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# The Asymmetric Hydroformylation of Vinyl Acetate

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**Synopsis.** Vinyl acetate gives selectively (*S*)-2-acetoxypropanal in 10—24% optical yields by the asymmetric hydroformylation with $\mu,\mu'$-dichlorotetracarbonyldirhodium–(−)-DIOP. (*R*)-Benzylmethylphenylphosphine and neomenthyldiphenylphosphine give low optical yields. The reaction depends essentially on the DIOP/rhodium ratio. Just 2 mol or more of (−)-DIOP per g-atm of rhodium is required for the asymmetric reaction. Other reaction variables (temperatures and pressures of hydrogen and carbon monoxide) have minor effects.

More recently, a chiral phosphine–rhodium complex system has been shown to be effective for the asymmetric hydroformylation of olefins.[1] These studies have been mainly concentrated on styrene and butenes. Styrene gives 2-phenylpropanal as the major product in moderately high optical yields up to 44%[1b] but such 1-alkenes as 1-butene and 1-octene give branched chain-aldehydes with optically active carbons as minor products in only low optical yields. Little attention, however, has been paid to the asymmetric hydroformylation of *O*- and *N*-vinyl compounds, which are selectively formylated on the inner carbon adjacent to the oxygen and nitrogen to produce aldehydes with an optically active carbon.[2] Thus, vinyl acetate gives 2-acetoxypropanal in an excellent yield. Compared with simple olefins, *O*- and *N*-vinyl compounds appear to be more suitable for the asymmetric hydroformylation.

The present study will deal with the asymmetric hydroformylation of vinyl acetate using a chiral phosphine–rhodium complex, and the effects of several reaction variables (ligands, temperatures, and pressures of hydrogen and carbon monoxide) will be described in some detail.

## Experimental

All the $^1$H NMR spectra were recorded on a JEOL JNM-PM-60 spectrometer, using $Me_4Si$ as the internal standard. The optical rotations were measured on a JASCO model DIP-180 automatic polarimeter using samples as a neat liquid. The GPC analysis was carried out on a Shimadzu model GC-3B apparatus equipped with a column (3 mm$\phi$, 3 m) packed with diethylene glycol adipate polyester on Chromosorb.

*Materials.* The vinyl acetate was refluxed over active calcium sulfate for one or two days, distilled, and stored in a refrigerator. Neomenthyldiphenylphosphine(abbreviated as nmdpp),[3] (*R*)-benzylmethylphenylphosphine(bmpp),[4] 2,2-dimethyl-4,5-bis(diphenylphosphino)-1,3-dioxolane ((−)-DIOP),[5] and $\mu,\mu'$-dichlorotetracarbonyldirhodium[6] were prepared according to the methods in the literature.

*Reaction Procedure.* The reaction was carried out in a manner similar to that described in a previous paper.[1a] The 2-acetoxypropanal was separated by vacuum distillation (bp, 65—68 °C/30 Torr), and then the optical rotation was measured. The 2- and 3-acetoxypropanal were identified by GPC and $^1$H NMR analysis. 2-Acetoxypropanal, $^1$H NMR ($CDCl_3$): $\delta$ (ppm) 1.35 (d, 3H, $J$=7.5 Hz, $CH_3$), 2.15 (s, 3H, $CH_3$), 4.95 (q, 1H, $J$=7.5 Hz, CH), 9.94 (s, 1H, CHO). 3-Acetoxypropanal, $^1$H NMR ($CDCl_3$): $\delta$ (ppm) 2.03 (s, 3H, $CH_3$), 2.83 (t, d, 2H, $J_t$=6, $J_d$=1 Hz, $CH_2$), 9.98 (t, 1H, $J$=1 Hz, CHO).

