Ruthenium Complex Catalyzed Regioselective Dehydrogenation of Unsymmetrical α,ω-Diols

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Ruthenium complex catalyzed regioselective dehydrogenation of unsymmetrically substituted 1,4- and 1,5-diols in the presence of such a hydrogen acceptor as α,β-unsaturated ketone gave predominantly β-substituted γ-lactones and γ-substituted δ-lactones, respectively. Among the ruthenium complexes examined, $RuH_2(PPh_3)_4$ was the most active and selective catalyst and showed high catalytic activity even at 20 °C. For example, 2,2-dimethyl-1,4-butanediol was quantitatively converted to dihydro-4,4-dimethyl-2(3*H*)-furanone and dihydro-3,3-dimethyl-2(3*H*)-furanone in a ratio of 99.6/0.4 in the presence of 4-phenyl-3-buten-2-one (hydrogen acceptor) and a catalytic amount of $RuH_2(PPh_3)_4$ at 20 °C. The proposed main factor controlling the regioselectivity is the steric constraints produced by the substituent(s) of a diol at the coordination step of alkoxy group to ruthenium.

Selective lactone synthesis has attracted increasing attention, since lactones are a highly desirable class of compounds as targets in organic synthesis because of their occurrence in natural products and biologically active compounds[1] as well as their versatility as synthetic intermediates for other classes of compounds.[2] A large number of lactone synthesis methods have appeared in literature.[3] Among them, ruthenium complex catalyzed hydrogen transfer reaction from a diol[4] is a promising choice because homogeneous metal complex catalyzed reactions often show high selectivity[5] and it is unnecessary to use an oxidant which is either poisonous (Cr(VI)), expensive (Ag(I)), or explosive (peroxide).

In the course of our study on ruthenium complex catalyzed asymmetric reactions, we reported the synthesis of optically active lactones by asymmetric hydrogen transfer from prochiral or meso diols catalyzed by ruthenium–DIOP complex.[6] In this reaction one of the enantiotopic hydroxymethyl groups of the diol is dehydrogenated to give a carbonyl group, so that the reaction belongs to the enantiotopos differentiating reaction,[7] which is rarely found in transition metal complex catalyzed reactions.[8] Its asymmetric induction mechanism is of great interest from the standpoint of improving the optical yields. In order to clarify the steric interaction between a diol and ruthenium catalyst, we examined a certain ruthenium complex catalyzed dehydrogenation of unsymmetrically substituted diols, and found this reaction to proceed with good to excellent regioselectivity.

Table I. Ruthenium Complex Catalyzed Regioselective Dehydrogenation of 2,2-Dimethyl-1,4-butanediol: Effect of Ruthenium Catalysts[a]

catalyst	time, h	yield,[b,c] %	ratio[b] 2a/3a
$RuH_2(PPh_3)_4$	10	96	96/4
$RuH_2(PMePh_2)_4$[d]	10	98	90/10
$RuH_2(PMe_2Ph)_4$[d]	10	64	88/12
$RuH_2(PHPh_2)_4$[d]	10	6	78/22
$RuHCl(PPh_3)_3$DMA	10	91	65/35
$RuHCl((+)\text{-BINAP})_2$	10	96	74/26
$RuCl_2(PPh_3)_3$	10	98	89/11
$RuCl_2(dppe)_2$	10	0	
$Ru_2Cl_4(dppb)_3$	20	61	97/3
$Ru_2Cl_4((-)\text{-DIOP})_3$	20	69	97/3
$Ru_2Cl_4((+)\text{-BINAP})_2(NEt_3)$	10	82	90/10
$RuH_2(CO)(PPh_3)_3$	10	31	67/33
$Ru_2Cl_4(CO)_2((-)\text{-DIOP})_3$	10	89	71/29
$RuCl(C_5H_5)(PPh_3)_2$	10	0	
$Ru(C_5H_5)(SnCl_3)(PPh_3)_2$	10	0	

[a] Reaction conditions: **1a** (1 mmol), catalyst (0.04 mmol as Ru atom), 4-phenyl-3-buten-2-one (2 mmol), triethylamine (0.024 mL), toluene (5 mL), reflux. [b] Determined by GC. [c] Based on the starting **1a**. [d] Triethylamine was not added.

The regioselective lactone synthesis from an unsymmetrically substituted diol was achieved under controlled oxidation conditions; $Ph_3C^+BF_4^-$,[9] Bz_2O_2/NiX_2,[9] $Br_2/Ni(OBz)_2$,[9b,10] or a stoichiometric amount of $RuCl_2(PPh_3)_3$[11] are used as oxidants in the oxidation of 2,2-dimethyl-1,4-butanediol or 2,2-diphenyl-1,4-butanediol. More recently reported was palladium(0) or palladium(II) complex catalyzed dehydrogenation of diols[12] to give lactones using aryl halide as a hydrogen acceptor, but its regioselectivity was still unsatisfactory. The hydrogenation of unsymmetrically substituted cyclic anhydrides[13] is an alternative choice from the viewpoint of utilizing ruthenium complex for the catalyst of regioselective lactone synthesis. The two ru-

