Linked Diene–Dienophile Ester 31. To 141 mg (0.68 mmol) of *N,N'*-dicyclohexylcarbodiimide in 0.1 mL of anhydrous THF at 0 °C under a nitrogen atmosphere was added dropwise 113 mg (0.51 mmol) of acid **5** in 0.7 mL of anhydrous THF. The mixture was stirred at 0 °C for 10 min, and 120 mg (0.34 mmol) of alcohol **28** in 2.5 mL of anhydrous THF was added. The mixture was stirred for 24 h at 0 °C and subsequently for 24 h at 25 °C. The product was diluted with ether and filtered. The filtrate was washed successively with water and brine and dried over anhydrous magnesium sulfate. The product was chromatographed on a 20 × 20 cm preparative layer Merck silica gel F254 plate in 1:3 ethyl acetate–hexane to afford (53%) of the acetal ester **29**: R_f 0.28; IR (TF) 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, J = 6.8 Hz, 3, C-8 CH_3), 1.02 (s, 3, C-4a CH_3), 3.40–3.65 (m, 2, $OCOCH_2$), 3.7–3.95 (m, 4, OCH_2CH_2O), 4.41 and 4.63 (AB q, J = 11.2 Hz, 2, $CH_2C_6H_5$), 5.13 (d, J = 10.6 Hz, 1, CH=CH_2), 5.19 (s, 1, acetal H), 5.56–5.72 (m, 2, CH=CH_2, and CHOCO), 5.96 (C-4 vinylic H), 6.40–6.56 (m, 2, CH=C(SPh)CH=CH_2), 7.05–7.40 (m, 10, aromatic H); ^{13}C NMR ($CDCl_3$) δ 64.56 and 64.95 (OCH_2CH_2O), 70.07 (C-2), 71.24 (C-7), 83.59 ($CH_2C_6H_5$), 102.89 (acetal C), 117.58 (CH=CH_2), 170.63 ($OCOCH_2$); mass spectrum (70 eV), m/e (relative intensity) 560 (M^+, 23), 341 (15), 233 (16), 204 (17), 192 (82), 176 (39), 175 (61), 160 (16), 110 (71), 109 (33), 91 (100); exact mass spectrum, calcd for $C_{34}H_{40}O_5S$ m/e 560.2597, found 560.2610.

The procedure of Snitman[30] was repeated by using 76.7 mg (0.14 mmol) of acetal ester **29** in 6 mL of 1:2:3 1 M hydrochloric acid–acetic acid–THF to afford, after preparative layer chromatography on a 20 × 20 cm Merck silica gel F254 plate in 1:3 ethyl acetate–hexane, 51 mg (72%) of **31**: R_f 0.36; IR (TF) 1733, 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (d, J = 6.5 Hz, 3, C-8 CH_3), 1.12 (s, 3, C-4a CH_3), 3.40–3.65 (m, 2, $OCOCH_2$), 4.43 and 4.65 (AB q, J = 11.7 Hz, 2, $CH_2C_6H_5$), 5.12 (d, J = 10.3 Hz, 1, CH=CH_2), 5.61 (d, J = 15.9 Hz, 1, CH=CH_2), 5.78 (t, J = 8.9 Hz, 1, CHOCO), 6.40–6.56 (m, 2, CH=C(SPh)CH=CH_2), 6.68 (s, 1, C-4 vinylic H), 7.05–7.43 (m, 10, aromatic H), 9.36 (s, 1, CHO); ^{13}C NMR ($CDCl_3$) δ 67.12 (C-2), 71.34 (C-7), 83.11 ($CH_2C_6H_5$), 117.41 (CH=CH_2), 162.68 (C-4), 170.37 ($OCOCH_2$), 191.86 (CHO); exact mass spectrum calcd for $C_{32}H_{36}O_4S$ m/e 516.2331, found 516.2336.

Linked Diene–Dienophile Ester 32. The procedure described for the preparation of **31** was repeated by using 35 mg (0.098 mmol) of alcohol **28** and 27.4 mg (0.24 mmol) of 3,5-hexadienoic acid to afford, after coupling and hydrolysis, 8.9 mg (22%) of **32**: IR ($CHCl_3$) 1725, 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (d, J = 5.9 Hz, 3, C-8 CH_3), 1.12 (s, 3, C-4a CH_3), 3.00–3.20 (m, 2, $OCOCH_2$), 4.44 and 4.66 (AB q, J = 11.4 Hz, 2, $CH_2C_6H_5$), 5.06 (d, J = 9.5 Hz, 1, CH=CH_2), 5.17 (d, J = 17.3 Hz, 1, CH=CH_2), 5.70–5.86 (m, 2, $CHOCOCH_2CH$=$CHCH$=CH_2), 6.08–6.22 (m, 1, CH_2CH=$CHCH$=CH_2), 6.25–6.43 (m, 1, CH_2CH=$CHCH$=CH_2), 6.71 (s, 1, C-4 vinylic H), 7.20–7.40 (m, 5, aromatic H), 9.4 (s, 1, CHO); exact mass spectrum calcd for $C_{26}H_{32}O_4$ m/e 408.2301, found 408.2307.

