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CATALYTIC REGIOSELECTIVE DEHYDROGENATION OF UNSYMMETRICAL α,ω-DIOLS USING RUTHENIUM COMPLEXES

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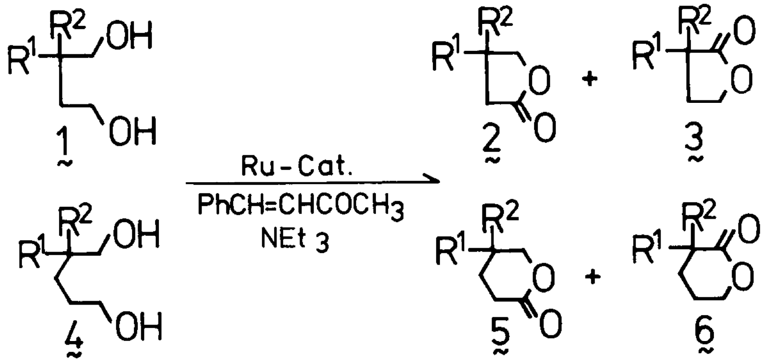
Summary: Ruthenium complex catalyzed regioselective dehydrogenation of unsymmetrically substituted 1,4- and 1,5-diols in the presence of α,β-unsaturated ketone as a hydrogen acceptor and triethylamine gave β-substituted γ-lactones and γ-substituted δ-lactones as major products, respectively.

In the course of stereoselective transformation of diols to lactones by ruthenium complexes with phosphine ligands, we have previously reported the hydrogen transfer reaction of prochiral or meso diols catalyzed by $Ru_2Cl_4((-)\text{-DIOP})_3$ to give optically active lactones.1) This asymmetric dehydrogenation of diols is classified as the enantiotopos differentiating reaction,2) where the catalyst could effectively distinguish the enantiotopic groups in a prochiral molecule. In this reaction we found that the substituent(s) of diol strongly influenced the stereoselectivity in the formation of optically active lactones. In order to clarify the detailed steric interaction between the substituents and phosphine ligand, the dehydrogenation of unsymmetrically substituted diols, which can potentially give two isomeric lactones as shown in scheme 1, was examined. Similar regioselective dehydrogenation of diols by Bz_2O_2 / $NiBr_2$,3a) $(C_6H_5)_3C^+BF_4^-$,3a) or a stoichiometric amount of $RuCl_2(PPh_3)_3$3b) are reported, but there are very few of such a reaction catalyzed by transition metal complexes.4) Further, in spite that several ruthenium catalysts are known to be effective for the hydrogen transfer reaction from diols to adequate

Scheme 1

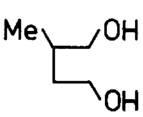
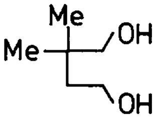
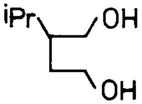
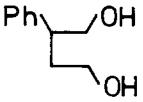


hydrogen acceptors to give lactones,5) only the selectivity between primary and secondary hydroxyl groups has been reported.5b)

The dehydrogenation of diols was carried out in a similar manner reported previously (see Table 1). After usual work-up the lactonic products were isolated by preparative GLC or HPLC and identified by ^{1}H-NMR and IR spectra, and the molar ratio of the products was determined by GLC using internal standards.

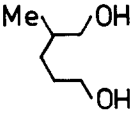
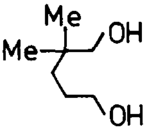
Table 1 shows the representative results obtained using unsymmetrically substituted 1,4-butanediols. In all cases the hydroxymethyl group not adjacent

Table 1. Regioselective Dehydrogenation of 1,4-Diolsa)

Entry	Diol	Catalyst	Temp.(°C)	Time(h)	Yield(%)b)	2 / 3
1		$RuCl_2(PPh_3)_3$	110	10	91	67 / 33
2c)		$RuCl_2(PPh_3)_3$	110	10	73	64 / 36
3		$Ru_2Cl_4((-)\text{-DIOP})_3$	110	20	52	73 / 27
4		$Ru_2Cl_4(dppb)_3$	110	20	55	72 / 28
5		$Ru_2Cl_4(dppb)_3$	140	5	77	69 / 31
6		$RuCl_2(PPh_3)_3$	110	10	98	89 / 11
7c)		$RuCl_2(PPh_3)_3$	110	10	71	85 / 15
8d)		$RuCl_2(PPh_3)_3$	110	10	95	85 / 15
9		$RuCl_2(dppe)_2$	110	10	0	–
10		$Ru_2Cl_4((-)\text{-DIOP})_3$	110	20	69	97 / 3
11		$Ru_2Cl_4(dppb)_3$	110	20	61	97 / 3
12		$Ru_2Cl_4(dppb)_3$	140	5	86	92 / 8
13		$RuCl_2(PPh_3)_3$	110	10	94	73 / 27
14		$Ru_2Cl_4(dppb)_3$	110	20	39	86 / 14
15		$RuCl_2(PPh_3)_3$	110	10	98	77 / 23
16		$Ru_2Cl_4(dppb)_3$	110	20	59	85 / 15

a) Diol (5 mmol), 4-phenyl-3-buten-2-one (hydrogen acceptor, 10 mmol), catalyst (0.2 mmol as Ru atom), and triethylamine (0.12 mL) were disolved in toluene (25 mL) and heated under argon. b) GLC yield based on the starting diol. c) 1,3-Diphenyl-2-propen-1-one was used as a hydrogen acceptor. d) 4-Methyl-3-penten-2-one was used as a hydrogen acceptor.

