An Efficient Synthesis of Optically Active 4-Methyloxetan-2-one: Asymmetric Hydrogenation of Diketene catalysed by binap–Ruthenium(II) Complexes [binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]

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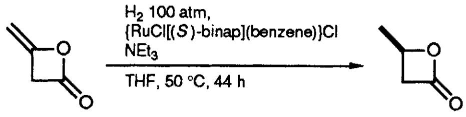
Highly enantioselective hydrogenation of diketene with the catalytic system derived from {RuCl[(*S*)- or (*R*)-binap](benzene)}Cl and triethylamine or with $Ru_2Cl_4[(S)$- or (R)-binap$]_2(NEt_3)$ [binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] in tetrahydrofuran gives optically active 4-methyloxetan-2-one in up to 97% selectivity and 92% enantiomeric excess (e.e.).

In recent years, polyesters derived from (*R*)-3-hydroxybutyric acid have been attracting much attention as biodegradable polymers. For example, the commercially available biodegradable plastic developed by ICI Co. Ltd is a linear block copolymer of (*R*)-3-hydroxybutyric acid and 3-hydroxypentanoic acid.[1] This material has been prepared by glucose fermentation by use of a bacterium of natural origin. Since use of environmentally friendly materials is one of the most important social needs at present, the development of new methods to prepare monomers which, upon polymerization, give polyesters of (*R*)-3-hydroxybutyric acid seems to be attractive in organic synthesis. In view of the recent progress in the ring opening polymerization of 4-methyloxetan-2-one **2**,[2] (*R*)-**2** is thought to be a promising starting compound.† We now report a highly efficient synthesis of (*R*)- and (*S*)-**2** by asymmetric hydrogenation of diketene **1** catalysed by binap–Ru^{II} complexes [eqn. (1)].[4]‡ Compound (*R*)-**2** has been synthesized by lactonization of (*S*)-3-bromobutyric acid obtained by optical resolution of racemic 3-bromobutyric acid with (*R*)-1-(1-naphthyl)ethylamine.[6]

The typical hydrogenation was performed as follows. A solution of triethylamine (3.6×10^{-2} mmol) in tetrahydrofuran (THF) (5.5 ml) was added to {RuCl[(*S*)-binap](benzene)}Cl (*S*)-**3** (4.0×10^{-2} mmol) under argon and the mxiture was stirred at 50 °C for 15 min. The resulting solution was concentrated under a reduced pressure to about a half of its initial volume. To this was added a solution of diketene **1** (22 mmol) in THF (10 ml) and then the mixture was transferred to a quartz vessel placed in a 50 ml stainless steel autoclave. Hydrogenation was carried out at 50 °C under the initial hydrogen pressure of 100 atm for 44 h. ^1H NMR analysis of the product obtained after removal of the solvent showed that it was composed of 4-methyloxetan-2-one **2** (97%) and butyric acid (3%). A part of the product was converted to methyl 3-hydroxybutyrate by the treatment of **2**



1 (*R*)-**2** (1)

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† Synthesis of methyl (*R*)-3-hydroxybutyrate, another important starting material for polyesters of (*R*)-3-hydroxybutyric acid, by asymmetric hydrogenation of methyl 3-oxobutyrate has been reported.[3]

‡ For the asymmetric hydrogenation of 5-methylene-2-oxotetrahydrofuran catalysed by binap–Ru^{II} complexes, see ref. 5.

Table 1 Asymmetric hydrogenation of diketene catalysed by binap–Ru^{II} complexes[a]

			Product		
Catalyst[b]	Solvent	t/h	Select. (%)[c]	E.e. (%)[d]	Config.[e]
(R)-**3**	CH_2Cl_2	40	60	70	S
(R)-**3** + 0.5 NEt_3	THF	44	97	92	S
(S)-**3** + 0.9 NEt_3	THF	44	97	92	R
(R)-**4**[f]	CH_2Cl_2	25	90	90	S
(R)-**4**	THF	60	95	90	S

[a] The reaction was carried out at 50 °C under initial hydrogen pressure of 100 atm. The substrate : catalyst ratios were 500–1000 : 1 and conversions were 100%. [b] (S)-**3**: {RuCl[(S)-binap](benzene)}Cl, (R)-**4**; Ru_2Cl_4[(R)-binap]$_2$(NEt_3). [c] The other product was butyric acid. [d] Determined by ^1H NMR spectroscopy of the (R)-MTPA ester of methyl 3-hydroxybutyrate derived from **2**. [e] Determined by optical rotation of (S)-**2** (95% e.e.); $[\alpha]_D^{22}$ −28.8 (c 4.3, $CHCl_3$); T. Sato, T. Itoh, C. Hattori and T. Fujisawa, *Chem. Lett.*, 1983, 1391. [f] At 70 °C.

with methanol containing a catalytic amount of KOH. This alcohol was further converted to the ester of (R)-2-methoxy-2-(trifluoromethyl)phenylacetic acid [(R)-MTPA] by the reaction with (R)-2-methoxy-2-(trifluoromethyl)phenylacetyl chloride in pyridine in the presence of 4-dimethylaminopyridine. The diastereoisomeric excess of this ester determined by ^1H NMR spectroscopy was 92%. Some other representative results and reaction conditions are listed in Table 1.

Among the catalytic systems used, the species derived from {RuCl[(S)- or (R)-binap](benzene)}Cl and NEt_3 gave the best results in both selectivity and enantiomeric excess (e.e.). In the absence of triethylamine, competitive hydrogenolysis occurred to give butyric acid in 30% yield. The role of the added amine has not been elucidated. Higher reaction temperature does not cause any substantial loss of enantioselectivity over the range 50–70 °C. Enantioselectivities were not so sensitive to the substrate to catalyst ratios. Use of aprotic solvents is important for high product selectivities. When a neutral binap–Rh^I species derived from $[Rh(cod)Cl]_2$ (cod = cycloocta-1,5-diene) and 2.05 equiv. of (R)-binap was used as catalyst, the major product was butyric acid accompanied by a small amount of the desired product **2**.

(R)-**2** produced by the present method is of particular interest as the starting compound for the synthesis of various important materials such as biodegradable polymers, since the starting diketene **1** is easily accessible in a large quantity under reasonable prices and, in many cases, enantiomeric excesses higher than 90% seem to meet requirements for optical purity.

This work was supported by the Grant-in-Aid for Scientific Research on Priority Areas of Organic Unusual Valency No. 04 217 103 and the Grant-in-Aid for Developmental Scientific Research No. 03 555 178 from the Ministry of Education, Science and Culture, Japan. The author (T. O.) is also indebted to the Watanabe Memorial Foundation and Naito Foundation for partial financial support.

Received, 3rd September 1992; Com. 2/04759D

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