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ENANTIOSELECTIVE CATALYTIC HYDROGENATION OF α-ACETAMIDOACRYLIC ACIDS. DIPHOSPHINITE-RHODIUM CATALYSTS DERIVED FROM A SUGAR

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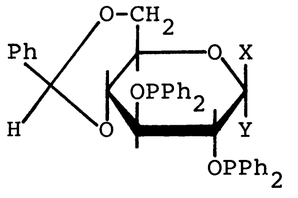
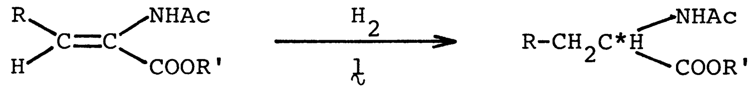
A chiral diphosphinite: methyl 4,6-O-benzylidene-2,3-bis-O-diphenylphosphino-β-D-glucopyranoside (β-POOP) was derived from D-glucose. High enantiomeric excess values of up to 91% were achieved in the hydrogenation of α-acetamidoacrylic acids using the rhodium complex of β-POOP.

Recently, enantioselective synthesis of amino acids by rhodium complexes has been of interest to many workers.[1,2] We previously reported the use of methyl 4,6-O-benzylidene-2,3-bis-O-diphenylphosphino-α-D-glucopyranoside (α-POOP) as a ligand in a rhodium complex for the enantioselective hydrogenation of α-acetamidoacrylic acids; the enantiomeric excess values were up to 80%.[2] In this paper, we wish to describe highly enantioselective hydrogenation catalyzed by a diphosphinite-rhodium complex derived from a sugar, D-glucose.



α-POOP: X=H, Y=OMe.
β-POOP: X=OMe, Y=H.

β-POOP was prepared from methyl 4,6-O-benzylidene-β-D-glucopyranoside, and was purified by recrystallization from tetrahydrofuran-petroleum ether, m.p. 117-118°, $[\alpha]_D^{25}$ -38.1 (c 1.1, chloroform).[2,3] A cationic complex $[(\beta\text{-POOP})\text{Rh(NBD)}]^+\text{PF}_6^-$ (**1**) was obtained from $[\text{RhCl(NBD)}]_2$, β-POOP, and AgPF_6 by known procedure (NBD=norbornadiene).[2,4]

(**2**)  (**3**)

$$\text{RHC=C(NHAc)COOR'} \xrightarrow[\mathbf{1}]{H_2} \text{R-CH}_2\text{C*H(NHAc)COOR'}$$

2a,**3**a: R=H, R'=H; **2**b,**3**b: R=Ph, R'=H, **2**c,**3**c: R=H, R'=Me; **2**d,**3**d: R=Ph, R'=Me.

Hydrogenation of α-acetamidoacrylic acids and their esters (**2**) was carried out in the presence of **1** in absolute ethanol at 0-30°C under 1 atm of hydrogen. The results are summarized in Table 1. The reaction is rapid and quantitative. High enantiomeric excess values are achieved; up to 91% for the acids and 88% for the esters. Product amino acid derivatives (**3**) have the natural, S, configuration as is the case for α-POOP, although the enantiomeric excess values are higher. The complex **1** is more active than its α-isomer. The configuration of the product will be determined mainly by the conformation of the diphosphinite moieties coordinated to the rhodium. The difference in activity and enantiomeric excess values between the complexes, **1** and its α-isomer, would be ascribed to a difference in congestion in the coordination sphere. The rhodium complex of α-POOP would be sterically more crowded than its β-isomer, because the 1-methoxy group of α-POOP is disposed as an axial substituent. High congestion in the complex of α-POOP would

Table 1. Hydrogenation of α-Acetamidoacrylic Acids and their Esters a)

Substrate	Substrate Rh ratio	Temperature (C°)	Time (min)	Conversion (%)	Enantiomeric Excess c) (%) (Coniguration)
2a	100	30	5	100	91 (S)
2a	200	30	6	100	90 (S)
2a	200	0	10	100	90 (S)
2a	100 d)	30	16(hr)	100	60 (S)
2b	200	30	8	100	91 (S)
2b	200	0	30	96	90 (S)
2b	100 d)	30	16(hr)	100	41 (S)
2c	200	30	5	100	84 (S)
2c	200	0	10	100	88 (S)
2d	200	30	25	100	80 (S)
2d	200	0	70	100	79 (S)

a) Hydrogenations were carried out with the substrate (2 mmol) and **1** ((1∿2)x10^{-2}mmol) in absolute ethanol under 1 atm of hydrogen. b) Estimated by proton NMR spectra. c) Calculated on the basis of the highest value of **3** described previously.2) d) In situ catalyst from [RhCl(cyclooctene)$_2$]$_2$ (0.01 mmol) and β-POOP (0.02 mmol) in ethanol/benzene(2/1) (15ml) under 50 atm initial pressure of hydrogen.

reduce the ease of access of the substrate and the selectivity in the coordination of the prochiral face of the substrate, resulting in a decrease of activity and enantiomeric excess values. Similar observations have been made regarding modified DIOP complexes (DIOP=2,3-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane).5)

A substrate which has no acetamido group, such as α- or β-methylcinnamic acid was not hydrogenated in this system, as was the case for the complex of α-POOP. These results suggest that the acetamido group is essential for the hydrogenation of α-acetamidoacrylic acids, and the coordination of the acetamido group plays an important role in obtaining reactivity and high enantiomeric excess values.6-8) Recently, the crystal structure of an intermediate, in which both the carbon-carbon double bond and the carbonyl group in the acetamido moiety are coordinated to the rhodium, has been reported by Halpern.7b)

A catalyst prepared in situ from [RhCl(cyclooctene)$_2$]$_2$ and β-POOP was less active than the cationic one, and the enantiomeric excess values were also lower.

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