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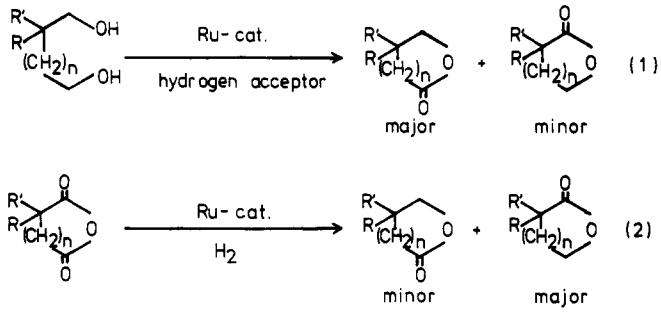
Table II. Ruthenium Complex Catalyzed Regioselective Dehydrogenation of 2,2-Dimethyl-1,4-butanediol: Effect of Reaction Conditions[a]

catalyst	hydrogen acceptor[b]	NEt_3	temp, °C	yield,[c,d] %	ratio[c] 2a/3a
$RuH_2(PPh_3)_4$	BA	+[e]	110	96	96/4
$RuH_2(PPh_3)_4$	BA	-	110	96	97/3
$RuH_2(PPh_3)_4$	BA	-	80	94	98/2
$RuH_2(PPh_3)_4$	BA	-	50	95	99.4/0.6
$RuH_2(PPh_3)_4$	BA	-	20	100	99.6/0.4
$RuH_2(PPh_3)_4$	CH	-	20	96	99/1
$RuH_2(PPh_3)_4$	MO	-	20	13	93/7
$RuCl_2(PPh_3)_3$	BA	+[e]	110	98	89/11
$RuCl_2(PPh_3)_3$	BA	+[e]	80	82	86/14
$RuCl_2(PPh_3)_3$	BA	+[e]	20	7	nd
$RuCl_2(PPh_3)_3$	CH	+[e]	110	71	85/15
$RuCl_2(PPh_3)_3$	MO	+[e]	110	95	85/15
$RuCl_2(PPh_3)_3$	BA	-	110	43	95/5

[a] Reaction conditions: **1a** (1 mmol), catalyst (0.04 mmol), hydrogen acceptor (2 mmol), toluene (5 mL), for 10 h. [b] BA, 4-phenyl-3-buten-2-one; CH, 1,3-diphenyl-2-propen-1-one; MO, 4-methyl-3-penten-2-one. [c] Determined by GC. [d] Based on the starting **1a**. [e] Triethylamine (0.024 mL) was added.

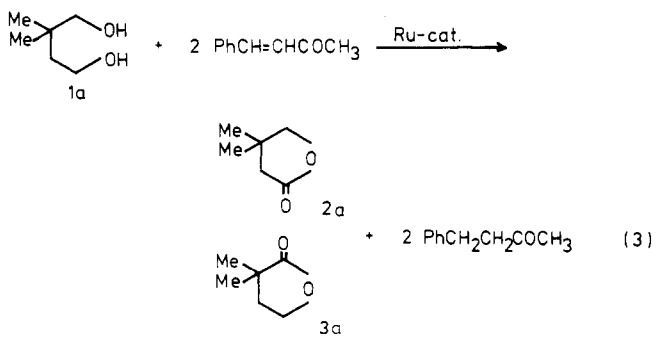
thenium complex catalyzed reactions, the hydrogenation of a cyclic anhydride[13] and the dehydrogenation of a diol,[14] completely differ in their selectivity of forming isomeric lactones (eq 1, 2). In this paper we wish to describe the



full detail of the regioselective dehydrogenation of unsymmetrical diols.[14]

Results

Effect of Catalyst. Dehydrogenation of 2,2-dimethyl-1,4-butanediol (**1a**) catalyzed by ruthenium complex in the presence of 4-phenyl-3-buten-2-one as a hydrogen acceptor afforded a mixture of regioisomeric γ-lactones, dihydro-4,4-dimethyl-2(3*H*)-furanone (**2a**) and dihydro-3,3-dimethyl-2(3*H*)-furanone (**3a**), as shown in eq 3. A wide range of ruthenium complexes including mono- and binuclear ones were found to be effective for this reaction. The results on the catalytic activity and regioselectivity obtained under toluene (solvent) reflux condition are shown in Table I, lactone **2a** being the major product in all cases examined.



Anionic ligands as well as phosphine ligands significantly influenced the regioselectivity. Thus, the former effect was found for the triphenylphosphine complexes examined; the regioselectivity increased in the order of $RuHCl(PPh_3)_3DMA < RuCl_2(PPh_3)_3 < RuH_2(PPh_3)_4$. On the other hand, the latter effects was shown by employing a series of *cis*-dihydridoruthenium complexes; $RuH_2(PPh_3)_4$ showed the highest regioselectivity and catalytic activity in comparison with $RuH_2(PMePh_2)_4$, $RuH_2(PMe_2Ph)_4$, and $RuH_2(PHPh_2)_4$. $RuH_2(PPh_3)_4$ was active enough to produce the lactone quantitatively even at 20 °C, at which temperature the dihydrido complexes of other phosphines showed low or no catalytic activity. For example, $RuH_2(PMePh_2)_4$, $RuH_2(PMe_2Ph)_4$, and $RuH_2(PHPh_2)_4$ gave product lactone only in 26%, 10%, and 0% yields (based on the starting diol), respectively, in the reaction with **1a** at 20 °C.

The binuclear ruthenium complexes of seven-membered chelating diphosphines, $Ru_2Cl_4(dppb)_3$ and $Ru_2Cl_4((-)\text{-DIOP})_3$ (dppb = 1,4-bis(diphenylphosphino)butane and (−)-DIOP[15] = (4*R*,5*R*)-4,5-bis((diphenylphosphino)-methyl)-2,2-dimethyl-1,3-dioxolane), showed relatively high regioselectivity, but the catalytic activity was moderate. The complex of five-membered chelating diphosphine, $RuCl_2(dppe)_2$ (dppe = 1,2-bis(diphenylphosphino)ethane), as well as cyclopentadienyl complexes, $RuCl(C_5H_5)(PPh_3)_2$ and $Ru(C_5H_5)(SnCl_3)(PPh_3)_2$, was completely inactive for this reaction. The regioselectivity brought about by the complexes containing carbonyl ligand, $RuH_2(CO)(PPh_3)_3$ and $Ru_2Cl_4(CO)_2((-)DIOP)_3$, was very low.

