Notes

Kinetic Resolution of Allyl Carbonates in Asymmetric Allylic Alkylation Catalyzed by Planar-Chiral Cyclopentadienyl-Ruthenium Complexes

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Summary: Planar-chiral cyclopentadienyl-ruthenium complexes serve as effective catalysts for the kinetic resolution of racemic allylic carbonates in asymmetric allylic alkylation. The absolute configurations of the recovered carbonates and the alkylation products are dependent on the substituent on the cyclopentadienyl group at the 4-position of the ruthenium catalyst.

Introduction

Kinetic resolution, the principle of which rests on the difference in the rate of transformation between enantiomers of substrates, represents an efficient method for producing enantiopure compounds, and both enzymatic and nonenzymatic resolution processes have been extensively studied.[1] Major developments using nonenzymatic catalysts for kinetic resolution have been achieved by transition-metal catalysts with various kinds of chiral ligands. In this context, the enantioselective substitution of allylic compounds with nucleophiles, which is a powerful tool for the controlled formation of carbon−carbon and carbon−heteroatom bonds, is of special interest because it has potential for the kinetic resolution of racemic allylic compounds.[2] Although Pd-based catalysts have been widely used in enantioselective allylic substitution,[3] recent studies have been aimed at identifying other transition metals having effects similar to or better than those of Pd catalysts.[4,5] However, there are very few reports on kinetic resolution in allylic substitution that uses metal catalysts other than Pd catalysts.[6]

Our research has been focused on the stereochemistry of planar-chiral cyclopentadienyl-ruthenium (Cp′Ru) complexes possessing an anchor phosphine ligand,[7] which have high ability to control the metal-centered chirality in some ligand-exchange reactions.[8] Recently, we showed that planar-chiral Cp′Ru complexes **1** catalyze asymmetric allylic amination and alkylation with high enantioselectivity.[9] We present herein an effective kinetic resolution of racemic allyl carbonates in asymmetric allylic alkylation via catalysis by planar-chiral Cp′Ru complexes **1**.

Results and Discussion

The reaction of a racemic mixture of (*E*)-ethyl pent-3-en-2-yl carbonate (**2a**) with 0.6 equiv of sodium dimethyl malonate (**3**) in the presence of 2.5 mol % (*S*)-

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Scheme 1

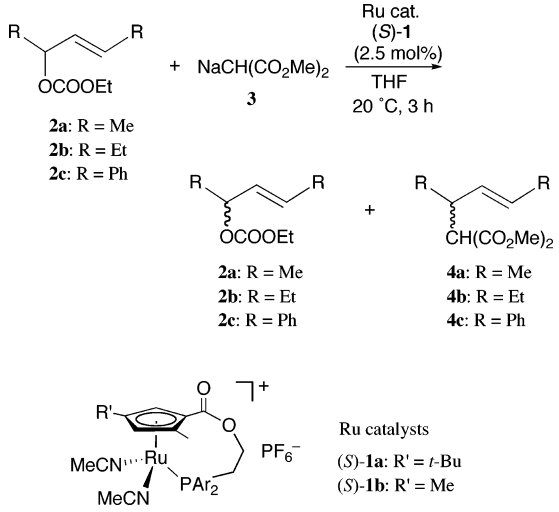

Table 1. Kinetic Resolution of (*E*)-Ethyl Pent-3-en-2-yl Carbonate 2a by Planar-Chiral Cp′Ru Complexes 1

entry	catalyst	ratio of **3**/**2a**	conversion (%) of **2a**[a]	% ee recovered **2a**[b,c]	k_{rel}[d]	yield (%) of **4a**[a]	% ee of **4a**[b,c]
1	(*S*)-**1a**	0.2	16	10(*R*)	3.5	13	80(*S*)
2	(*S*)-**1a**	0.3	25	24(*R*)	7.7	24	85(*S*)
3	(*S*)-**1a**	0.4	34	39(*R*)	10.6	33	87(*S*)
4	(*S*)-**1a**	0.6	48	72(*R*)	17.3	48	91(*S*)
4	(*S*)-**1a**	0.7	54	84(*R*)	15.6	50	91(*S*)
5	(*S*)-**1a**	0.8	60	94(*R*)	14.7	55	92(*S*)
7	(*S*)-**1a**	1.0	65	94(*R*)	10.0	61	89(*S*)
8	(*S*)-**1a**	1.2	69	93(*R*)	7.5	65	89(*S*)
9	(*S*)-**1b**	0.2	15	10(*S*)	4.0	15	72(*R*)
10	(*S*)-**1b**	0.4	33	22(*S*)	3.2	30	83(*R*)
11	(*S*)-**1b**	0.6	44	33(*S*)	3.3	41	87(*R*)
12	(*S*)-**1b**	0.7	54	43(*S*)	3.2	51	87(*R*)
13	(*S*)-**1b**	0.8	61	51(*S*)	3.1	57	87(*R*)
14	(*S*)-**1b**	1.0	72	64(*S*)	2.9	68	87(*R*)
15	(*S*)-**1b**	1.2	80	72(*S*)	2.7	77	87(*R*)

