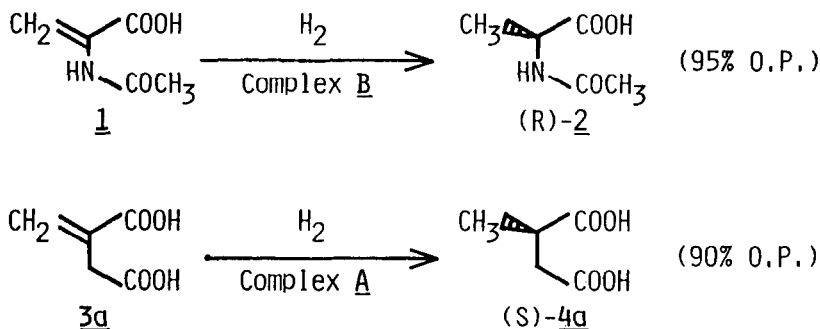


**RUTHENIUM(II)-BINAP COMPLEX CATALYZED ASYMMETRIC HYDROGENATION  
OF UNSATURATED DICARBOXYLIC ACIDS**

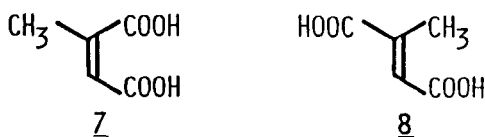
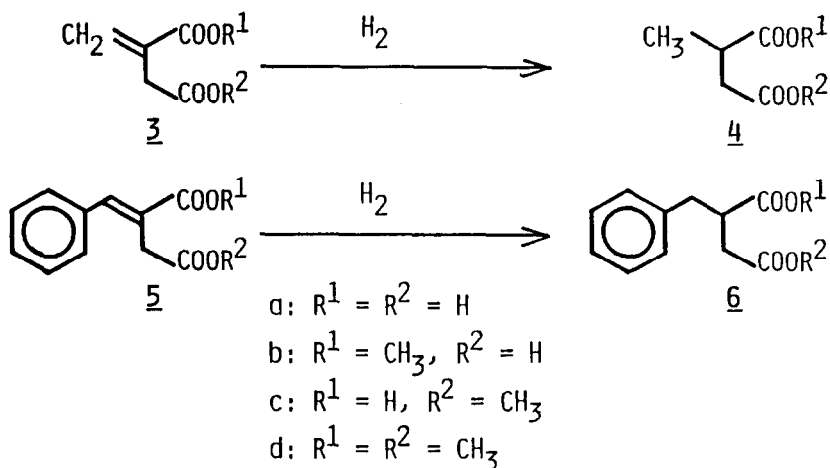
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Summary: Asymmetric hydrogenation of unsaturated dicarboxylic acids employing ruthenium-BINAP complexes as catalyst gave optically active 2-alkylsuccinic acids with high enantioselectivities.

Catalytic asymmetric hydrogenation by means of a wide variety of rhodium-bisphosphine complex catalyst has been developed to achieve very high e.e., and further, its asymmetric induction mechanism has been recently revealed in detail.<sup>1)</sup> The major interest has been focused on the asymmetric hydrogenation of dehydroamino acids, and few examples were reported on highly stereoselective rhodium-bisphosphine complex catalyzed asymmetric hydrogenation of dicarboxylic acids such as itaconic acid, which have the structural feature closely related to dehydroamino acids. Exceptionally, rhodium-BPPM complex was reported to be an effective catalyst for this reaction, affording a high optical yield under practical conditions.<sup>2)</sup>



We have recently reported the synthesis of novel ruthenium complexes of (+)-BINAP ((R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl);<sup>3)</sup>  $\text{Ru}_2\text{Cl}_4((+)\text{-BINAP})_2(\text{NEt}_3)$  A and  $\text{RuHCl}((+)\text{-BINAP})_2$  B. We also reported that these complexes worked as catalysts for the asymmetric hydrogenation of dehydroamino acids such as 1 to give the products with high optical yields.<sup>4)</sup> Here we wish to report



that ruthenium-BINAP complexes **A** and **B** are effective catalysts for the asymmetric hydrogenation of itaconic acid and related dicarboxylic acid.

Itaconic acid **3a** (1.5 mmol) was dissolved in toluene-THF (1:1; 30 ml) and stirred at 35°C under hydrogen atmosphere (3 kgw/cm<sup>2</sup>) in the presence of complex **A** (0.030 mmol) and triethylamine (1.8 mmol). The hydrogenation of **3a** occurred smoothly. After 24 h the reaction mixture was evaporated to dryness, and the residue was dissolved in 0.5 M NaOH, and washed with ether. The aqueous layer was acidified with 1 M HCl to pH 1 and extracted repeatedly with ether. After being dried over MgSO<sub>4</sub>, ether was removed to give (S)-methylsuccinic acid **2a** having 88% O.P. An NMR analysis showed no starting material remained. To the best of our knowledge, the value of optical purity obtained here is the highest among the reported ones provided by the asymmetric hydrogenation using ruthenium-bisphosphine catalysts.<sup>5)</sup> The enantioface selection by the catalyst in the hydrogenation of **3a** is the same as that of structurally related dehydroamino acid,  $\alpha$ -acylaminoacrylic acid **1**. This result suggests that at the transition state **3a** should form a chelate ring to ruthenium with the olefinic moiety and the 4-carbonyl group, in a similar manner to **1**.