Effect of Reaction Condition. The optimization of reaction condition was attempted using $RuH_2(PPh_3)_4$ or $RuCl_2(PPh_3)_3$ as a catalyst, and the results are listed in Table II. When 4-phenyl-3-buten-2-one was used as a hydrogen acceptor, $RuH_2(PPh_3)_4$ was active enough at 20 °C and showed almost complete regioselectivity. 1,3-Diphenyl-2-propen-1-one and 4-methyl-3-penten-2-one were inferior hydrogen acceptors to 4-phenyl-3-buten-2-one from viewpoints of both reaction rate and regioselectivity.

$RuCl_2(PPh_3)_3$, contrary to $RuH_2(PPh_3)_4$, was a poor catalyst at 20 °C, though it showed high catalytic activity at 110 °C. Triethylamine was an effective additive for the catalysis of $RuCl_2(PPh_3)_3$. The amine probably acts as a trapping agent of hydrogen chloride formed through the reaction of $RuCl_2(PPh_3)_3$ with substrate diol. It could promote acetal formation[4c] and/or polymerization of formed hemiacetals[4b] (vide infra) to suppress the lactone

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Table III. Ruthenium Complex Catalyzed Dehydrogenation of 1,4-Butanediols[a]

diol	catalyst[b]	temp, °C	time, h	yield,[c,d] %	ratio[c] 2/3
2,2-Me_2 (1a)	A	20	10	100	99.6/0.4
	B[e]	110	10	98	89/11
	C[e]	110	20	61	97/3
	C[e]	140	5	86	92/8
2-Me (1b)	A	20	10	94	93/7
	B[e]	110	10	91	67/33
	C[e]	110	20	55	72/28
	C[e]	140	5	77	69/31
2-*i*-Pr (1c)	A	20	10	100	98/2
	B[e]	110	10	94	73/27
	C[e]	110	20	39	86/14
2-Ph (1d)	A	20	10	90[f]	97/3[g]
	B[e]	110	10	98	77/23
	C[e]	110	20	59	85/15
2-MeO (1e)	A	20	10	100	98/2
	B[e]	110	10	100	69/31
2-BuO (1f)	A	20	10	100	98/2
2-BnO (1g)	A	20	10	100	96/4
	B[e]	110	10	100	79/21
2-MOMO (1h)	A	20	10	91[f]	99/1

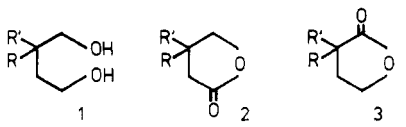
[a] Reaction conditions: 1 (1 mmol), catalyst (0.04 mmol as Ru atom), 4-phenyl-3-buten-2-one (2 mmol), toluene (5 mL). [b] A, $RuH_2(PPh_3)_4$; B, $RuCl_2(PPh_3)_3$; C, $Ru_2Cl_4(dppb)_3$. [c] Determined by GC. [d] Based on the starting 1. [e] Triethylamine (0.024 mL) was added. [f] Isolated yield. [g] Determined by 400-MHz ^1H NMR analysis.

Table IV. Ruthenium Complex Catalyzed Dehydrogenation of 1,5-Pentanediols[a]

diol	catalyst[b]	temp, °C	time, h	yield,[c,d] %	ratio[c] 5/6
2,2-Me_2 (4a)	A	20	10	100	99.5/0.5
	B[e]	110	10	88	95/5
	C[e]	110	20	33	98/2
	C[e]	140	5	84	92/8
2-Me (4b)	A	20	10	100	84/16
	B[e]	110	10	75	75/25
	C[e]	110	20	55	84/16
2-Ph (4c)	A	20	10	93[f]	98/2[g]
	B[e]	110	10	79[f]	88/12[g]

[a] Reaction Conditions: 4 (1 mmol), catalyst (0.04 mmol as Ru atom), 4-phenyl-3-buten-2-one (2 mmol), toluene (5 mL). [b] A, $RuH_2(PPh_3)_4$; B, $RuCl_2(PPh_3)_3$; C, $Ru_2Cl_4(dppb)_3$. [c] Determined by GC. [d] Based on the starting 4. [e] Triethylamine (0.024 mL) was added. [f] Isolated yield. [g] Determined by 400-MHz ^1H NMR analysis.

Chart I



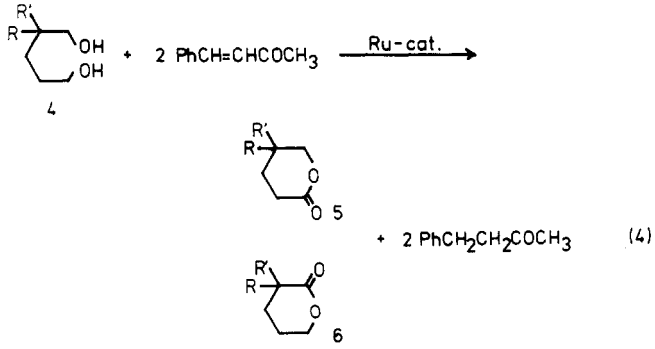
1 2 3

a, R = CH_3; R′ = CH_3
b, R = CH_3; R′ = H
c, R = $(CH_3)_2CH$; R′ = H
d, R = C_6H_5; R′ = H
e, R = CH_3O; R′ = H
f, R = $CH_3CH_2CH_2CH_2O$; R′ = H
g, R = $C_6H_5CH_2O$; R′ = H
h, R = CH_3OCH_2O; R′ = H

formation. In fact, triethylamine hydrochloride was isolated from the reaction mixture in some cases. $RuH_2(PPh_3)_4$ which has no chloride ligand showed no loss of lactone yield in the absence of triethylamine.