1,2,4a,5,6,7,8,8aα-Octahydro-7β-(benzyloxy)-4aβ,8α-dimethyl-2α-hydroxynaphthalene-3-carboxaldehyde (34). The procedure of Snitman[31] was repeated by using 31.3 mg (0.087 mmol) of **28** in 11.5 mL of 1:2:3 1 M hydrochloric acid–acetic acid–THF to afford, after preparative layer chromatography on a Merck silica gel F254 plate in 1:3 ethyl acetate–dichloromethane, 18 mg (66%) of **34**: IR ($CHCl_3$) 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (d, J = 6.6 Hz, 3, C-8 CH_3), 1.12 (s, 3, C-4a CH_3), 4.44 (part of AB q, J = 11 Hz, 1, $CH_2C_6H_5$), 4.57–4.70 (m, 2, CHOH and $CH_2C_6H_5$), 6.57 (s, 1, C-4 vinylic H), 7.20–7.50 (m, 5, aromatic H), 9.41 (s, 1, (CHO); exact mass spectrum calcd for $C_{20}H_{26}O_3$ m/e 314.1884, found 314.1882.

Linked Diene–Dienophile Ester 35. The procedure described for the preparation of **31** was repeated by using 339 mg (1.53 mmol) of acid **5**, 423 mg (2.04 mmol) of *N,N'*-dicyclohexylcarbodiimide, and 171 mg (1.02 mmol) of 3-hydroxy-2,6,6-trimethyl-1-cyclohexenecarboxaldehyde[31] to afford, after chromatography on two 20 × 20 cm Macherey Nagel silica gel plates in dichloromethane, 235 mg (63%) of **35**: R_f 0.44; IR (TF) 1734, 1677, 1615, 1580 cm^{-1}; NMR ($CDCl_3$) δ 1.20 and 1.27 (2 s, 6, $C(CH_3)_2$), 2.00 (s, 3, vinylic CH_3), 3.57 (d, J = 7.3 Hz, 2, $CHOCOCH_2$), 5.14 (d, J = 11 Hz, 1 vinylic H), 5.33 (t, J = 5.9 Hz, 1, $CHOCOCH_2$), 5.65 (d, J = 17 Hz, vinylic H), 6.45 (m, 2, vinylic H), 7.10–7.40 (m, 5, aromatic H), 10.13 (s, 1, CHO); exact mass spectrum, calcd for $C_{22}H_{26}O_3S$ m/e 370.1602, found 370.1602.

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Registry No. (*Z*)-**5**, 84132-29-6; (*E*)-**5**, 84132-30-9; **6**, 5296-64-0; (±)-**7**, 84132-31-0; **8Z**, 84132-32-1; **8E**, 84132-33-2; (*Z*)-**12**, 84132-34-3; (±)-**13**, 84132-35-4; (±)-**14**, 84132-36-5; (±)-**16**, 84132-37-6; (±)-**17**, 84132-38-7; **18**, 84132-39-8; **19**, 84132-40-1; (±)-**21**, 84132-41-2; (±)-**22**, 84132-42-3; (±)-**23**, 84132-43-4; (±)-**24**, 84132-44-5; (±)-**25**, 84132-45-6; (±)-**26**, 84132-46-7; (±)-**27**, 84132-47-8; (±)-**28**, 84132-48-9; (±)-2,β-**28**, 84132-49-0; (±)-**29**, 84143-11-3; (±)-**31**, 84132-50-3; (±)-**32**, 84132-51-4; (±)-**34**, 84132-52-5; (±)-**35**, 84132-53-6; ethyl (2*E*,4*E*)-4,5-epoxy-2-hexenoate, 84173-36-4; (±)-3′,4′,4a′,5′,6′,7′-hexahydro-4a′,8′-dimethylspiro[1,3-dioxolane-2,2′-(1′*H*)-naphthalene], 84132-54-7; (*E*)-3,5-hexadienoic acid, 32775-95-4; (±)-3-hydroxy-2,6,6-trimethyl-1-cyclohexenecarboxaldehyde, 60078-92-4; ethylene oxide, 75-21-8; maleic anhydride, 108-31-6.

