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STERIC SELECTIVITY IN OXIDATIONS OF DIOLS

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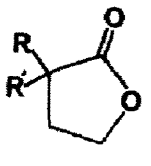
Oxidations of 2,2-disubstituted-1,4-butanediols by the combination of nickel(II) bromide and benzoyl peroxide and by trityl tetrafluoroborate produce β,β-disubstituted-γ-butyrolactones with exceptional selectivity.

Considerable attention has recently been directed towards the design of effective methods for selective oxidation in polyhydroxylated molecules. The primary focus of this attention has been associated with selective oxidations of secondary alcohols in primary,secondary diols, for which differential electronic stabilization resulting from hydrogen abstraction could be expected to direct the course of the oxidation. Selectivity in these oxidations is now conveniently achieved through the use of trityl salts,[1] of trichloroacetaldehyde on dehydrated chromatographic alumina,[2] of bromine or chlorine in the presence of hexamethylphosphoric triamide,[3] of bromine in the presence of distannoxane,[4] and of other active halogen reagents.[5-7] In contrast, the effectiveness of chemical oxidants in selective oxidations of primary,primary- and secondary,secondary-diols, where steric factors play a major role in directing the course of oxidation, has received scant attention. We now report methods for the conversion of 2,2-disubstituted-1,4-butanediols to the corresponding β,β-disubstituted-γ-butyrolactones (eq 1) with exceptional selectivity.



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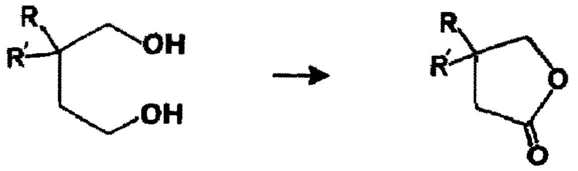

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(1)

The transformations represented by equation 1 were chosen for this investigation because of the relative accessibility of α,α-disubstituted-γ-butyrolactones (2) from γ-butyrolactone.[9] The combination of reductive conversion of 2 to 2,2-disubstituted-1,4-butanediols followed by selective oxidation to 1 would represent a facile method for transposition of substituents on γ-butyrolactone. Realization of this transformation is evidenced in the selectivity of oxidations of 2,2-diphenyl-1,4-butanediol by the nickel(II) bromide-benzoyl peroxide combination and by trityl tetrafluoroborate (Table I). Chromium(VI) and halogen oxidants exhibit limited selectivity for the production of 1. The dimethyl sulfoxide-oxalyl chloride oxidant[10] gives a complex mixture of products without appreciable selectivity.

Table I. Selectivity in Oxidations of 2,2-Diphenyl-1,4-butanediol by Representative Chemical Oxidants

Oxidant	Solvent	Temp., C°	R = R' = C_6H_5 %2	%1	Isolated Yield, %
$Bz_2O_2/NiBr_2$	CH_3CN	60	0	100	91
$Bz_2O_2/LiBr$	CH_3CN	60	50	50	91
$Bz_2O_2/Me_4N^+Br^-$	CH_3CN	60	51	49	98
Br_2/HMPT[3]	CH_2Cl_2	0	88	12	48
$C_5H_5N\cdot HCl\cdot CrO_3$[13]	CH_2Cl_2	25	30	70	99
$HCrO_4^-$	$(CH_3)_2CO/H_2O$	25	35	65	99
$(C_6H_5)_3C^+BF_4^-$	CH_3CN	60	0	100	77