Dehydrogenation of Various Unsymmetrically Substituted Diols. Dehydrogenation of unsymmetrically substituted diols other than **1a** was also attempted. Various 2-substituted or 2,2-disubstituted 1,4-butanediols (**1a–h**) including 2-alkoxy-1,4-butanediols were successfully dehydrogenated by $RuH_2(PPh_3)_4$, $RuCl_2(PPh_3)_3$, or $Ru_2Cl_4(dppb)_3$ to give a mixture of γ-lactones, **2a–h** and **3a–h** (see Chart I). As is shown in Table III, β-substituted or β,β-disubstituted γ-lactones (**2**) are the major products in all cases. The regoselectivity increased in the order of the bulkiness of the substituent(s): dimethyl > isopropyl, phenyl > methyl. It is noteworthy that $RuH_2(PPh_3)_4$ catalyzed reactions provide extremely high regioselectivities as well as excellent chemical yields for all substrates examined.

When 2-substituted or 2,2-disubstituted 1,5-pentanediol (**4**) are used as a substrate, a pair of regioisomeric δ-lactones, **5** and **6**, are expected as the products (eq 4). Again



4 5 6

a, R = CH_3; R′ = CH_3
b, R = CH_3; R′ = H
c, R = C_6H_5; R′ = H

the dehydrogenation was successfully achieved with high yield and high regioselectivity (Table IV). The dehydrogenation of 2,2-dimethyl-1,5-pentanediol (**4a**) catalyzed by $RuH_2(PPh_3)_4$ showed a substantially perfect regioselectivity so that tetrahydro-5,5-dimethyl-2-pyranone (**5a**) was obtained almost quantitatively.

1,4-Pentanediol, having both a primary and a secondary hydroxyl group, gave γ-valerolactone quantitatively in a $RuH_2(PPh_3)_4$-catalyzed dehydrogenation at 20 °C, using

4-phenyl-3-buten-2-one as a hydrogen acceptor. However, usual monohydric alcohol was a poor substrate under the same reaction conditions; 1-octanol gave only 3% of octanal, and 77% of 1-octanol was recovered.

Discussion

The observed regioselectivity was highly sensitive to the ligands of catalyst, providing some information with regard to the catalytically active species. Some preceding reports described the active species in the ruthenium catalyzed hydrogen transfer from an alcohol.[16]

The active species for the dihydrido–ruthenium complex catalyzed hydrogen transfer was supposed to be a ruthenium(0) complex[16a] which was formed by the dissociation of phosphine ligand from $RuH_2(PR_3)_4$ accompanied with the hydrogen transfer from ruthenium(II) dihydride species to olefinic hydrogen acceptor.[16a,17] It is plausible that the steric bulkiness and low electron donating ability of triphenylphosphine enhance its dissociation from ruthenium so that it is reasonably understood that $RuH_2(PPh_3)_4$ has the highest catalytic activity among dihydrido complexes. The steric bulkiness of phosphine ligands seems to play an important role in the regioselection, that is, the complex of the sterically bulkiest triphenylphosphine was the catalyst giving the highest regioselectivity, while less bulky phosphines, PMe_2Ph and $PHPh_2$, showed only moderate selectivity.

$RuCl_2(PPh_3)_3$ was shown to generate $RuHCl(PPh_3)_3$ and hydrogen chloride[18] during a reaction with an alcohol at moderate temperature (60 °C). However, $RuCl_2(PPh_3)_3$ and $RuHCl(PPh_3)_3$DMA exhibited clearly different regioselectivities in the dehydrogenation of **1a** under the same reaction condition. This strongy indicates that definitely different catalytically active species should be formed from $RuCl_2(PPh_3)_3$ and $RuHCl(PPh_3)_3$DMA, although the active species have not been clarified.

The catalytic ineffectiveness of $RuCl_2(dppe)_2$, $RuCl(C_5H_5)(PPh_3)_2$, and $Ru(C_5H_5)(SnCl_3)(PPh_3)_2$ is probably due to the fact that they provide no or insufficient vacant coordination sites necessary for the reaction, because of the rigid coordination of cyclopentadienyl or dppe ligands. A similar catalytic ineffectiveness (or low activity) due to the lack of ligand dissociation was reported in the ruthenium complex catalyzed hydrogenation of olefins.[19]

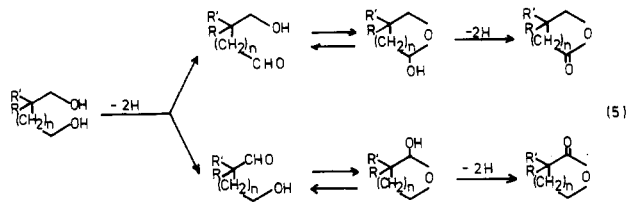
The bulkiness of the substituent(s) of a diol is also an important factor controlling the regioselectivity of these reactions. Thus, in the dehydrogenation of both 1,4- and 1,5-diols, the hydroxymethyl group not adjacent to the substituent(s) was preferably dehydrogenated to give the lactones **2** and **5** as the major products, and the bulkier the substituent of a diol was, the higher the regioselectivity became. Diols bearing polar alkoxy substituents also showed a similar trend of regioselectivity. This suggests that alkoxy substituents are recognized by ruthenium catalyst through their steric factors. It should be noted that the lactones **2g** and **2h** are hydroxy-protected forms of dihydro-4-hydroxy-2(3*H*)-furanone, a potential synthetic intermediate for natural products such as an insect pheromone.[20] This demonstrates the usefulness of the present reaction as a synthetic tool.

