (12), 118 (96), 91 (5), 90 (63), 89 (100), 87 (14), 86 (8), 85 (4), 64 (12), 63 (54), 62 (25), 61 (12), 59 (17), 51 (10), 50 (13), 43 (12), 41 (8), 40 (5), 39 (37), 38 (16), 37 (12).

6: ¹H NMR^{23,24b} δ 5.36* (s, 2 H); MS²⁴ *m/z* 134 (33), 133 (16), 106 (29), 105 (85), 89 (8), 78 (18), 77 (100), 76 (14), 75 (10), 74 (19), 73 (7), 63 (10), 62 (8), 61 (6), 53 (8), 52 (16), 51 (71), 50 (48), 49 (9), 39 (19), 38 (13), 37 (13).

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Stereoselectivity of the α-Sulfonylation of 4-Phenylbutyrolactone. Configurational and Conformational Analyses by ¹H NMR Spectroscopy¹

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γ-Butyrolactones have emerged as important synthons and building blocks for the synthesis of complex natural products.² Their stereochemistry and conformational

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