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Enantioselective hydrogenation of olefins with axial chiral iridium QUINAP complex

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Abstract—(*S*)-QUINAP reacted with $[Ir(cod)Cl]_2$ to form a new chelating iridium complex in 77.4% yield. The iridium complex was proved to be a highly efficient catalyst for the enantioselective hydrogenation of olefins. 33.4–95.1% ee were obtained for the hydrogenation of unfunctionalized olefins and 90.8–96.1% ee were obtained for functionalized olefins.

Chiral N–P ligands are the most widely used heterodentate ligands in metal-catalyzed asymmetric reactions.[1] Among these, enantioselective hydrogenation, one of the most powerful methods in the asymmetric synthesis, has become a growing field of interest in organic chemistry. During the past few decades, much progress has been made to catalyze asymmetric hydrogenation of olefins by use of ruthenium or rhodium complexes.[2] However, these systems did not always produce satisfactory results in the hydrogenation of unfunctionalized olefins or some functionalized olefins.[3]

In 1976, Crabtree[4] disclosed the first homogeneous achiral iridium catalyst, $[Ir(cod)(py)Pcy_3]PF_6$, for the hydrogenation of tri- and tetrasubstituted olefins. The Pfaltz's group[5] developed an optically active phosphinooxazoline (PHOX) ligand to replace pyridine and tricyclohexylphosphine in the Crabtree's catalyst. The resulting mimic chiral catalysts could afford an excellent enantioselectivity of up to 99% ee in the hydrogenation of (*E*)-1,2-diphenyl-1-propene derivatives. Following this discovery, many kinds of chiral Ir-(PHOX)[6] and Ir-phosphiniteoxazoline complexes[7] have been intensively investigated and successfully applied to the hydrogenation of unfunctionalized and functionalized olefins.

Recently, Andersson,[8] Knochel,[9] and Pfaltz[10] developed phosphinooxazol and phosphinopyridine as a new kind of chiral N–P ligands, which have one or more chiral carbon centers on the branch of the aromatic ring. These corresponding Ir-complexes are structurally similar to the Crabtree's catalyst compared with Ir-PHOX complexes, but provided much better catalytic activity and enantioselectivity.

Since QUINAP was for the first time introduced by Alcock et al.[11] in 1993, the axial chiral ligand has been extensively used in a number of transition metal complexes catalyzed asymmetric reactions.[12] Taking advantage of precedent studies, it was assumed in current study that a chiral Ir-complex like the achiral Crabtree's catalyst formed by combination of quinoline ring and triaryphosphine structure could provide high enantioselectivity due to the axial chirality and rigid six-member ring. Herein, we wish to report our recent study on the use of QUINAP as a ligand in the enantioselective hydrogenation of olefins with cationic iridium catalyst.

The iridium complex was synthesized from (*S*)-QUINAP, $[Ir(cod)Cl]_2$, and Na[BARF] in 77.4% yield under mild conditions (Scheme 1).[13] The hydrogenation of (*E*)-1,2-diphenyl-1-propene was carried out at room temperature under 50 bar of hydrogen pressure by using CH_2Cl_2 as the solvent (Table 1).[14] A higher catalyst loading (2 mol %) could not increase enantioselectivity (entry 1), but a lower catalyst loading (0.2 mol %) resulted in extremely low conversion (entry 2). By running

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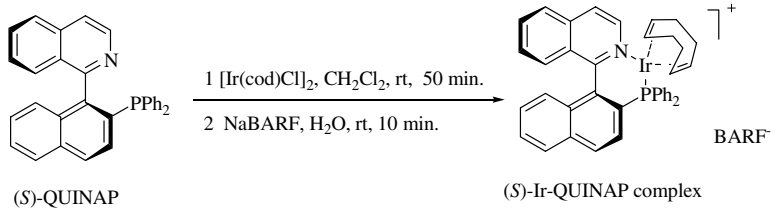
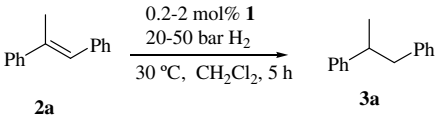
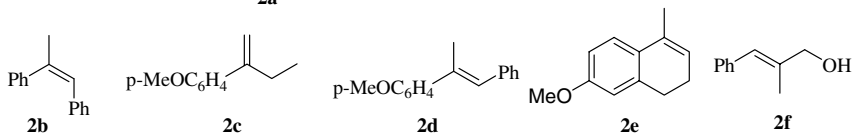


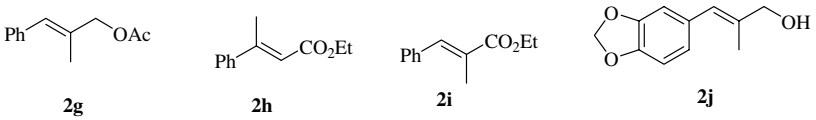
NaBARF = sodium tetrakis [3,5-bis(trifluoromethyl)phenyl]borate

Scheme 1. Synthesis of iridium QUINAP complex.