Table V. Regioselective Dehydrogenation of 2-Methyl-1,4-butanediol Catalyzed by Ru_2Cl_4((−)-DIOP)$_3$ or Ru_2Cl_4((+)-DIOP)$_3$[a]

diol	catalyst	yield,[b,c] %	ratio[b] **2b**/**3b**
(R)-**1b**	Ru_2Cl_4((−)-DIOP)$_3$	55	76/24
(R)-**1b**	Ru_2Cl_4((+)-DIOP)$_3$	72	69/31
(RS)-**1b**	Ru_2Cl_4((−)-DIOP)$_3$	52	73/27

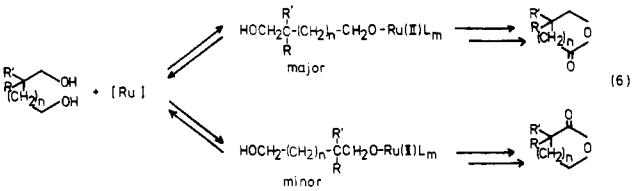
[a] Reaction conditions: **1b** (1 mmol), catalyst (0.02 mmol), 4-phenyl-3-buten-2-one (2 mmol), triethylamine (0.024 mL), toluene (5 mL), reflux for 20 h. [b] Determined by GC. [c] Based on the starting **1b**.

Based on the fact that the GC analysis occasionally indicates the existence of hemiacetals in some reaction mixtures, the formation of a lactone from a diol seems to consist of the following steps: (i) the dehydrogenation of a diol to give ω-hydroxyaldehydes, (ii) the cyclization of the hydroxyaldehydes to give hemiacetals, and (iii) the dehydrogenation of hemiacetals to afford lactones (eq 5).[4a,b]



(5)

From kinetic experiments,[15b] a ruthenium alkoxide, which was generated through the reaction of active ruthenium species and an alcohol, was supposed to be an intermediate in ruthenium catalyzed dehydrogenation of an alcohol. When an unsymmetrically substituted diol is used as a substrate, two regioisomeric ruthenium alkoxide intermediates can be formed (eq 6). Taking account of the



(6)

L = phosphine, hydrogen acceptor, or other ligands

facts that the less sterically hindered hydroxymethyl group is preferentially dehydrogenated and that the diol with bulkier substituent(s) exhibited higher selectivity, the regioselectivity of the reaction could be attributed to the facility in the coordination of the less hindered hydroxymethyl group to the ruthenium catalyst to give a ruthenium alkoxide intermediate.

1,4-Pentanediol afforded exclusively γ-valerolactone through the dehydrogenation catalyzed by $RuH_2(PPh_3)_4$ at 20 °C. The observed selectivity can be ascribed to the difference in the stereochemical congestion between the primary and secondary hydroxyls. The favored reactivity of primary hydroxyl groups over secondary ones was also pointed out by Descotes[4b] and Murahashi.[4c] The above-mentioned high selectivity for the primary hydroxyl group suggests a possibility of selective oxidation of a primary alcohol in a mixture of primary and secondary ones. It was found, however, that the dehydrogenation of 1-octanol was very slow at 20 °C compared with the reaction of a diol. It seems, therefore, that, for the reaction of a diol, the dehydrogenation of a hydroxyl group is promoted by the nearby hydroxyl group in the same molecule.

It can be supposed that the diastereomeric combination of a chiral substrate and a chiral ruthenium catalyst may result in the formation of lactones with different regioselectivity. From this standpoint, the dehydrogenation of

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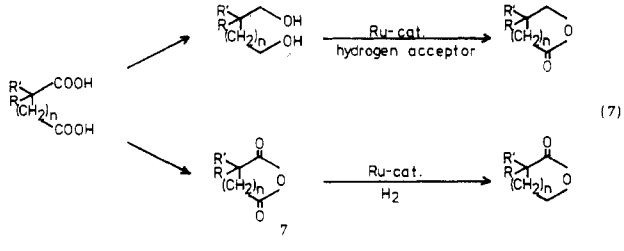
(*R*)-2-methyl-1,4-butanediol ((*R*)-**1b**) and (*RS*)-2-methyl-1,4-butanediol ((*RS*)-**1b**) was examined by using Ru_2Cl_4-((−)-DIOP)$_3$ or Ru_2Cl_4((+)-DIOP)$_3$ as a catalyst (Table V). Actually observed was that the regioselectivity for the dehydrogenation of (*R*)-**1b** by Ru_2Cl_4((−)-DIOP)$_3$ was higher than that of (*R*)-**1b** with Ru_2Cl_4((+)-DIOP)$_3$, and that (*RS*)-**1b** showed an averaged value of the above selectivities. From the theoretical point of view, optically active lactones will be obtained from the reaction products of the racemic substrate by making use of the differential regioselectivities between the enantiomers of the substrate. Unfortunately, however, the difference in regioselectivity for the above system was not large enough to affect the asymmetric synthesis of lactone.

