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# KINETIC RESOLUTION OF 4-HYDROXY-2-CYCLOPENTENONE BY RHODIUM-CATALYZED ASYMMETRIC ISOMERIZATION

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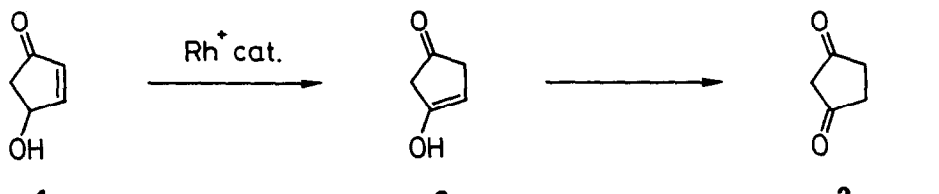
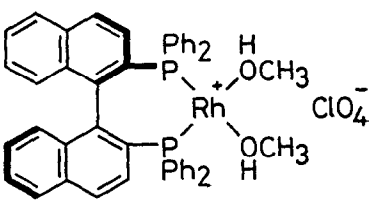
*Summary:* Cationic Rh—BINAP complexes catalyze isomerization of racemic 4-hydroxy-2-cyclopentenone to 1,3-cyclopentanedione with 5:1 enantiomeric discrimination.

(*R*)-4-Hydroxy-2-cyclopentenone [(*R*)-**1**] is a key chiral building block in our three-component coupling prostaglandin synthesis.[2] This compound has been obtained by the BINAL-H asymmetric reduction of 4-cyclopentene-1,3-dione,[3] synthesis from (2*S*,3*S*)-tartaric acid,[4] terrein,[5] or 2,4,6-trichlorophenol (including resolution),[6] chromatographic separation via the diastereomeric[7] or racemic[8] hydroxyl-protected derivatives, enzymatic kinetic resolution of the acetate[9] or related compound,[10] etc. We describe here the chemical kinetic resolution based on a new transition metal-catalyzed asymmetric 1,3-hydrogen migration.

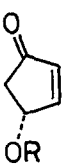
In the presence of cationic Rh—phosphine complexes, the allylic alcohol **1** undergoes isomerization, leading to the keto enol **2** and ultimately the 1,3-diketone **3**. When racemic **1** was exposed to the (*R*)-BINAP complex, (*R*)-**4**,[11] the *S* enantiomer was consumed more readily. The asymmetric isomerization[12] in THF at 0 °C afforded $k_{fast}/k_{slow}$ = 5:1 discrimination, providing a convenient method for resolution of readily accessible (±)-**1**[13] to give the important *R* enantiomer. Thus the reaction with 0.5 mol% of (*R*)-**4** gave (*R*)-**1** in 91% ee at 72% conversion, and the extremely high crystallinity of the diketone **3** allowed easy




**1** **2** **3**




(*R*)- **4**




(*R*)-**1**, R = H
(*R*)-**5**, R = *t*-$C_4H_9(CH_3)_2Si$

separation of (*R*)-**1** from the reaction mixture. The enantiomerically pure enone was obtained by conversion to the crystalline *O*-silyl derivative, (*R*)-**5**.[14] The 1,3-diketone **3** is also useful but difficult to make.[15]

The experimental procedure is as follows. A dry 300-mL Schlenk tube was charged with (*R*)-**4** (845 mg, 0.951 mmol) and anhydrous degassed THF (240 mL) under argon stream. To the resulting yellowish red solution cooled to -70 °C was added degassed (±)-**1** (16.9 g, 0.172 mol) by syringe, and the mixture was kept at 0 °C for 14 days. After separation of crystalline **3** (10.3 g), mp 151—153 °C, by filtration, the filtrate was subjected to column chromatography (silica gel, Fuji Devison Chemical Co., BW 300, 250 g; eluent, ether) to give (*R*)-**1** in 91% ee (4.60 g, 27% yield). This product (4.60 g, 46.9 mmol) was dissolved in dichloromethane (40 mL) and the solution was cooled to 0 °C. To this was added 4-dimethylaminopyridine (573 mg, 4.69 mmol), triethylamine (7.19 mL, 51.5 mmol), and *t*-butyldimethylsilyl chloride (7.77 g, 51.5 mmol), and the mixture was stirred at 26 °C for 2 h. After removal of the resulting precipitate by filtration, the filtrate was evaporated and the residue was diluted with hexane (300 mL). This was washed successively with water, saturated aqueous potassium hydrogensulfate solution, saturated aqueous sodium hydrogencarbonate, and brine. Drying over anhydrous magnesium sulfate, evaporation of the solvent, and distillation (80 °C/0.5 mmHg) afforded (*R*)-**5** (9.24 g, 93% yield). Recrystallization from pentane gave (*R*)-**5** in >99% ee, mp 29—30 °C (6.7 g, 18% yield from **1** (36% of theory)). HPLC analysis of **5**: column, DAICEL Chemical Industries Ltd. CHIRALCEL OC; eluent, 1% 2-propanol in hexane; flow rate, 0.5 mL/min; detection, 215-nm light; $t_R$ 13.9 min (*R*), 17.8 min (*S*).

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