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Asymmetric Hydrogenation of Unsaturated Carbonyl Compounds Catalyzed by BINAP—Ru(II) Complexes. Enantioselective Synthesis of γ-Butyrolactones and Cyclopentanones

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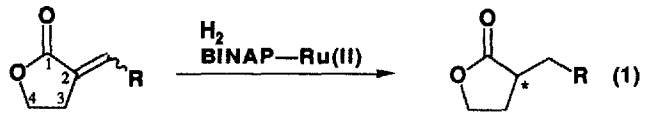
Key Words: Asymmetric Hydrogenation; BINAP—Ru(II); Optically active γ-butyrolactones; 2-alkylcyclopentanones

Abstract: *Asymmetric hydrogenation of 2- and 4-alkylidene-γ-butyrolactones and 2-alkylidenecyclopentanones catalyzed by BINAP—Ru(II) complexes affords the corresponding γ-butyrolactones and cyclopentanones in 94—98% ee. Hydrogenation of (E)- and (Z)-2-propylidene-γ-butyrolactone catalyzed by the same catalyst gave the products with the same absolute configuration and in almost equal enantioselectivities, which shows that olefin geometry does not affect the stereochemistry and enantioselectivity.*

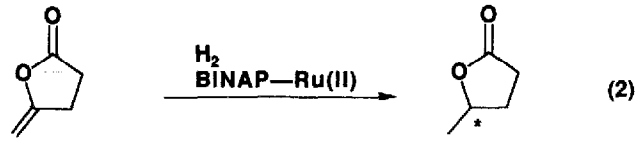
Asymmetric hydrogenation of unsaturated compounds is one of the most useful tools for the synthesis of optically active organic compounds.[1] We have already reported several BINAP—Ru(II) complexes, highly efficient catalysts for asymmetric hydrogenation of enamides, α,β- and β,γ-unsaturated carboxylic acids, allylic and homoallylic alcohols, and α- and β-functionalized ketones.[2] Optically active carbonyl compounds are important not only as physiologically active materials but also as intermediates for the synthesis of various useful compounds. Highly enantioselective hydrogenation of olefinic part of α,β-unsaturated carbonyl compounds, however, has been rarely attained with conventional chiral catalysts[3,4] except for more functionalized carbonyl compounds such as α-acylaminoacrylic acids and itaconic acid. We here describe highly enantioselective hydrogenation of 2- and 4-alkylidene-γ-butyrolactones and 2-alkylidenecyclopentanones catalyzed by BINAP—Ru(II) complexes.

A degassed mixture of 2-methylene-γ-butyrolactone (**1a**) (1 mmol) and [RuCl((*S*)-binap))(benzene)]Cl[5] (1×10^{-2} mmol) in CH_2Cl_2 (10 ml) was stirred under hydrogen pressure (100 atm) in an autoclave at 50 °C for 20 h. The product **2a** was purified by distillation followed by silica gel column chromatography (hexane—ether 4 : 1). The enantiomeric excess was determined to be 95% by HPLC analysis (column, Chiralcel OD; hexane—2-propanol 994 : 6; flow rate, 1 ml/min; detection, UV (230 nm)). Similarly, substrates **3**, **5**, **6**, and **7** were also hydrogenated to give the corresponding optically active γ-butyrolactones and cyclopentanones. Some representative results are shown in Table 1.



1a: R = H
1b: R = Et

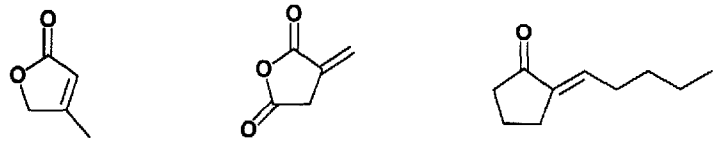
2a: R = H
2b: R = Et



3 **4**

Hydrogenation was usually carried out at 50 °C since the reaction proceeds sluggishly at lower temperature. Among several BINAP—Ru(II) complexes used as catalysts in the hydrogenation of **1a**, the complex bearing chloride ion showed the highest catalytic activities and enantioselectivities. Higher enantioselectivities were obtained in CH_2Cl_2 (run 1) or in THF (run 5) than in MeOH (run 6). Hydrogen pressure influenced reaction rate but did not affect the enantiomeric excesses of the products.

Various substrates were investigated under selected conditions (Table 1). γ-Butyrolactones **1** and **3** were hydrogenated in high enantiomeric excesses (>90% *ee*), while hydrogenation of **5** proceeded in very low enantioselectivity (run 12). Itaconic anhydride (**6**), the compound structurally related to **1**, was also hydrogenated smoothly to give the product arisen from the same sense of enantioselectivity with that of **1**, though the optical yield is still unsatisfactory. Thus, the stereoselectivity depends highly on relative positions of olefin and oxygen functional group(s) of unsaturated carbonyl compounds. Usually high enantioselectivities have been attained for hydrogenation of unsaturated compounds catalyzed by BINAP—Ru(II) complexes only in case that substrates have another functional group at a neighboring position.[2] Such reactions are considered to proceed by chelation control. In the present reaction, however, it is still not clear whether the interaction of both C=C and oxygen atom in the substrates with rhuthenium is requisite or not, though etheral oxygen has also been shown to act as coordinating group in the hydrogenation using Rh and Ir complexes.[6]