The dehydrogenation of an unsymmetrically substituted diol was also catalyzed by certain rhodium complexes in the presence of α,β-unsaturated carbonyl compounds.[21] The observed regioselectivity found for this system was closely similar to that for the ruthenium catalyst. It was proposed for $RhH(PPh_3)_4$ catalyzed hydrogen transfer that an alkylphenylcarbinol having a bulky alkyl substituent showed lower coordinating ability to rhodium in comparison with an alcohol with a smaller alkyl group, and, consequently, suffers slow dehydrogenation.[22] It is plausible that the kinetic control of the same type occurs in the lactone formation reaction catalyzed by ruthenium complex.

On the other hand, palladium complex catalyzed dehydrogenation of unsymmetrical diols[12] **1a** and **4a**, which proceeds in the presence of aryl bromide as a hydrogen acceptor, has been reported to give lactones **3a** and **6a** as the major products, respectively. The palladium catalyzed reaction was considered to be affected by so called "steric acceleration" at the β-hydrogen elimination step of alkoxypalladium intermediate, which determined the regioselectivity of the reaction. This forms a striking contrast to the steric effect observed in the ruthenium or rhodium catalyzed reaction.

Finally it should be pointed out that the lactones obtained through the dehydrogenation of diols can also be obtained by the hydrogenation of cyclic anhydrides **7** using the ruthenium complexes as catalyst.[13] However, the latter reaction gives α-substituted lactone **3** or **6** as the major product due to the steric effect of the substituents. Consequently the distributions of the products are in opposite trend in these two reactions in spite of the fact that they are catalyzed by the same ruthenium complex. Therefore, these ruthenium complex catalyzed reactions should provide a novel methodology of selective lactone synthesis since a diol and a cyclic anhydride are easily derived from the common dicarboxylic acid (eq 7).



(7)

Experimental Section

Proton NMR spectra were taken on a Hitachi R-40 (90 MHz) spectrometer a or JEOL JNM-GX400 (400 MHz) spectrometer using chloroform-*d* as a solvent, and all chemical shifts were recorded as δ values in ppm downfield from internal Me_4Si. Singlet, doublet, triplet, and multiplet are abbreviated to s, d, t, and m, respectively. NMR spectra listed below were recorded on a 90-MHz apparatus unless otherwise noted. IR spectra were taken on a Shimadzu IR-400 spectrophotometer as neat film unless otherwise noted. Analyses by gas chromatography were performed on a Shimadzu GC-6AM instrument equipped with a flame ionization detector and a Shimadzu Chromatopac C-E1B calculating integrator using an appropriate internal standard. A 2-m steel column filled with 60/80 mesh Uniport HB with 2% Carbowax 40M was used. A Hitachi 163 instrument fitted with a thermal conductivity detector was used for preparative scale gas chromatography.

2,2-Dimethyl-1,4-butanediol (**1a**), (*R*)-2-methyl-1,4-butanediol ((*R*)-**1b**), (*RS*)-2-methyl-1,4-butanediol ((*RS*)-1b), 2-isopropyl-1,4-butanediol (**1c**), 2-phenyl-1,4-butanediol (**1d**), 2-methoxy-1,4-butanediol (**1e**), 2-butoxy-1,4-butanediol (**1f**), 2,2-dimethyl-1,5-pentanediol (**4a**), 2-methyl-1,5-pentanediol (**4b**), and 2-phenyl-1,5-pentanediol (**4c**) were prepared by $LiAlH_4$ reduction of 2,2-dimethylsuccinic acid, (*R*)-methylsuccinic anhydride, (*RS*)-diethyl methylsuccinate, isopropylsuccinic acid, phenylsuccinic acid, dimethyl 2-methoxysuccinate, dibutyl 2-butoxysuccinate, 2,2-dimethylglutaric acid, 2-methylglutaric acid, and 2-phenylglutaric anhydride, respectively. 2-(Benzyloxy)-1,4-butanediol (**1g**) was prepared by O-benzylation (NaH, benzyl chloride/DMF) of 1,4-bis(trityloxy)-2-butanol[23] followed by acid hydrolysis. 2-(Methoxymethoxy)-1,4-butanediol (**1h**) was prepared by methoxymethylation[24] of dimethyl malate followed by $LiAlH_4$ reduction. All of ruthenium complexes, $RuH_2(PPh_3)_4$,[25] $RuH_2(PMePh_2)_4$,[26] $RuH_2(PMe_2Ph)_4$,[27] $RuH_2(PHPh_2)_4$,[28] $RuHCl(PPh_3)_3$DMA,[29] RuHCl((+)-BINAP)$_2$[30] ((+)-BINAP[31] = (*R*)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), $RuCl_2(PPh_3)_3$,[32] $RuCl_2(dppe)_2$,[19a] $Ru_2Cl_4(dppb)_3$,[33] Ru_2Cl_4((−)-DIOP)$_3$,[34] Ru_2Cl_4-((+)-DIOP)$_3$,[34] Ru_2Cl_4((+)-BINAP)$_2$(NEt_3),[30] $RuH_2(CO)(PPh_3)_3$,[35] $Ru_2Cl_4(CO)_2$((−)-DIOP)$_3$,[36] $RuCl(C_5H_5)(PPh_3)_2$,[37] and Ru-$(C_5H_5)(SnCl_3)(PPh_3)_2$[38] were prepared according to the literature methods. Toluene was dried over sodium, distilled, and kept under an argon atmosphere. Other chemicals were purchased from Tokyo Kasei Ind. Co. and purified by recrystallization of distillation if needed.