*Reduction of 2-Acetoxypropanal.* Optically active 2-acetoxypropanal, whose configuration and maximum rotation are unknown, was reduced to a known compound, (*S*)-1,2-propanediol ($[\alpha]_{D\,max}$=+16.28°[7]): To a suspension of lithium aluminum hydride (3 g) in tetrahydrofuran (20 ml) was added, drop by drop, a 2-acetoxypropanal (5 ml, $[\alpha]_D$=−11.26°) solution in tetrahydrofuran (20 ml), and then the mixture was refluxed for 4 h. The resultant solution was hydrolyzed with 1M HCl (30 ml), and the precipitates thus formed were filtered off. The filtrate was dried with disodium sulfate, concentrated, and analyzed by GPC. $[\alpha]_D$=+2.35°; optical yield, 14.4%.

## Results and Discussion

Under the typical oxo reaction conditions (120 °C and $CO/H_2$=50/50 atm) using a rhodium catalyst such as $[RhCl(CO)_2]_2$, vinyl acetate is readily hydroformylated to give 2-acetoxypropanal selectively. The reaction is completed in less than 1 h. A chiral phosphine–$[RhCl(CO)_2]_2$ system is effective for the asymmetric hydroformylation. The reaction was examined in some detail by changing several reaction variables, using (−)-DIOP, (*R*)-bmpp, and nmdpp as chiral phosphines. Some typical results are summarized in Table 1.

$$AcOCH{=}CH_2 \xrightarrow[[RhL^*]]{CO,\ H_2} AcOC^*(CHO)-CH_3 + AcOCH_2CH_2CHO$$

A tertiary phosphine–rhodium catalyst requires a much longer reaction time for completion than does $[RhCl(CO)_2]_2$; even at the DIOP/Rh ratio of 1.0, the product yields amounted to only 25% even after 18 h (Run 1). Such a retardation effect appears to come from the coordination of the phosphine to the rhodium, showing that the active catalyst species are $HRh(CO)_{3-n}L_n$ ($n$=1, 2, L=ligand) in place of $HRh(CO)_3$. The retardation effect appears to be largest with bmpp, followed by (−)-DIOP and nmdpp. The stereochemical control, however, is largest with (−)-DIOP. (*R*)-Bmpp and nmdpp are much less effective (Runs 13 and 14).

With (−)-DIOP, the (−)-DIOP/Rh ratio has a great effect on the stereoselectivity (see Runs 1—3), while the other reaction conditions are fixed. At the ratios of 1.0 and 1.5, the stereochemical control was not effective, giving only low optical yields, 0.8 and

Table 1. Asymmetric hydroformylation of vinyl acetate with $[RhCl(CO)_2]_2$-(−)-DIOP

| Run | Reaction conditions: Molar ratio (−)-diop/Rh | $CO/H_2$ atm/atm | Temp °C | Time h | Product yield[a] % | 2-Acetoxypropanal: Selectivity % | $[\alpha]_D$ ° | Optical yield[b] % |
|---|---|---|---|---|---|---|---|---|
| 1 | 1.0 | 50/50 | 120 | 18 | 25 | 100 | −0.60 | 0.8 |
| 2 | 1.5 | 50/50 | 120 | 16 | 45 | 100 | −1.29 | 1.7 |
| 3 | 2.0 | 50/50 | 120 | 15 | 61 | 100 | −11.26 | 15 |
| 4 | 4.0 | 50/50 | 120 | 18 | 50 | 100 | −11.72 | 15 |
| 5 | 2.0 | 50/50 | 70 | 42 | 13 | 92 | −18.4 | 23 |
| 6 | 2.0 | 50/50 | 80 | 17 | 12 | 89 | −17.32 | 22 |
| 7 | 2.0 | 50/50 | 100 | 20 | 56 | 87 | −12.60 | 16 |
| 8 | 2.0 | 50/50 | 140 | 3 | 45 | 100 | −9.25 | 12 |
| 9 | 2.0 | 20/50 | 120 | 2 | 59 | 100 | −11.54 | 15 |
| 10 | 2.0 | 65/50 | 120 | 6 | 61 | 100 | −9.18 | 12 |
| 11 | 2.0 | 50/20 | 120 | 6 | 45 | 100 | −10.40 | 13 |
| 12 | 2.0 | 50/70 | 120 | 8 | 43 | 100 | −8.55 | 11 |
| 13[c] | 4.0 | 50/50 | 120 | 21 | 25 | 100 | −1.63 | 2.1 |
| 14[d] | 8.0 | 50/50 | 120 | 1 | 73 | 100 | −0.36 | 0.5 |

a) Isolated yields of 2- and 3-acetoxypropanal. b) Calcd from the $[\alpha]_D$ values of 1,2-propanediol derived from 2-acetoxypropanal. c) (*R*)-Benzylmethylphenylphophine was used. d) Neomenthyldiphenylphophine was used.