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Regioselectivity in Nickel(II)-Mediated Oxidations of Diols

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Oxidations of 2- and 4-substituted 1,4-butanediols to their corresponding γ-butyrolactones by the combination of molecular bromine and nickel(II) alkanoate occur with a high degree of regioselectivity. The influence of the alkanoate ligand, of substituents at the 2-position of 1,4-butanediols, and of solvent on oxidation regiocontrol is examined, and comparison of regioselectivity in diol oxidations is made with representative conventional oxidative methods. Regiocontrol in nickel(II)-mediated reactions is proposed to be derived from steric constraints for oxidative hydrogen transfer to the alkanoate ligand of nickel(II) in the diol-associated complex. Alternate use of cobalt(II) alkanoates provides regiocontrol in diol oxidations that is comparable or superior to that obtained with nickel(II) alkanoates in bromine oxidations.

We have previously reported the facile oxidation of alcohols by benzoyl peroxide in combination with nickel(II) bromide[1] and by molecular bromine in combination with nickel(II) benzoate.[2] Nickel(II) bromide serves as a cat-

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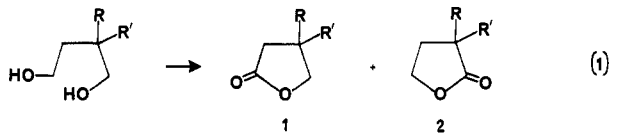
Table I. Regioselectivity in Oxidations of 2,2-Disubstituted 1,4-Butanediols[a]

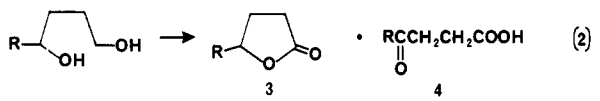
oxidant (amount)[b]	mediator (amount)[b]	temp, °C	R = R′ = Ph yield, %[c]	R = R′ = Ph %1:%2	R = Et, R′ = Me yield, %[c]	R = Et, R′ = Me %1:%2	R = R′ = Me yield, %[c]	R = R′ = Me %1:%2
Br_2 (8.0)	$Ni(OAc)_2$ (5.0)	20	90	20	77	1.5	95	1.4
Br_2 (8.0)	$Ni(OBz)_2$ (5.0)	20	99	24	99	19	87	6.5
Br_2 (8.0)	$Ni(OOCCMe_3)_2$ (5.0)	20	99	>100	88	23	99	6.6
Br_2 (8.0)	$Ni[OOCCH(Et)Bu]_2$ (5.0)	20	99	>100	93	35	82	14
Cl_2[d]	$Ni(OBz)_2$ (5.0)	20	99	>100	99	3.8	86	1.2
$(CH_3)_3COCl$ (10)	$Ni(OBz)_2$ (5.0)	20			55	3.2		
Br_2 (8.0)	LiOBz (10)	20	40[e]	0.50	58	0.45	43	0.39
Bz_2O_2 (3.0)	$NiBr_2$ (10)	60	99	>100	60	9.1	60	6.7
Bz_2O_2 (3.0)	LiBr (10)	60	99	1.0	60	2.4		
Br_2 (3.2)	HMPA (0.6)[f]	0	48	0.14	54	0.93	55	0.83
$HCrO_4^-$[g]		20	99	1.9	64	1.9	89	2.1
$C_5H_5N{\cdot}HCl{\cdot}CrO_3$ (4.0)[h]		25	99	2.4				
$Ph_3C^+BF_4^-$ (2.6)		60	77	>100	59	49	47	24

[a] Unless specified otherwise, reactions were performed in anhydrous acetonitrile. [b] Number of moles based on diol. [c] Yield of isolated products. [d] Gaseous chlorine was bubbled through reaction solution until oxidation was complete. [e] A 58% yield of unreacted diol was recovered. [f] Reaction was performed in methylene chloride (ref 5). [g] Diol in aqueous acetone was titrated with chromic acid (ref 7). [h] Reaction was performed in methylene chloride (ref 8).

alyst for the oxidation of alcohols by benzoyl peroxide, whereas oxidations by bromine require the use of a molar excess of the nickel(II) alkanoate. The principal advantages of these oxidative methods are exemplified in the regioselective oxidations of 2,2-disubstituted 1,4-butanediols (eq 1), which occur with a high degree of selectivity



(1)



(2)

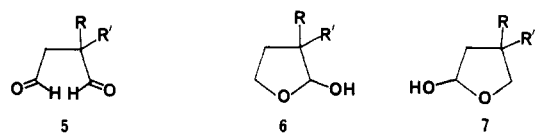
at the 4-position,[2,3] and of primary alcohols in 4-substituted 1,4-butanediols (eq 2).[4] The selectivity that is afforded to diol oxidations by nickel(II) has been suggested to be steric in origin and to arise from oxidation of a coordination complex between the diol and nickel(II).[3,4] We now report results from detailed investigations of these oxidative methods that exemplify their unique advantages for selective oxidations of diols, that define the nature of their selectivity, and that offer alternatives to nickel(II) for selective oxidations of diols.