5 **6** **7**

When a mixture of (*E*)- and (*Z*)-2-propylidene-γ-butyrolactone [(*E*)-**1b** and (*Z*)-**1b**] was used as starting material, hydrogenation catalyzed by (*R*)-**9** gave (*S*)-**2b** in 92% *ee* (run 8). The reaction of stereomerically pure (*E*)-**1b** or (*Z*)-**1b** also proceeded smoothly and the products with the same absolute configuration were obtained in almost the same enantioselectivities (runs 9 and 10). The above results show that the proportion of (*E*)-

Table 1. Asymmetric Hydrogenation of 2- and 4-Alkylidene-γ-butyrolactones and 2-Alkylidenecyclopentanones Catalyzed by BINAP—Ru(II) Complexes.[a]

run	substrate	cat.[b]	product % *ee* [c,d]	product config[e]
1	**1a**	(*S*)-**8**	95 (91)	*R*
2	**1a**	(*S*)-**9**	93 (96)	*R*
3	**1a**	(*R*)-**10**	92	*S*
4	**1a**	(*S*)-**11**	84	*R*
5[f]	**1a**	(*R*)-**8**	94	*S*
6[g]	**1a**	(*S*)-**8**	82	*R*
7[h]	**1a**	(*S*)-**8**	95	*R*
8	**1b** (7/3)[i]	(*R*)-**9**	92 (98)	*S*
9[j]	**1b** (0/1)[i]	(*S*)-**9**	95	*R*
10	**1b** (1/0)[i]	(*R*)-**9**	95	*S*
11	**3**	(*S*)-**8**	94[k] (99)	*R*
12[l]	**5**	(*R*)-**9**	— (6)	*S*
13	**6**	(*R*)-**9**	— (54)	*S*
14	**7**	(*R*)-**8**	94[m]	*S*[n]
15	**7**	(*R*)-**10**	>98[m,o]	*S*[n]

a) Reactions were carried out in CH_2Cl_2 at 50 °C under 100 atm of hydrogen for 20—60 h and conversions of substrates determined by GLC were 100% unless otherwise mentioned.

b) **8**: [RuCl(binap)(benzene)]Cl,[5] **9**: $Ru_2Cl_4(binap)_2NEt_3$,[7] **10**: $Ru(OCOCH_3)_2$(binap),[8] **11**: [RuI(binap)(*p*-cymene)]I.[5]

c) Enantiomeric excess was determined by HPLC (Chiralcel OD, hexane—2-propanol 994 : 6, 1 ml/min, UV (230 nm)).

d) Optical purity calculated based on the following optical rotation values is given in parenthesis. (*R*)-2-Methyl-γ-butyrolactone; $[\alpha]_D$ +23.1° (*c* 9.7, EtOH).[9] (*R*)-2-Propyl-γ-butyrolactone (73% *ee*); $[\alpha]_D$ -8.05° (*5.7, EtOH*).[10] (*S*)-4-Methyl-γ-butyrolactone; $[\alpha]_D$ -31.6° (*c 0.95, $CHCl_3$*).[11] (*S*)-3-Methyl-γ-butyrolactone; $[\alpha]_D$ -24.7° (*c* 4, MeOH).[12] (*R*)-2-Methylsuccinic anhydride; $[\alpha]_D$ +32.1° (*c* 4.0, EtOH).[13]

e) Absolute configuration was determined based on optical rotation.

f) Tetrahydrofuran was used as solvent.

g) Methanol was used as solvent.

h) The initial hydrogen pressure was 3 atm. The conversion was 96% by GC.

i) Figures in parentheses are the *E/Z* ratios of substrate **1b**.

j) The conversion was 67% by ^{1}H-NMR.

k) Enantiomeric excess was determined by GLC (CP Cyclodex-B-236M, 0.25 mm x 50 m, 80 °C, He).

l) The conversion was 98% by ^{1}H-NMR.

m) Enantiomeric excess was determined by HPLC (Wakosil 5sil (4.6 mm x 30 mm) and Chiralcel OJ (4.6 mm x 250 mm), hexane—2-propanol 199 : 1, 1 ml/min, UV (230 nm)).

n) Absolute configuration was determined based on optical rotation of 5-pentyl-δ-valerolactone which was prepared by Baeyer-Villiger oxidation of 2-pentylcyclopentanone with *m*-chroloperbenzoic acid in CH_2Cl_2.

o) $[\alpha]_D^{25}$ +55.82° (*c* 1.93, MeOH). The optical rotation value of the pure sample has not been reported.

and (*Z*)-isomers does not affect the enantioselectivity. This suggests that the BINAP—Ru(II) complex differentiates the enantioface of sp^2 carbon α to carbonyl moiety regardless of the geometry at β-sp^2 carbon.[14] At present, however, the possibility that hydrogenation proceeds through a $Z \rightarrow E$ isomerization can not be ruled out, because a controlled experiment shows that the *Z* isomer was isomerized to *E* isomer to a considerable extent during the catalysis.[15]

Interestingly, 2-alkylidenecyclopentanones such as **7** were also hydrogenated smoothly to give 2-alkylcyclopentanones. Among the BINAP—Ru(II) complexes used, $Ru(OCOCH_3)_2$(binap) afforded the highest enantioselectivity (>98% *ee*, run 15). Thus, the present asymmetric hydrogenation catalyzed by BINAP—Ru(II) complexes provides us a new route to optically active γ-butyrolactones and cyclopentanones in high optical purity.

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