Tetrahedron Letters No. 22, pp 1889 - 1892, 1974. Pergamon Press. Printed in Great Britain.

ASYMMETRIC REDUCTION OF α-KETO ESTERS VIA HYDROSILYLATION CATALYZED BY A RHODIUM(I) COMPLEX WITH CHIRAL PHOSPHINE LIGANDS

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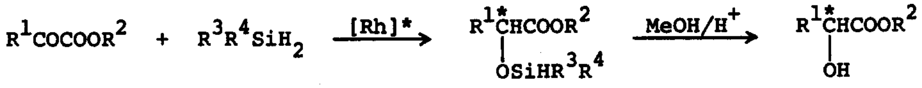
(Received in Japan 16 April 1974; received in UK for publication 22 April 1974)

Asymmetric syntheses of α-hydroxy carboxylic acids have gathered much interest for a long time, and a large number of reports have been made on the Grignard reaction and the reduction of α-keto esters.[1] As for the asymmetric reduction of α-keto esters, catalytic hydrogenation and metal hydride reduction of chiral esters of α-keto acids have been extensively studied.[1] However, relatively little is known about the asymmetric reduction of the α-keto esters by chiral reducing agents, and only the reductions of arylglyoxylic acid and its esters by the use of chiral magnesium alkoxides[2] and lithium aluminum hydride - chiral alcohol complexes[3] were reported. The optical yield attained by chiral magnesium alkoxides was reported to be 15-33%,[2] and that obtained by lithium aluminum hydride - chiral alcohol complexes was reported to be 4-17%.[3] No catalytic asymmetric reduction of α-keto esters has been performed, however. We wish to describe in this communication the first and effective asymmetric reduction of α-keto esters as an application of our work on the reduction of carbonyl[4] and imino[5] functionalities using hydrosilylation catalyzed by a rhodium(I) complex with phosphine ligands.

We chose propyl pyruvate and ethyl phenylglyoxylate as a substrate and (+)-BMPP[6] and (+)-DIOP[6] as chiral phosphine ligands for the rhodium(I) complex. The asymmetric reduction of propyl pyruvate is typically described. To a solution of the catalyst which was prepared from 12 mg of [Rh(1,5-cyclooctadiene)-Cl]$_2$ (0.02 mmol) and 25 mg of (+)-DIOP (0.05 mmol) in 15 ml of benzene, were added 3.90 g (30 mmol) of propyl pyruvate and 5.80 g (31.5 mmol) of diphenylsilane. The mixture was cooled with ice-water and stirred for 12 hr and then the reaction completed. Methanol(30 ml) was poured into the reaction mixture and 10 mg of p-toluenesulfonic acid was added. Methanolysis readily proceeded within 10 minutes at ice-cooled temperature and methanol was evaporated. Then, the residue was distilled under reduced pressure after rough separation with short colum chromatography on silica gel. The optically active (S)-(-)-propyl lactate [bp. 70°/15 mm, $[\alpha]_D^{20}$ -9.11 (neat), 75.3% e.e.] was obtained in 87% yield.

When (+)-BMPP was used as a chiral ligand, (R)-(+)-propyl lactate was obtained. Results are summarized in Table 1.



$$R^1COCOOR^2 + R^3R^4SiH_2 \xrightarrow{[Rh]^*} R^1\underset{OSiHR^3R^4}{\overset{*}{C}H}COOR^2 \xrightarrow{MeOH/H^+} R^1\underset{OH}{\overset{*}{C}H}COOR^2$$

As shown in Table 1, optical yields depend on the nature of hydrosilane used and the configuration of propyl lactate derived by the use of (+)-BMPP is opposite to that derived by using (+)-DIOP. The optical yields realized for the asymmetric reduction of propyl pyruvate by this method are much higher than those obtained by other methods,[1] and especially, the optical yield attained by the use of α-naphthylphenylsilane (81.5% e.e.) is the highest one ever known. The similar asymmetric reduction of ethyl phenylglyoxylate resulted in rather low optical yields at this stage, however.

Next, we performed the asymmetric reduction of menthyl pyruvate via catalytic asymmetric hydrosilylation using the same catalysts mentioned above in the hope of estimating the efficiency of the "double asymmetric induction".[7]

The silylated menthyl lactate was hydrolyzed by KOH-MeOH, and both lactic acid and (-)-menthol were obtained. Lactic acid thus obtained was further esterified to propyl lactate. The results of the "double asymmetric induction" are also listed in Table 1. The optical yields attained by the system are not