Table 2. Regioselective Dehydrogenation of 1,5-Diols[a)]

Entry	Diol	Catalyst	Temp.(°C)	Time(h)	Yield(%)[b)]	5 / 6
1		$RuCl_2(PPh_3)_3$	110	10	75	75 / 25
2		$Ru_2Cl_4((-)\text{-}DIOP)_3$	110	20	47	80 / 20
3		$Ru_2Cl_4(dppb)_3$	110	20	55	84 / 16
4		$Ru_2Cl_4(dppb)_3$	140	5	89	71 / 29
5		$RuCl_2(PPh_3)_3$	110	10	88	95 / 5
6		$Ru_2Cl_4((-)\text{-}DIOP)_3$	110	20	54	96 / 4
7		$Ru_2Cl_4(dppb)_3$	110	20	33	98 / 2
8		$Ru_2Cl_4(dppb)_3$	140	5	84	92 / 8

a) See footnote a) in Table 1. b) GLC yield based on the starting diol.

to the substituent was preferentially dehydrogenated to yield β-substituted or β,β-disubstituted γ-butyrolactone 2. Moreover the regioselectivity increased in the order 2-methyl- < 2-isopropyl-, 2-phenyl- < 2,2-dimethyl-1,4-butanediol, which is the order of the steric bulkiness of the substituents. 2,2-Dimethyl-1,4-butanediol showed a particularly high regioselectivity up to 97/3. These results clearly show that the main factor which governs the regioselectivity in this reaction should be the steric repulsion between the substituent(s) of diol and those of phosphines.

The activities and regioselectivities of the catalyst complexes are largely affected by their phosphine ligands. The complexes containing seven membered chelating ligands, $Ru_2Cl_4(dppb)_3$[6)] and $Ru_2Cl_4((-)\text{-}DIOP)_3$,[7)] showed higher regioselectivities than $RuCl_2(PPh_3)_3$ in each case. On the contrary catalytic activity of $RuCl_2(PPh_3)_3$, estimated from the yields of lactonic products, was higher than those of $Ru_2Cl_4(dppb)_3$ and $Ru_2Cl_4((-)\text{-}DIOP)_3$. When $RuCl_2(dppe)_2$[8)] was used as a catalyst, no reaction occurred and the catalyst was recovered unchanged. $RuCl_2(dppe)_2$ seems to provide no or insufficient vacant coordination sites necessary for this reaction, because dppe forms a rigid five membered chelate ring and hardly disociates.

Higher reaction temperature improved chemical yields in shorter reaction time, but lowered the regioselectivities. When 1,3-diphenyl-2-propen-1-one or 4-methyl-3-penten-2-one was used as a hydrogen acceptor in the place of 4-phenyl-3-buten-2-one, chemical yields and regioselectivities were somewhat lowered.

Unsymmetrically substituted 1,5-pentanediols gave similar results which are shown in Table 2. Again the less hindered hydroxymethyl group was preferentially dehydrogenated to afford γ-substituted or γ,γ-disubstituted δ-valerolactone 5. In the case of 2,2-dimethyl-1,5-pentanediol a high regioselectivity up to 98/2 was achieved.

The fact that the hemiacetals are detected by GLC in a reaction mixture suggests that the stepwise dehydrogenation involving the dehydrogenation of a diol to give hydroxyaldehydes followed by cyclization to give hemiacetals and the succesive dehydrogenation of hemiacetals to afford lactones, would be a possible mechanism. In $RuCl_2(PPh_3)_3$ catalyzed hydrogen transfer reaction from alcohols to α,β-unsaturated ketones the catalytic cycle is inferred to contain the coordination of the alcohol to give a metal alkoxide,9) so that the regioselectivity of this dehydrogenation could be attributed to the facility of the coordination of the less hindered hydroxyl group.

It should be pointed that the lactones obtained in this reaction can also be prepared by hydrogenation of cyclic anhydrides by using the same ruthenium complexes used here. The hydrogenation, however, gives α-substituted lactones 3 and 6 as major products, and so the regioselectivities of the two reactions are in opposite directions.10) With the combination of these two reactions either of the lactones can be preferentially obtained and the investigation along this line is in progress.

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