Results and Discussion

Comparative results for the oxidation of representative 2,2-disubstituted 1,4-butanediols to their corresponding lactone products (eq 1) by methods utilizing nickel(II) compounds to mediate oxidation selectivity are reported in Table I. In the series of nickel(II) alkanoates, selectivity for oxidation at the 4-position leading to lactone 1 increases with increasing steric bulk of the alkanoates: acetate < benzoate < pivalate < 2-ethylhexanoate. Furthermore, the use of bromine in combination with nickel(II) benzoate provides greater selectivity than the corresponding use of chlorine or *tert*-butyl hypochlorite. Molecular iodine was relatively ineffective and unselective for these transformations; with 2-ethyl-2-methyl-1,4-butanediol in the presence of nickel(II) benzoate at 20 °C, lactones 1 and 2 were produced in only 22% yield after 5 h (1:2 = 5.8). Substitution of lithium benzoate for nickel(II) benzoate results in low yields for lactone formation, and a reversal in product selectivity is observed.

In reactions with benzoyl peroxide at 60 °C, nickel(II) bromide drastically increases oxidation selectivity relative to lithium bromide (Table I). For comparison, neither oxidations by molecular bromine in acetonitrile,[5] the solvent employed for nickel(II)-mediated reactions, nor bromine oxidations in the presence of HMPA[6] exhibits any significant relationship to the nickel(II)-mediated transformations.

Chromic acid oxidations, although resulting in high yields of lactone products (Table I), are characteristically unselective. Use of the Swern oxidant (Me_2SO/oxalyl chloride)[9] with 2,2-diphenyl-1,4-butanediol produced a complex product mixture of which dialdehyde **5** (28% yield) and hemiacetals **6** and **7** (12% and 6% yield, respectively) were major components; lactones **1** and **2** were not produced in meaningful amounts from either 2,2-diphenyl-1,4-butanediol or 2-ethyl-2-methyl-1,4-butanediol.



Trityl tetrafluoroborate, an alcohol oxidant[10] whose kinetic activation parameters in ether oxidations[11] suggest its capability for oxidative selectivity based on steric factors, is the only reagent of those examined whose selectivity in oxidations of 2,2-disubstituted-1,4-butanediols is comparable to that obtained in nickel(II)-mediated reactions.

The extent to which substituents at the 2-position of 1,4-butanediols affect oxidative selectivity is exemplified in the results presented in Tables I and II. Oxidations

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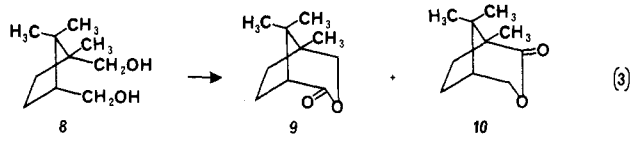
Table II. Regioselectivity in Oxidations of 2-Phenyl-1,4-butanediol and of the 1,5-Diol 8[a]

			R = Ph; R′ = H		8 → 9 + 10	
oxidant (amount)[b]	mediator (amount)[b]	temp, °C	yield, %[c]	1:2	yield, %[c]	9:10
Bz_2O_2 (3.0)	$NiBr_2$ (5.0)	60	54	8.2	57	0.90
Br_2 (9.0)	$Ni(OAc)_2$ (5.0)	20			57	1.6
Br_2 (9.0)	$Ni(OBz)_2$ (5.0)	20	76	12	97	2.0
Br_2 (9.0)	$Ni[OOCCH(Et)Bu]_2$ (5.0)	20			88	2.2
$C_5H_5N{\cdot}HCl{\cdot}CrO_3$ (3.0)		20	94	1.5	63	1.1

[a] Except for oxidations by pyridinium chlorochromate, which were performed in methylene chloride (ref 8), reactions were performed in anhydrous acetonitrile. [b] Number of moles based on diol. [c] Yield of isolated products.