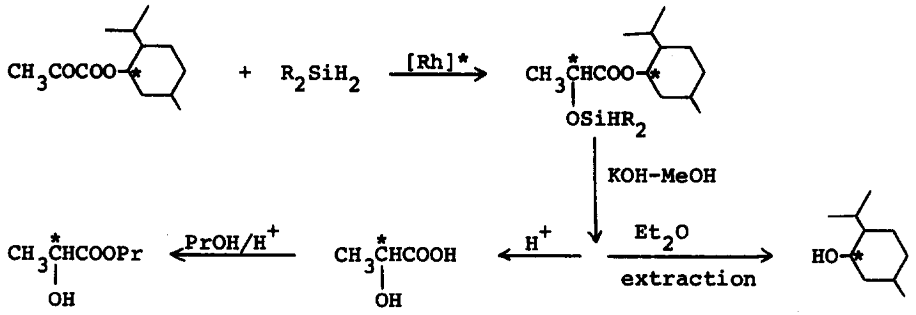
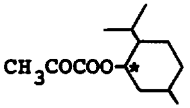


Table 1. Catalytic Asymmetric Reduction of Propyl Pyruvate, Ethyl Phenylglyoxylate and Menthyl Pyruvate

α-Keto Ester	Hydrosilane[8]	Chiral Rigand	Product	$[\alpha]^{20}_{D}$[a]	Optical Yield (% e.e.)[b]
$CH_3COCOOPr$	Et_2SiH_2	(+)-BMPP	$\underset{OH}{CH_3\overset{*}{C}HCOOPr}$	+ 3.67[c]	30.3
	$PhMeSiH_2$	(+)-BMPP		+ 6.05[c]	50.0
	Ph_2SiH_2	(+)-BMPP		+ 7.30[c]	60.3
	Ph_2SiH_2	(+)-DIOP		- 9.11	75.3
	α-$NpPhSiH_2$	(+)-DIOP		- 9.86	81.5
$PhCOCOOEt$	Et_2SiH_2	(+)-BMPP	$\underset{OH}{Ph\overset{*}{C}HCOOEt}$	+ 8.20[c,d]	6.4
	Ph_2SiH_2	(+)-BMPP		-13.24[c,d]	10.3
	Ph_2SiH_2	(+)-DIOP		+ 1.73	1.4
 CH_3COCOO	Et_2SiH_2	(+)-BMPP	$\underset{OH}{CH_3\overset{*}{C}HCOOPr}$	+ 1.99	16.4
	Et_2SiH_2	(+)-DIOP		- 5.12	42.3
	Ph_2SiH_2	(+)-DIOP		- 7.55	62.4
	Ph_2SiH_2	(-)-DIOP		+ 7.96	65.8

a Optical rotations are for the neat liquid in the case of propyl lactate, and as for ethyl mandelate those are measured in chloroform. b Optical yields were calculated from the specific rotation of the pure enantiomer which is reported in the literature[9] and confirmed on the basis of nmr spectra using a shift reagent, $Eu(TFC)_3$ [TFC: 3-trifluoromethylhydroxymethylene-d-camphor]. c Optical rotation is calibrated by the purity of (+)-BMPP (77.7%). d c 1.57 ($CHCl_3$). e c 7.07 ($CHCl_3$).

so high as expected, and are rather low compared with those obtained in the case of the asymmetric reduction of propyl pyruvate. Thus, the effect of menthyl group was by no means remarkable. However, a possibility of a partial racemization during the alkaline hydrolysis cannot be excluded. Accordingly, we intend to continue the investigation of the "double asymmetric induction".

A further investigation on the asymmetric reduction of α-keto esters, their Schiff bases and the mechanism of the reaction is now undergoing.

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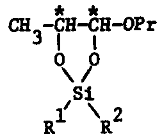
5. I. Ojima, T. Kogure and Y. Nagai, Tetrahedron Lett., 2475 (1973); cf. N. Langlois, T-P. Dang and H. B. Kagan, ibid., 4865 (1973).
6. BMPP: benzylmethylphenylphosphine, DIOP: 2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane.
7. See ref. 1, pp 206-208, and ref. 3.
8. When (+)-DIOP was employed as a chiral ligand for the rhodium catalysts, the hydrosilylation of propyl pyruvate using diethylsilane or phenylmethylsilane seemed to proceed in somewhat different fashion. Thus, a double hydrosilylation occurred as the reaction proceeded, and a cyclic silyl ether shown below was a main product at the end of the reaction. The double hydrosilylation could not be observed when $[(+)\text{-BMPP}]_2Rh(S)Cl$ or $(Ph_3P)_3RhCl$ was employed.



e.g., $R^1 = R^2 = Et$, bp. 86°/ 10 mm
$[\alpha]_D^{20} = + 29.0$ (c 2.02, C_6H_6)

9. As for propyl lactate, see E. Wassmer and P. A. Guye, Chem. Zentr., (II) 1418 (1903): $[\alpha]_D^{18} = 12.1$ (neat). This value is well corresponding to that calculated for the pure enantiomer on the basis of nmr spectra using $Eu(TFC)_3$, $[\alpha]_D^{20} = 12.1 \pm 0.2$. As for ethyl mandelate, see P. Walden, Z. Physik. Chem., 17, 705 (1895); R. Roger, J. Chem. Soc., 2178 (1932).