We have recently reported that the combination of nickel(II) bromide with benzoyl peroxide serves as an effective reagent for the conversion of secondary alcohols to ketones and, when nickel(II) bromide is employed as an alcohol template, for the oxidation of primary alcohols to aldehydes.[11] The active oxidan in these reactions is understood to be benzoyl hypobromite, whose concentration is effectively mediated by nickel(II) bromide. In the present study, nickel(II bromide is observed to have a pronounced influence on the selectivity of diol oxidations, presumsably resulting from association of the diol with the metal halide. Results from reactions in which lithium bromide and tetramethylammoniu bromide are employed to generate benzoyl hypobromite show no apparent influence of the cation on oxidation selectivity. In a typical procedure for these oxidations, the alcohol was treated with 3.0 molar equivalents of benzoyl peroxide and a variable amount of anhydrous nickel(II) bromide[12] (or bromide salt), usua ly 2.5 equivalents, in acetonitrile at 60°C for 24 hr. Following treatment wi aqueous potassium iodide to decompose excess peroxide and the usual aqueous wor up,[11] the lactone was isolated as the sole product.

The use of trityl salts for the direct oxidation of secondary alcohols has recently been reported.[1a] Although trityl salts are not normally employed for oxidations of aliphatic primary alcohols and are, expectedly, unreactive towards 2,2-disubstituted-1,4-butanediols under the reaction conditions generally used for oxidations of secondary alcohols, treatment of the diol with 2.5 equivalents of trityl tetrafluoroborate in acetonitrile at 60°C for 24 hr afforded β,β-diphenyl-γ-butyrolactone in good yield. The selectivity observed in this oxidation reflects the severe steric requirements for hydrogen transfer from trityl ethers.[14]

As indicated by the results presented in Table II, trityl tetrafluoroborate provides greater selectivity in oxidations of 2,2-disubstituted-1,4-butanediols than does the benzoyl peroxide-nickel(II) bromide combination. However, product yields for oxidations by trityl salts are lower, even though triphenylmethane is obtained in yields consistent with the stoichiometry of 2 $(C_6H_5)_3C^+BF_4^-$/diol. For comparison, chromic acid oxidations of 2-ethyl-2-methyl-1,4-butanediol and 2,2-dimethyl-1,4-butanediol gave the corresponding lactone mixtures in ratios (% **1**/% **2**) of 1.9 and 2.1, respectively (60-65% isolated yield). The use of lithium bromide in place of nickel(II) bromide for the benzoyl peroxide oxidation of 2-ethyl-2-methyl-1,4-butanediol resulted in the production of the corresponding lactones in a % **1**/% **2** ratio of 2.4 (60% isolated yield).

Table II. Oxidations of Representative 2,2-Disubstituted-1,4-butanediols by Sterically Selective Oxidizing Agents

R	R'	Oxidant[a]	% **2**	% **1**	Isolated yield, %
C_6H_5	C_6H_5	$Bz_2O_2/NiBr_2$	0	100	91
		$(C_6H_5)_3C^+BF_4^-$	0	100	77
C_2H_5	CH_3	$Bz_2O_2/NiBr_2$	10	90	60
		$(C_6H_5)_3C^+BF_4^-$	2	98	59
CH_3	CH_3	$Bz_2O_2/NiBr_2$	13	87	60
		$(C_6H_5)_3C^+BF_4^-$	4	96	47

[a] All reactions were performed in anhydrous acetonitrile at 60°C.

As expected from the mechanistic interpretation that the observed high selectivity in oxidations by $Bz_2O_2/NiBr_2$ results from association of nickel(II) bromide with the diol,[15] increasing the molar ratio of nickel(II) bromide to diol results in increased selectivity for the production of β,β-disubstituted-γ-butyrolactones. For example, from reactions with 2,2-dimethyl-1,4-butanediol, increasing the molar ratio of nickel(II) bromide to diol from 0.5 to 2.5 resulted in an increase in the lactone product ratio (% **1**/% **2**) from 4.8 to 6.6. Nickel(II) bromide modifies the steric requirements of diols for oxidation through reversible association in a scheme that is analogous to that for reversible formation of trityl ethers in trityl cation oxidations of alcohols. However, nic el(II) bromide is not the oxidant in these transformations; therefore, altern uses of this reagent for selective structural modifications can be envisioned.

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