1.7% respectively. A small increase in the ratio to 2.0, however, resulted in a larger stereoselectivity, an optical yield of up to 15%. Additional increases in the ratio, to 3.0, 4.0, and 8.0, however, showed no additional increase in the stereoselectivity. Thus, the (−)-DIOP/Rh ratio clearly has a critical point at 2.0 in the reaction. The efficiency of the DIOP ligand in some asymmetric reactions has been considered to come from its chelating ability as a bidentate,[8] and some metal complexes chelated by DIOP are known.[9] The results obtained here, however, appear to throw doubt on the idea that (−)-DIOP acts as a bidentate ligand in this reaction.

The active catalyst species for the asymmetric hydroformylation has normally been considered to be $HRh(CO)L_2$* rather than $HRh(CO)_2L$*, where L* is a chiral ligand.[1] Even at the (−)-DIOP/Rh ratio of 1.0, a retardation in the reaction rate was observed, showing that the rhodium catalyst is changed into the $HRh(CO)_2P^\frown P$ species (DIOP is presented as $P^\frown P$), still with no effect on the stereochemical control. Just one additional mole of (−)-DIOP per g-atm of rhodium seems to change the rhodium catalyst into another species, $HRh(CO)(P^\frown P)_2$, with a conformational rigidity; this species is really active in the asymmetric reaction. Thus, the fact described above could be explained by considering that the DIOP acts as a monodentate ligand. A similar doubt has been suggested in the asymmetric hydrocarboxylation catalyzed by (−)-DIOP–palladium chloride.[10]

Among other reaction variables, such as the reaction temperatures and partial pressures of carbon monoxide and hydrogen, the reaction temperature has the largest effect on the stereoselectivity (see Runs 3, 5—8). Under fixed conditions, a (−)-DIOP/Rh ratio of 2.0 and an initial partial pressure of 50 atm of either carbon monoxide or hydrogen, a lower reaction temperature (70—140 °C) gave a higher stereoselectivity. At 70 °C the highest optical yield of 23% was achieved, but the reaction rate became remarkably slow. At lower temperatures (70—100 °C), 3-acetoxypropanal was produced as a by-product. Lowering the reaction temperature exhibits the same tendency as with styrene.[1]

The stereoselectivity of this reaction, however, was not significantly affected by changing the initial pressures of carbon monoxide and hydrogen. Under the fixed conditions, a (−)-DIOP/Rh ratio of 2.0 and at 120 °C, the effects of the pressures on the stereoselectivity were examined. When the pressure of hydrogen was fixed at 50 atm, the stereoselectivity was almost unchanged, giving 15% optical yields at 20—50 atm of carbon monoxide, but it decreased to 12% at 65 atm (Runs 3, 9, and 10). When the pressure of carbon monoxide was fixed at 50 atm, the stereoselectivity was the largest (15% optical yield) at 50 atm of hydrogen, but decreased to 13 and 11% at higher (70 atm) and lower (20 atm) pressures of hydrogen respectively (Runs 3, 11, and 12). Accordingly, the pressures have a minor effect on the reaction of vinyl acetate.

In the present study, vinyl acetate shows a larger stereoselectivity than any other olefins except styrene. The largest stereoselectivity with styrene has been considered to arise from the conformational rigidity concerned with the phenyl group,[1a] though the mechanism of the asymmetric induction is not clear. With vinyl acetate, the acetoxyl group seems to play some role in the asymmetric induction.

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