[a] Conversion and yield were determined by HPLC. [b] The ee values were determined by GLC (Chirasil-DEX capillary column, 25 m × 0.25 mm) or HPLC (Daicel Chiralcel OD, hexane/i-PrOH, 99/1). [c] Configuration of the products was assigned on the basis of the sign of specific rotation according to the literature (see Supporting Information). [d] $k_{rel} = k_{fast}/k_{slow} = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (*C*: conversion, ee: enantiomeric excess of the recovered substrate).

1a at 20 °C in THF for 3 h gave the alkylation product (**4a**) in 48% yield with 91% enantiomeric excess (ee) (*S*) as well as 48% yield of the recovered carbonate **2a**. GLC analysis showed that the recovered **2a** was an *R* isomer with 72% ee, suggesting that the *S* enantiomer reacted significantly faster than the *R* enantiomer ($k_{rel} = 17.3$). To control the conversion of the substrate, we performed the reaction with various amounts of **3**, and the representative results are shown in Table 1. Although the ee of the recovered **2a** was increased with an increase in conversion of up to 60% (entries 1−6), the ee value was almost unchanged at greater than 60% conversion (entries 6−8). The best result was attained in the reaction with 0.8 equiv of **3** to give (*S*)-**4a** in 55% yield with 92% ee and (*R*)-**2a** in 40% yield with 94% ee (entry 6). No significant difference was observed in the ee of the alkylation product **4a** except for the result at the lowest conversion (entries 2−8), suggesting that the absolute configuration of the substrate does not affect the enantioselectivity in allylic alkylation using complex **1a**.

Table 2. Kinetic Resolution of Allyl Carbonates 2 by Planar-Chiral Cp′Ru Complexes 1

entry	cat.	substr.	conversion (%) of **2**[a]	% ee of recovered **2**[b,c]	k_{rel}[d]	yield (%) of **4**[a]	% ee of **4**[b,c]
1	(*S*)-**1a**	**2b**	58	90(*R*)	14.0	55	>99(*S*)
2	(*S*)-**1b**	**2b**	57	30(*S*)	2.1	53	91(*R*)
3	(*S*)-**1a**	**2c**	58	50(*R*)	3.4	55	92(*S*)
4	(*S*)-**1b**	**2c**	54	18(*S*)	1.6	50	95(*R*)

[a] Conversion and yield were determined by HPLC. [b] The ee values were determined by GLC (Chirasil-DEX capillary column, 25 m × 0.25 mm) or HPLC (Daicel Chiralcel OD, hexane/i-PrOH, 99/1). [c] Configuration of the products was assigned on the basis of the sign of specific rotation according to the literature (see Supporting Information). [d] $k_{rel} = k_{fast}/k_{slow} = \ln[(1 - C/100)(1 - ee/100)]/\ln[(1 - C/100)(1 + ee/100)]$ (*C*: conversion, ee: enantiomeric excess of the recovered substrate).

Complex (*S*)-**1b**, having a methyl group at the 4-position of the Cp′ ring, was also employed for the kinetic resolution of **2a** (entries 9−15). Although the enantioselectivity of **4a** was similar to that in the reaction using (*S*)-**1a**, the ee values of **2a** were slightly lower. To our surprise, the absolute configurations of not only the product **4a** but also the recovered substrate **2a** were opposite of those in the reactions using complex (*S*)-**1a**.[9] Thus, the treatment of racemic **2a** with 0.8 equiv of **3** in the presence of 2.5 mol % (*S*)-**1b** under the same conditions gave (*R*)-**4a** in 57% yield with 87% ee and (*S*)-**2a** in 39% yield with 51% ee (entry 13).