An Example of Catalytic Dehydrogenation of a Diol. A mixture of 0.118 g (1.0 mmol) of 2,2-dimethyl-1,4-butanediol (**1a**) and 0.292 g (2.0 mmol) of 4-phenyl-3-buten-2-one was dissolved in 5 mL of toluene under argon and 46.1 mg (0.04 mmol) of $RuH_2(PPh_3)_4$ was added in one portion. The resulting blackish yellow solution was stirred for 10 h at 20 °C. At the end of the reaction the color of the reaction mixture changed to orange. GC analysis of the reaction mixture using an internal standard indicated that the dehydrogenation of **1a** proceeded quantitatively to give a mixture of dihydro-4,4-dimethyl-2(3*H*)-furanone (**2a**) and dihydro-3,3-dimethyl-2(3*H*)-furanone (**3a**) in the ratio

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99.6/0.4. The structures of the products were identified by ^1H NMR and IR spectroscopy after purification by preparative GC.

Dihydro-4,4-dimethyl-2(3*H*)-furanone (2a): ^1H NMR 1.19 (s, 6 H, Me), 2.32 (s, 2 H, 3-H), 3.97 (s, 2 H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-methyl-2(3*H*)-furanone (2b): ^1H NMR 1.15 (d, 3 H, Me, J = 7 Hz), 2.0–2.8 (m, 3 H, 3-H, 4-H), 3.85, 4.41 (2 dd, 2 × 1 H, 5-H, J_{gem} = 9 Hz, J_{vic} = 6 Hz); IR 1780 cm^{-1} (C=O).

Dihydro-4-isopropyl-2(3*H*)-furanone (2c): ^1H NMR 0.90, 0.94 (2 d, 2 × 3 H, Me, J = 6 Hz), 1.4–1.9 (m, 1 H, $(CH_3)_2CH$), 2.0–2.6 (m, 3 H, 3-H, 4-H), 3.8–4.0, 4.25–4.45 (2 m, 2 × 1 H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-phenyl-2(3*H*)-furanone (2d): ^1H NMR (400MHz) 2.69 (dd, 1 H, 3-H, J_{gem} = 17.4 Hz, J_{vic} = 9.2 Hz), 2.93 (dd, 1 H, 3-H, J_{gem} = 17.4 Hz, J_{vic} = 8.5 Hz), 3.75–3.84 (m, 1 H, 4-H), 4.28 (dd, 1 H, 5-H, J_{gem} = 9.2 Hz, J_{vic} = 7.6 Hz), 4.68 (fortuitous t, 1 H, 5-H, J_{gem} = 9.2 Hz, J_{vic} = 7.9 Hz), 7.18–7.41 (m, 5 H, C_6H_5); IR 1780 cm^{-1} (C=O).

Dihydro-4-methoxy-2(3*H*)-furanone (2e): ^1H NMR 2.4–2.85 (m, 2 H, 3-H), 3.34 (s, 3 H, Me), 4.1–4.4 (m, 3 H, 4-H, 5-H); IR 1775 cm^{-1} (C=O).

Dihydro-4-butoxy-2(3*H*)-furanone (2f): ^1H NMR 0.91 (t, 3 H, Me, J = 6 Hz), 1.15–1.8 (m, 4 H, $CH_3CH_2CH_2$), 2.35–2.85 (m, 2 H, 3-H), 3.42 (t, 2 H, CH_2CH_2O, J = 6 Hz), 4.1–4.4 (m, 3 H, 4-H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-4-(benzyloxy)-2(3*H*)-furanone (2g): ^1H NMR 2.5–2.7 (m, 2 H, 3-H), 4.2–4.4 (m, 3 H, 4-H, 5-H), 4.48 (s, 2 H, $PhCH_2$), 7.2–7.4 (m, 5 H, C_6H_5); IR (KBr) 1780 cm^{-1} (C=O).

Dihydro-4-(methoxymethoxy)-2(3*H*)-furanone (2h): ^1H NMR 2.4–2.95 (m, 2 H, 3-H), 3.37 (s, 3 H, Me), 4.3–4.6 (m, 3 H, 4-H, 5-H), 4.66 (s, 2 H, OCH_2O); IR 1780 cm^{-1} (C=O).

Dihydro-3,3-dimethyl-2(3*H*)-furanone (3a): ^1H NMR 1.27 (s, 6 H, Me), 2.11 (t, 2 H, 4-H, J = 7 Hz), 4.26 (t, 2 H, 5-H, J = 7 Hz); IR 1770 cm^{-1} (C=O).

Dihydro-3-methyl-2(3*H*)-furanone (3b): ^1H NMR 1.28 (d, 3 H, Me, J = 6 Hz), 1.8–2.9 (m, 3 H, 3-H, 4-H), 4.1–4.5 (m, 2 H, 5-H); IR 1765 cm^{-1} (C=O).

Dihydro-3-isopropyl-2(3*H*)-furanone (3c): ^1H NMR 0.93, 1.04 (2 d, 2 × 3 H, Me, J = 7 Hz), 1.8–2.6 (m, 4 H, 3-H, 4-H, $(CH_3)_2CH$), 4.05–4.4 (m, 2 H, 5-H); IR 1765 cm^{-1} (C=O).

Dihydro-3-phenyl-2(3*H*)-furanone (3d): ^1H NMR (400 MHz) 2.40–2.51, 2.69–2.77 (2 m, 2 × 1 H, 4-H), 3.82 (fortuitous t, 1 H, 3-H, J_{vic} = 9.6 Hz, 9.6 Hz), 4.33–4.39, 4.46–4.52 (2 m, 2 × 1 H, 5-H), 7.26–7.40 (m, 5 H, C_6H_5); IR 1765 cm^{-1} (C=O).