of 2-phenyl-1,4-butanediol, for which the single phenyl substituent offers effective control of selectivity in nickel(II)-mediated reactions, and of the sterically encumbered diol 8 (eq 3), whose *gem*-dimethyl group influences oxi-



(3)

dative selectivity at both carbinol centers, suggest the general features of substituent control of oxidation selectivity. In acyclic systems a single phenyl substituent at the 2-position of 1,4-butanediols offers somewhat greater oxidative regiocontrol than do two methyl substituents, also at the 2-position. Lactone production from diol 8, even with the combination of molecular bromine and nickel(II) 2-ethylhexanoate (Table II), remains a relatively unselective process.[12] Attempts to extend this methodology to the production of δ-valerolactones from acyclic 1,5-pentanediols resulted in complex product mixtures and low yields of the desired lactones; however, 1,8-naphthalenedimethanol was oxidized to the corresponding lactone by the combination of benzoyl peroxide and nickel(II) bromide in nearly quantitative yield.

Oxidation of diols to lactones occurs in two stages. Regioselectivity is achieved in the initial oxidation of diol to hydroxyaldehyde. The extent of intramolecular hemiacetal formation is critical to the outcome of these oxidations since α-halogenation of the aldehyde and intermolecular hemiacetal formation cause decreased yields of lactone products.[13] The inverted selectivities obtained in oxidations of 1,4-diols by molecular bromine and their corresponding low yields of lactone products (Table I), as well as the lack of success in attempts to produce δ-valerolactones from acyclic 1,5-pentanediols, are direct consequences of these competing reactions. Furthermore, whereas nickel(II)-mediated oxidations of 4-substituted 1,4-butanediols (eq 2) produce the corresponding lactones in relatively high yields,[4] similar oxidations of 2,2,4-trimethyl-1,3-pentanediol resulted in nearly exclusive oxidation of the primary alcohol (aldol:ketol > 8), but even with the benzoyl peroxide/nickel(II) bromide combination, which has been successful for oxidations of primary alcohols to aldehydes,[1] the hydroxy aldehyde could be obtained in only 60% yield.

Acyl hypohalites, formed by interaction of the peroxide (eq 4) or halogen (eq 5) reactant with the appropriate

$$NiBr_2 + Bz_2O_2 \rightarrow (BzO)NiBr + BzOBr \quad (4)$$

$$Ni(OOCR) + X_2 \rightarrow (RCOO)NiX + RCOOX \quad (5)$$

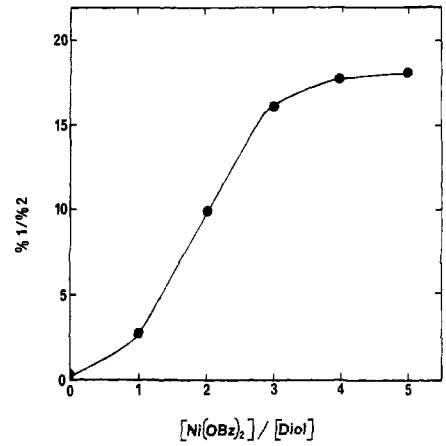


Figure 1. Dependence of selectivity for lactone formation (%1/%2) on the molar ratio of nickel(II) benzoate to 2-ethyl-2-methyl-1,4-butanediol. Reactions were performed at 20 °C in acetonitrile at a constant $[Br_2]/[Ni(OBz)_2]$ of 1.6.

nickel(II) compound, are plausible oxidants for the conversion of alcohols to carbonyl compounds. Benzoyl peroxide is known to form benzoyl hypohalites in reactions with ionic halides[14,15] and with nickel(II) bromide results in the eventual production of nickel(II) benzoate. Reactions of nickel(II) alkanoates with molecular bromine that are performed in the presence of primary or secondary alcohols form nickel(II) bromide as the sole nickel-containing product. However, attempts to trap acyl hypohalites through electrophilic addition to olefins were unsuccessful; reactions of benzoyl peroxide with nickel(II) bromide at 60 °C that were performed with styrene resulted in the exclusive formation of 1,2-dibromo-1-phenylethane and with cyclohexene gave *trans*-1,2-dibromocyclohexane and a minor amount (<10% yield) of *N*-(2-bromocyclohexyl)acetamide as the sole addition products. Furthermore, bromobenzene, anticipated from decarboxylation of benzoyl hypobromite,[16] was not produced in $Br_2/Ni(OBz)_2$ oxidations of alcohols and was only a minor product in $Bz_2O_2/NiBr_2$ oxidations (<5% yield).[17]

Molecular bromine is an alternate choice as the alcohol oxidant in nickel(II)-mediated reactions. However, in the absence of nickel(II) compounds bromine is a relatively unselective oxidant of diols and intercepts the intermediate hydroxyaldehyde to form derivative brominated products. In addition, there is no apparent difference in selectivity or product yields when bromine oxidations are performed in the presence or absence of nickel(II) bromide. In the absence of alcohol, nickel(II) benzoate decolorizes molec-

(12) Attempts to utilize trityl tetrafluoroborate for the oxidation of 8 at 60 °C in acetonitrile resulted in the recovery of starting material.