This kinetic resolution system could also be extended to other allylic carbonates (Table 2). The reaction of racemic (*E*)-ethyl hept-4-en-3-yl carbonate **2b** with 0.8 equiv of **3** catalyzed by complex (*S*)-**1a** gave (*S*)-**4b** in 55% yield with >99% ee and (*R*)-**2b** in 40% yield with 90% ee (entry 1), whereas (*R*)-**4b** in 53% yield with 91% ee and (*S*)-**2b** in 43% yield with 30% ee were obtained from a similar reaction using complex (*S*)-**1b** as a catalyst (entry 2). The reaction of (*E*)-1,3-diphenylallyl ethyl carbonate **2c** resulted in a decrease in the ee of the recovered carbonate, although the alkylation product **4c** was produced in high enantioselectivity (entries 3 and 4). The stereochemistry of both the alkylation product and the recovered substrate was also opposite of each other between the reactions catalyzed by complexes (*S*)-**1a** and (*S*)-**1b**.

It is generally accepted that allylic substitutions using transition-metal catalysts proceed via π-allyl complexes that are produced by the oxidative addition of allylic compounds. There are some reports on the oxidative addition of allyl halides to $CpRuL_3$ complexes to give π-allyl Ru complexes, in which the π-allyl groups coordinate in an endo fashion.[10] As complexes (*S*)-**1a** and

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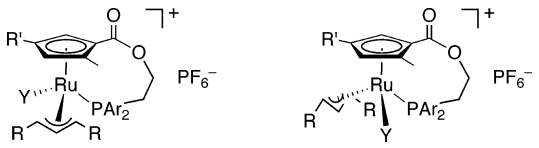
Chart 1



(*S*)-**1b** gave products with different absolute configurations, it seems reasonable that complex (*S*)-**1a** generates the π-allyl Ru complex with a different configuration at the metal center relative to that from complex (*S*)-**1b** (Chart 1). We have already found similar phenomena in the reaction of **1** with allyl chloride.[8f] The highly diastereoselective oxidative addition to planar-chiral Cp′ complexes was also reported by other groups.[11]

In conclusion, we have demonstrated that the planar-chiral Cp′Ru complexes are effective catalysts for the kinetic resolution of allyl carbonates. This is the first example of kinetic resolution in allylic alkylation using Ru catalysts. Further studies on the mechanism of the allylic alkylation are in progress.

Experimental Section

General Procedures. All reactions were carried out under an atmosphere of argon, and the workup was performed in air. ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-LA400 and -LA600 spectrometers using $SiMe_4$ as an internal standard. IR and mass spectra were taken on a Perkin-Elmer system 2000 FT-IR and a JEOL JMS-600H, respectively. Optical purity was determined by GLC using a Chirasil-DEX capillary column (25 m × 0.25 mm) except for **4c**, for which HPLC equipped with a DAICEL chiral cell OD column (eluent: hexane/i-PrOH = 99/1) was used. The absolute configurations of the allyl ethyl carbonate derivatives **2a**,[3h] **2b**,[3h] and **2c**[12] and alkylation products **4a**,[13] **4b**,[14] and **4c**[15] were assigned referring to the literature.

THF was distilled over sodium benzophenone ketyl under argon just before use. Other chemicals available commercially were used without further purification. Ruthenium complexes **1a** and **1b** were prepared as reported previously.[7] Identification of the products was performed by spectral analyses referring to the literature.[9,13−15]

General Procedure of the Reaction of Allylic Carbonates (2) with Sodium Dimethyl Malonate (3). Sodium hydride (60% dispersion in mineral oil, 220 mg, 5.5 mmol) was washed with dry hexane three times and dried in vacuo. After addition of THF (8 mL), dimethyl malonate (456 μL, 4 mmol) was added at 0 °C. The reaction mixture was stirred for 10 min and filtered through Celite. An appropriate amount of the filtrate (0.5 M solution) was measured by microsyringe and added dropwise to a solution containing allyl carbonate (**2**) (0.1 mmol) and Ru complex (**1**) (2.5 mmol) in THF (0.5 mL) at 20 °C, and the mixture was stirred for 3 h. The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel using hexane/diethyl ether = 9/1 (v/v) as an eluent. The yield and enantioselectivity were examined by using GLC and HPLC.

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