Table 1. Asymmetry hydrogenation with iridium QUINAP complex







Entry	Substrate	Conversion[a] (%)	ee[b] (%)
1	**2a**	100	95.1 (*S*)[c]
2	**2a**	26	92.0 (*S*)[d]
3	**2a**	100	94.5 (*S*)
4	**2b**	100	70.0 (*S*)
5	**2c**	100	33.4[e] (*R*)
6	**2d**	100	83.0 (*R*)
7	**2e**	95	92.5 (*S*)
8	**2f**	100	95.0[f]
9	**2g**	100	96.1[f]
10	**2h**	100	90.8 (*R*)
11	**2i**	90	93.1 (*R*)
12	**2j**	100 (65)[g]	95.2 (*R*)

[a] Determined by ^{1}H NMR.
[b] Determined by HPLC (Chiracel OJ-H for substrates **2a**, **2b**, and **2c**; Chiracel OD-H for substrates **2e**, **2f**, **2g**, and **2j**; Chiracel OB-H for substrates **2h** and **2i**). The absolute configurations were assigned by comparison of the HPLC retention times with the literature values.[5,6a,8a,15]
[c] 2 mol % of catalyst was used.
[d] 0.2 mol % of catalyst was used. Other runs used 0.5 mol % of catalyst unless otherwise indicated.
[e] 20 bar pressure was used. Other runs used 50 bar pressure unless otherwise indicated.
[f] The absolute configurations were not determined.
[g] Bracketed value was an isolated yield.

a series of parallel reactions, it was found that the optimal amount of the catalyst loading was 0.5 mol % of the substrate. Thus, the hydrogenation afforded complete conversion and 94.5% ee in the presence of 0.5 mol % of iridium complex (entry 3). (*Z*)-1,2-Diphenyl-1-propene underwent the catalytic hydrogenation to afford 70% ee with predominant (*S*) configuration of the product (entry 4). Substrates **2c**, **2d**, and **2e** gave 33.4%, 83.0%, and 92.5% ee, respectively (entries 5–7). The exceptional low enantioselectivity of **2c** (entry 5) was due to its terminal olefin function. Excellent conversions and enantioselectivities were also observed in the hydrogenation of functionalized trisubstituted olefins. The functionalized 2-methyl-3-phenylpropenol **2f** and 3-acetoxy-2-methylphenylpropene **2g** afforded 95.0% and 96.1% ee with complete conversion (entries 8 and 9). β-Methyl cinnamic ester **2h** and α-methyl cinnamic ester **2i** could also be hydrogenated in 90.8% ee and 93.1% ee value, respectively (entries 10 and 11). The products are useful intermediates for the synthesis of natural and unnatural compounds. The asymmetric hydrogenation of piperonyl allyl alcohol **2j** gave 100% conversion

(65% isolated yield) and 95.2% ee of the corresponding alcohol. Oxidation of the product could lead chiral fragrance helional.[15]

In conclusion, the cationic iridium QUINAP complex from QUINAP, $[Ir(cod)Cl]_2$, and Na[BARF] was prepared and applied in the enantioselective hydrogenation of various olefins. The complex showed excellent catalytic activity and enantioselectivity in the hydrogenation of olefins except for the terminal olefin. Further modification of ligands and the applications in asymmetric catalysis are in progress in our lab.

Acknowledgments

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13. *Preparation of Ir-QUINAP complex*: To a schlenk flask were added QUINAP (43.9 mg, 0.1 mmol), $[Ir(cod)Cl]_2$ (33.6 mg, 0.05 mmol), and CH_2Cl_2 (5 mL) under N_2. The solution was stirred at room temperature for 50 min until ^{31}P NMR indicated that the ligand had been consumed. Na[BARF] (138 mg, 0.15 mmol) was added, followed by the addition of H_2O (5 mL), The resulting two-phase mixture was stirred vigorously for 10 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic phases were washed with H_2O (5 mL), dried over Na_2SO_4, and evaporated. The residue was purified by flash column chromatography under N_2 with 50% of CH_2Cl_2 in hexane as eluent to afford the air-sensitive Ir-QUINAP complex. Additional purification can be effected by layering a concentrated CH_2Cl_2 solution of the complex with pentane at −20 °C and collecting the precipitated red solids: Yield, 77.4%; Mp 161–163 °C; $[\alpha]_D^{20}$ +924.4 (*c* 0.17, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 1.26–1.31 (m, 1H), 1.68–1.71 (m, 2H), 1.73–1.81 (m, 2H), 2.19–2.38 (m, 5H), 2.22–2.70 (m, 1H), 3.05–3.11 (m, 1H), 4.72–4.74 (m, 1H), 4.90–4.96 (m, 1H), 6.94–7.36 (m, 13H), 7.49 (s, 4H), 7.53–7.61 (m, 3H, PhH), 7.72 (s br, 8H), 7.98–8.02 (m, 1H), 8.06–8.09 (m, 1H), 8.24–8.28 (m, 2H), 8.52–8.53 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8 (q), 142.2, 134.7, 133.0, 129.8–129.0 (m), 128.7 (m), 128.5 (d, $J = 5.6$ Hz), 125.8, 123.1, 117.4 (m), 95.6, 94.2, 75.6, 75.2, 48.3, 45.4 38.9. ^{31}P NMR (160 MHz, $CDCl_3$) 13.1. Anal. Calcd for $C_{71}H_{46}BF_{24}IrNP$: C, 53.19; H, 2.89; N, 0.87. Found: C, 52.91; H, 2.76; N, 0.86.
14. *The typical procedure for the enantioselective hydrogenation of olefins*: (*E*)-1,2-Diphenylpropene (97 mg, 0.5 mmol) and Ir-QUINAP complex (4 mg, 0.0025 mmol) in dry degassed CH_2Cl_2 (2 mL) were added to the autoclave under inert atmosphere. The autoclave was sealed immediately and pressurized to 50 bar of H_2. The mixture was stirred for 5 h. The CH_2Cl_2 was removed and the crude product was passed through a short silica-gel column with hexane as eluent. After evaporation of the solvent, (*S*)-**3a** was obtained in a quantitative yield and analyzed for conversion (^1H NMR) and % ee (HPLC).
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