(13) Ester formation and α-halogenation were separately investigated with primary alcohols under reaction conditions identical with those reported in Table I.

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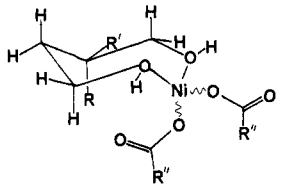
(16) Wilson, C. V. *Org. React.* **1957**, *9*, 332.

(17) Bromobenzene is a characteristic product, formed in as high as 35% yield based on limiting bromide, of alcohol oxidations performed with benzoyl peroxide in the presence of LiBr or $MgBr_2$.

ular bromine, but in less than equivalent molar amounts, and attempts to identify a unique nickel product from this transformation were not successful. $Ni(dmgH)_2$ (dmgH = dimethylglyoximate) and $Ni(Me_2dtc)_2$ (Me_2dtc = *N,N*-dimethyldithiocarbamate) actually inhibit alcohol oxidations by bromine that are performed in their presence, probably as a result of ligand oxidation by bromine.[18]

Nickel(II) compounds are capable of molecular associations with alcohols and ethers,[19,20] and it is attractive to speculate that selectivity in diol oxidations is derived from diol-associated nickel complexes. Oxidation selectivity is dependent on the number of molar equivalents of nickel(II) alkanoate employed (Figure 1) and is responsive to the steric bulk of the alkanoate employed (Tables I and II).[21] Diol association with the nickel(II) alkanoate places the alkanoate ligand in close proximity to hydrogens on the carbinol carbon (11). Although the proximal distance from



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the alkanoate carbonyl group to a hydrogen on the carbinol carbon will be dependent on the geometry of the complex at nickel, there is certain to be less steric interference with hydrogen transfer from the 4-position to the alkanoate than from the 1-position. The dependence of oxidation selectivity on the relative amount of $Ni(OOCR)_2$ employed and on the structure of the alkanoate, as well as the lack of involvement by $NiBr_2$ in bromine oxidations, suggests this intimate participation of the alkanoate ligand. Whether molecular bromine undergoes direct electron transfer with the carbinol that is associated with nickel(II) alkanoate[22] (Scheme I) or initiates electron transfer

Scheme I

$$HO\sim CH_2OH + Ni(OOCR)_2 \rightleftharpoons (HO\sim CH_2OH)Ni(OOCR)_2 \quad (6)$$

$$(HO\sim CH_2OH)Ni(OOCR)_2 + X_2 \rightarrow (HO\sim CH{=}^{+}OH)Ni(OOCR)_2 + HX + X^- \quad (7)$$

$$(HO\sim CH{=}^{+}OH)Ni(OOCR)_2 + HX + X^- \rightarrow HO\sim CHO + NiX_2 + 2RCOOH \quad (8)$$

Scheme II

$$(HO\sim CH_2OH)Ni(OOCR)_2 + X_2 \rightarrow [(HO\sim CH_2OH)NiX(OOCR)_2]^+(X^-) \quad (9)$$

12

$$12 \rightarrow [(HO\sim CH{=}^{+}OH)NiX(OOCR)](X^-) + RCOOH \quad (10)$$

$$[(HO\sim CH{=}^{+}OH)NiX(OOCR)](X^-) \rightarrow HO\sim CHO + NiX_2 + RCOOH \quad (11)$$

through nickel (Scheme II) is not defined by this investigation. In Scheme I molecular halogen is the hydride receptor for the coordinated diol, and the function of the nickel(II) alkanoate is to provide a steric bias at the sites from which hydride transfer can occur. In Scheme II **12**, either as a short-lived intermediate or as a transition state in the oxidation step, is proposed to provide activation of alkanoate ligands which serve as intramolecular hydride receptors. This latter mechanistic possibility describes a direct participatory role for nickel(II) in these oxidations and provides an efficient accounting of the influence of oxidant (Br_2, Cl_2, or *t*-BuOCl) and nickel(II) alkanoate on selectivity.