Dihydro-3-methoxy-2(3*H*)-furanone (3e): ^1H NMR 2.1–2.8 (m, 2 H, 4-H), 3.54 (s, 3 H, Me), 3.95–4.5 (m, 3 H, 3-H, 5-H); IR 1780 cm^{-1} (C=O).

Dihydro-3-butoxy-2(3*H*)-furanone (3f): ^1H NMR 0.91 (t, 3 H, Me, J = 7 Hz), 1.15–2.0 (m, 4 H, $CH_3CH_2CH_2$), 2.0–2.8 (m, 2 H, 4-H), 3.4–4.5 (m, 5 H, 3-H, 5-H, CH_2CH_2O); IR 1780 cm^{-1} (C=O).

Dihydro-3-(benzyloxy)-2(3*H*)-furanone (3g): ^1H NMR 2.0–2.6 (m, 2 H, 4-H), 3.9–4.5 (m, 3 H, 3-H, 5-H), 4.69, 4.86 (AB signal, 2 H, $PhCH_2$, J = 12 Hz), 7.1–7.4 (m, 5 H, C_6H_5); IR 1780 cm^{-1} (C=O).

Dihydro-3-(methoxymethoxy)-2(3*H*)-furanone (3h): ^1H NMR 2.0–2.8 (m, 2 H, 4-H), 3.42 (s, 3 H, Me), 4.1–4.5 (m, 3 H, 3-H, 5-H), 4.71, 4.93 (AB signal, 2 H, OCH_2O, J = 6 Hz); IR 1790 cm^{-1} (C=O).

Tetrahydro-5,5-dimethyl-2*H*-pyran-2-one (5a): ^1H NMR 1.05 (s, 6 H, Me), 1.69 (t, 2 H, 4-H, J = 7 Hz), 2.55 (t, 2 H, 3-H, J = 7 Hz), 3.96 (s, 2 H, 6-H); IR 1735 cm^{-1} (C=O).

Tetrahydro-5-methyl-2*H*-pyran-2-one (5b): ^1H NMR 1.00 (d, 3 H, Me, J = 6 Hz), 1.3–2.3 (m, 3 H, 4-H, 5-H), 2.4–2.7 (m, 2 H, 3-H), 3.91 (dd, 1 H, 6-H, J_{gem} = 11 Hz, J_{vic} = 10 Hz), 4.28 (ddd, 1 H, J_{gem} = 11 Hz, J_{vic} = 4 Hz, ^4J = 2 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-5-phenyl-2*H*-pyran-2-one (5c): ^1H NMR (400 MHz) 2.13–2.23 (m, 2 H, 4-H), 2.66 (ddd, 1 H, 3-H, J_{gem} = 18.0 Hz, J_{vic} = 7.4 Hz, 10.1 Hz), 2.78 (ddd, 1 H, 3-H, J_{gem} = 18.0 Hz, J_{vic} = 4.3 Hz, 6.7 Hz), 3.16–3.22 (m, 1 H, 5-H), 4.31 (fortuitous t, 1 H, 6-H, J_{gem} = 11.0 Hz, J_{vic} = 11.0 Hz), 4.48 (ddd, 1 H, 6-H, J_{gem} = 11.1 Hz, J_{vic} = 4.9 Hz, ^4J = 2.0 Hz), 7.24–7.38 (m, 5 H, C_6H_5); IR (KBr) 1730 cm^{-1} (C=O).

Tetrahydro-3,3-dimethyl-2*H*-pyran-2-one (6a): ^1H NMR 1.30 (s, 6 H, Me), 1.7–2.1 (m, 4 H, 4-H, 5-H), 4.35 (t, 2 H, 6-H, J = 5 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-3-methyl-2*H*-pyran-2-one (6b): ^1H NMR 1.26 (d, 3 H, Me, J = 9 Hz), 1.4–2.3 (m, 4 H, 4-H, 5-H), 2.4–2.8 (m, 1 H, 3-H), 4.32 (t, 2 H, 6-H, J = 6 Hz); IR 1730 cm^{-1} (C=O).

Tetrahydro-3-phenyl-2*H*-pyran-2-one (6c): ^1H NMR (400 MHz) 1.93–2.14 (m, 3 H, 4-H, 5-H), 2.25–2.34 (m, 1 H, 4-H), 3.78 (dd, 1 H, 3-H, J = 9.7 Hz, 7.1 Hz), 4.41–4.51 (m, 2 H, 6-H), 7.20–7.40 (m, 5 H, C_6H_5).

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A Synthesis of 4-Oxo Carboxylic Acids, 4-Oxo Aldehydes, and 1,4-Diketones from γ-Lactones[1]

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The α-methyldiphenylsilyl derivatives of γ-butyrolactone, γ-valerolactone, and the cis lactone of 2-hydroxycyclohexaneacetic acid have been reacted with Grignard reagents. The α-silylated lactones of γ-butyrolactone and γ-valerolactone react with a single equivalent of Grignard reagent to give a 2-substituted 4,5-dihydrofuran, which can be hydrolyzed and oxidized to 4-oxo carboxylic acids, 1,4-diketones, or 4-oxo aldehydes. The α-silylated fused lactone failed to react with ethylmagnesium bromide in refluxing tetrahydrofuran. An X-ray crystal structure of this silylated lactone indicated that this lack of reactivity is due to steric factors.

The preparation of 4-oxo acids, precursors to 5-substituted γ-lactones and of 1,4-diketones and 4-oxo aldehydes, valuable precursors to cyclopentenones, and important units in organic synthesis, as well as biologically and in-

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