The results of asymmetric hydrogenation of some unsaturated dicarboxylic acids and their esters are summarized in Table I. The free acids, itaconic acid and benzylidenesuccinic acid **5a**, were hydrogenated with good to excellent optical purity by either of the complexes, while citraconic acid **7** and mesaconic acid **8** were hardly hydrogenated. Interestingly, the esters of **3a** and **5a** were hydrogenated with somewhat lower enantioselectivities than those

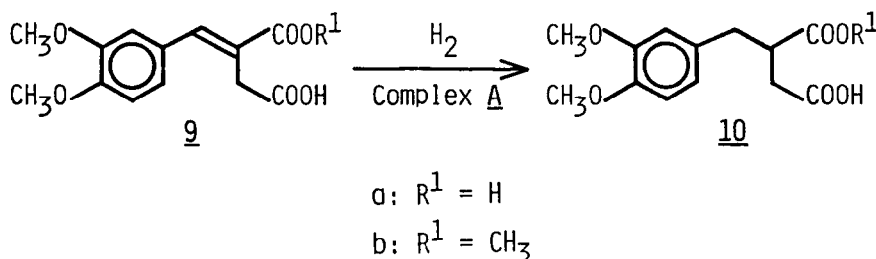
Table I. Hydrogenation of Unsaturated Dicarboxylic Acids and Their Esters.

Substrate	Product	Catalyst <sup>a)</sup>	Time/h	Conversion/% <sup>b)</sup>	O.P./% <sup>c)</sup>
3a	(S)-4a	A	24	100	88
		B	24	100	86
3b	(S)-4b	A	24	100	79
3c	(S)-4c	A	24	100	60
		B	24	100	54
3d	(S)-4d	A	24	96	68
		B	24	71	54
5a	(S)-6a	A	24	94	90
		B	24	56	88
5c	(S)-6c	A	48	100	72
		B	48	17	48
5d	(S)-6d	A	48	20	0
		B	48	10	0
7	(R)-4a	B	24	39	34
8	—	B	24	0	—

a) 2 mol % as Ru atom. b) Determined by an NMR analysis. c) Based on the values for optically pure (R)-4a,  $[\alpha]_D = +16.88^\circ$  (c = 2.2, ethanol) (E. Berner and R. Leonardsen, *Ann.* **538**, 1 (1939)) and (S)-6a,  $[\alpha]_D = -27^\circ$  (c = 2, ethyl acetate) (S. G. Cohen and A. Milovanovic, *J. Am. Chem. Soc.*, **90**, 3495 (1968)).

for the free acids. Especially, methyl esters of the 4-carboxyl group were unsuitable for the asymmetric hydrogenation by A and B. This fact makes a striking contrast to that of rhodium-dipamp catalyzed hydrogenation,<sup>6)</sup> where 3a was reported to be hydrogenated with low optical yield because of its dimer formation through hydrogen bonding, nevertheless the methyl esters 3b and 3d gave much higher optical yields. The fact that the substrates having C-4 carboxylate are reduced with higher e.e. than the C-4 esters suggests that the 4-carboxylate group, which coordinate to ruthenium at the transition state, plays an important role in the enantioselection effected by ruthenium-BINAP catalysts, and that the hydrogen bonding interference to the chelate formation,

which occurs in the rhodium-dipamp system, probably affects little in the enantioface discrimination by the ruthenium catalysts. These results can be explained by supposing that ruthenium complexes have a rather strong interaction with carboxyl group to break the hydrogen bonding between the substrates and prefer a free acid group rather to an ester group.



Finally, veratrylidene succinic acid 9a was also asymmetrically hydrogenated by complex A to afford optically active veratrylsuccinic acid 10a with as high as 84 % of optical purity.<sup>7)</sup> This is the first example that 10a is obtained by means of the asymmetric hydrogenation instead of the optical resolution of racemic 2-veratrylsuccinic acid-1-methyl ester 10b. The half ester 10b is a well known chiral starting material for some optically active lignans such as kusunokinin,<sup>8)</sup> which involve the chiral  $\gamma$ -lactone framework in their molecules. The optically active dicarboxylic acid 10a obtained here will also be a potential starting material for lignan synthesis. Further studies along this line are in progress.

#### References and notes

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- 7) Hydrogenation of 9a is carried out in similar procedure to the case of 3a except for the ratio of substrate to catalyst (100:1). Specific rotation of 10a is increased by recrystallization from  $-19.3^\circ$  to  $-22.3^\circ$ , which can be considered as that of optically pure (S)-veratrylsuccinic acid.
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