The solvent employed for these reactions has a remarkable influence on oxidation selectivity. For bromine oxidations of 2,2-dimethyl-1,4-butanediol performed in the presence of $Ni(OBz)_2$, the use of trimethylacetonitrile resulted in a 99% yield of lactone products but with a selectivity (**1:2**) of only 2.4 (compare with Table I). Similarly, use of methylene chloride provided the corresponding lactones in 81% yield (**1:2** = 2.2). Combination of acetonitrile with methylene chloride (20:80) resulted in an increase in oxidation selectivity (**1:2** = 4.1, 81% yield) over that obtained with methylene chloride alone. Use of DMF resulted in only a 30% yield of lactone products (**1:2** = 4.0). Obviously acetonitrile, which is an exceptionally effective coordinating ligand for nickel(II),[23] plays a special role in these reactions. This solvent dependence suggests that acetonitrile coordination with the nickel(II) alkanoate complex of the diol, which is consistent with either Scheme I or Scheme II, is integral to effective regiocontrol in these oxidations.

Representative metal alkanoates were utilized to mediate the oxidation of 2,2-disubstituted 1,4-butanediols to determine if nickel(II) alkanoates are unique among metal alkanoates in their promotion of bromine oxidation and influence on regioselectivity. As is evident from the results in Table III, cobalt(II) alkanoates exhibit a similar influence on oxidation selectivity, which in select cases is superior to that observed with the corresponding nickel(II) alkanoates. Lead(II), iron(III), and copper(II) alkanoates are comparatively unsuitable as a result of low yields for lactone products and relative lack of regioselectivity. Chromium(III) 2-ethylhexanoate was ineffective for bromine oxidation of 1-phenylethanol, and its use in oxidations of diols was not pursued.

Cobalt(II) alkanoates are also effective for regioselective oxidations of primary alcohols in 4-substituted 1,4-butanediols.[4] With 1,4-decanediol, bromine oxidation in the presence of $Co(OBz)_2$ yielded 42% of the corresponding lactone (**3**) and 31% of the keto acid (**4**), which is somewhat greater than the selectivity achieved by using $Ni(OBz)_2$ under identical conditions.[4] Cobalt(II) cyclohexanebutyrate is comparatively unselective. Trityl tetrafluoroborate, Br_2/HMPA, and pyridinium chlorochromate are highly selective for oxidation of the secondary alcohol in 4-substituted 1,4-butanediols.

Experimental Section

Materials and Methods. Instrumentation has been previously described.[24] Use was made of 1-m 20% Carbowax 20M, 10% OV-275, and 15% SE-30 columns for GC separations of isomeric products. Benzyl ether was employed as an internal standard for quantitative GC analyses, and yields were calculated with the use of separately determined relative thermal conductivity values. 2,2-Dimethyl-1,4-butanediol, 2,2-dimethyl-1,5-pentanediol, 2-

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(21) At a constant molar ratio of benzoyl peroxide to 2,2-dimethyl-1,4-butanediol of 5.0, increasing the molar ratio of nickel(II) bromide to diol from 0.5 to 2.5 results in a moderate increase in selectivity (**1:2**) of from 4.8 to 6.6.
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Table III. Comparative Selectivities from Metal Alkanoate Mediated Bromine Oxidations of 2,2-Disubstituted 1,4-Butanediols[a]

	R = R′ = Ph		R = Et; R′ = Me		R = R′ = Me	
mediator	yield, %[b]	%1:%2	yield, %[b]	%1:%2	yield, %[b]	%1:%2
$Ni(OAc)_2$	90	20	77	1.5	95	1.4
$Co(OAc)_2$	99	17	76	12	90	5.4
$Cu(OAc)_2$[c]					63	1.7
$Pb(OAc)_2$	49	3.5				
$Ni(OBz)_2$	99	24	99	19	87	6.5
$Co(OBz)_2$			99	22	98	6.0
$Pb(OBz)_2$	88	4.2			71	0.7
$Ni[OOCCH(Et)Bu]_2$	99	>100	93	35	82	14
$Fe[OOCCH(Et)Bu]_3$	67	1.9			52	0.7

[a] Reactions were performed in acetonitrile at 20 °C with 5.0 mol equiv of the mediator and 8.0 equiv of molecular bromine, based on diol. [b] Yield of isolated products. [c] In comparable reactions with $Zn(OAc)_2$, an 89% yield of lactone products were obtained from 2,2-dimethyl-1,4-butanediol (1:2 = 2.0). Minor products present in these reaction mixtures were not identified.

ethyl-2-methyl-1,4-butanediol, 2-phenyl-1,4-butanediol, and 8 were prepared from their corresponding commercially available dicarboxylic acids by lithium aluminum hydride reduction. 2,2-Diphenyl-1,4-butanediol was obtained by lithium aluminum hydride reduction of α,α-diphenylbutyrolactone. Nickel(II) pivalate[25] and $Ni(dmgH)_2$[26] were prepared by standard methods; other metal alkanoates and anhydrous $NiBr_2$ were commercially available. Acetonitrile was distilled from calcium hydride prior to use.

General Procedure: $Bz_2O_2/NiBr_2$ Method. The combination of diol, benzoyl peroxide, and anhydrous $NiBr_2$ dissolved in acetonitrile (10 mL/mmol of diol) was heated at 60 °C for 48 h. The reaction solution was characteristically green throughout this time. With lithium bromide as mediator, an analogous procedure was employed. After the reaction mixture cooled, a saturated solution of potassium iodide (2 mL/mmol Bz_2O_2 employed) was added to reduce unreacted peroxide. Ether was then added, and the resulting solution was washed with 10% aqueous hydrochloric acid and 20% aqueous sodium hydroxide solutions. After the mixture dryed over anhydrous magnesium sulfate, ether was distilled off under reduced pressure. Reaction products were characterized and yields were determined as previously described.[1,3]

General Procedure: $Br_2/Ni(OOCR)_2$ Method. Bromine (8.0 mmol/mmol of diol) in anhydrous acetonitrile (5.0 mL/8.0 mmol of Br_2) was added dropwise to a continuously stirred mixture of the alcohol and anhydrous nickel(II) alkanoate (5.0 mmol/mmol of diol) in acetonitrile (10 mL/mmol of diol) at 20 °C over 1 h. The color of the reaction solution was characteristically green unless excess molecular bromine was employed. Excess bromine was employed to compensate for bromine consumption by nickel(II) alkanoate, which occurred without oxidation of acetonitrile but afforded $NiBr_2$ and, presumably, peroxide. The molar amount of bromine used was adjusted to the molar ratio of $Ni(OOCR)_2$ to diol that afforded optimum regioselectivity. Molecular chlorine was added at a rate of 10–15 mL/min to the combination of diol and $Ni(OBz)_2$ in acetonitrile; *tert*-butyl hypochlorite was added in a manner analogous to the addition of molecular bromine. After a 4-h reaction time, the reaction mixture was poured into 10% aqueous hydrochloric acid and extracted with ether. The resultant ether solution was washed with 20% aqueous sodium hydroxide and water and then dried over anhydrous magnesium sulfate. Ether was distilled off under reduced pressure. Reaction products were characterized and yields were determined as previously described.[2,4] Weight yields of isolated products corresponded to those determined by GC analyses. Identical procedures were employed with the metal alkanoates that are listed in Table III.

General Procedure: Trityl Tetrafluoroborate Method. The combination of diol (2.0 mmol) and trityl tetrafluoroborate (5.2 mmol) dissolved in 20 mL of anhydrous acetonitrile was heated at 60 °C for 24 h. After cooling, the homogeneous dark solution was diluted with ether and extracted with 10% aqueous hydrochloric acid, 20% aqueous sodium hydroxide, and water. The resulting ether solution was dried over anhydrous magnesium sulfate, and ether was then removed under reduced pressure.

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Registry No. 2,2-diphenyl-1,4-butanediol, 69177-61-3; 2-ethyl-2-methyl-1,4-butanediol, 76651-98-4; 2,2-dimethyl-1,4-butanediol, 32812-23-0; 2-phenyl-1,4-butanediol, 6837-05-4; Br_2, 7726-95-6; Cl_2, 7782-50-5; $(CH_3)_3COCl$, 507-40-4; Bz_2O_2, 94-36-0; $HCrO_4^-$, 15596-54-0; $Ph_3C{\cdot}BF_4$, 341-02-6; $C_5H_5N{\cdot}HCl{\cdot}CrO_3$, 26299-14-9; $Ni(OAc)_2$, 373-02-4; $Ni(OBz)_2$, 553-71-9; $Ni(OOCCMe_3)_2$, 84215-34-9; $Ni[OOCCH(Et)Bu]_2$, 4454-16-4; $NiBr_2$, 13462-88-9; $Co(OAc)_2$, 71-48-7; $Cu(OAc)_2$, 142-71-2; $Pb(OAc)_2$, 301-04-2; $Co(OBz)_2$, 932-69-4; $Pb(OBz)_2$, 873-54-1; $Fe[OOCCH(Et)Bu]_3$, 7321-53-1.

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