

## ASYMMETRIC CATALYSIS

## A N,O hope

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The past decade has seen half-sandwich complexes of Ir find many applications in asymmetric hydrogenation catalysis. These complexes are often of the form  $[\text{Ir}(\text{C}_5\text{Me}_5)(\text{bidentate ligand})\text{X}]$ , with  $\text{X}^-$  being a weakly bound ligand that can be displaced by substrates. A more crucial factor is the bidentate ligand, which can be chiral and may bind through one of several different coordination modes. The influence of different modes on catalytic activity and enantioselectivity is not well understood. However, a team of researchers in China and the UK have made progress on this front by uncovering a striking reversal of activity in two Ir catalysts featuring different ligand coordination modes.

Jianliang Xiao of the University of Liverpool collaborated with Weiping Chen of the Fourth Military Medical University in Xi'an with the intention of developing a catalyst for the asymmetric transfer hydrogenation of imines. Their previous work had made use of hydrogen-bonding interactions to promote asymmetric

induction. Graduate student Gang Zhou made use of these interactions by incorporating a carboxylate group into his bidentate ligand. “What happened next is the story talked about in the *ACS Catalysis* paper,” recalls Xiao.

Zhou designed a ligand derived from serine methyl ester, which was intended to chelate Ir through an oxazoline N atom and an aryl C atom. This well-known N,C coordination mode features in a number of iridacyclic complexes — including catalysts for hydrogenations. But surprisingly, the ligand bound Ir through an alternative N,O mode involving the oxazoline and the carboxylate formed by hydrolysis of the ester.

“Gang showed that the unexpected N,O-chelated Ir catalyst was far superior to the targeted N,C-chelated analogue for the asymmetric transfer hydrogenation of ketones, even though the ligand was derived from the same precursor,” says Xiao.

Combining the ligand methyl ester and  $[\text{Ir}(\text{C}_5\text{Me}_5)\text{Cl}_2]$  in  $\text{CH}_2\text{Cl}_2$  containing adventitious  $\text{H}_2\text{O}$  leads to ester hydrolysis, after which Ir binds the resulting carboxylate rather than performing C–H activation to give the expected complex. Rigorously removing water from the solvent allows the N,C-complex to be obtained.

The two complexes exhibit strikingly different behaviours in the asymmetric transfer hydrogenation of acetophenones. The N,C-complex performs poorly, giving low conversions and single-digit enantiomeric excesses. By contrast, the N,O-complex affords consistently higher conversions and enantiomeric excesses of up to 99%. Furthermore,

the two complexes mediate the formation of products with opposite absolute configuration.

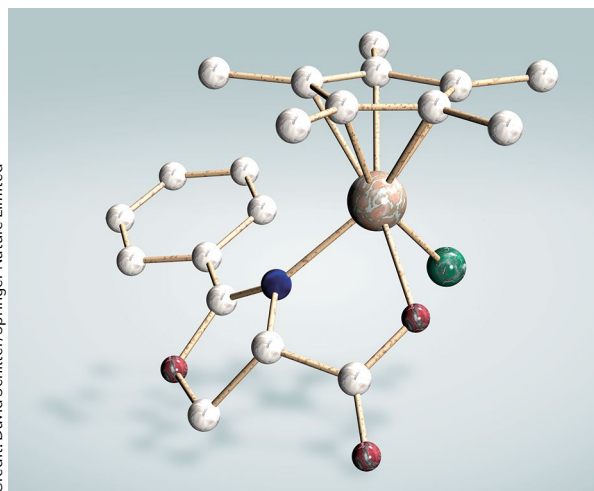
The authors use  $\text{HCO}_2\text{H}$  as a convenient  $\text{H}_2$  source, and the ratio of  $\text{HCO}_2\text{H}$  to the base used also influences the yield and selectivity. The choice of base is important —  $\text{NEt}_3$  is often the base of choice for transfer hydrogenations but is inferior here to primary amines such as  $i\text{PrNH}_2$ . Density functional theory calculations suggest that the protonated amine is involved in the transition state, engaging in hydrogen bonding with both the carboxylate ligand and the  $\text{C}=\text{O}$  group of the substrate. It is this former interaction that is made possible by the ligand binding Ir in an N,O mode.

Sadly, despite the valuable lessons learned from the study of the N,O complex using ketones, neither catalyst proved to be effective for the asymmetric hydrogenation of imines.

It may be that related examples of ambidenticity are lurking undetected in the literature. “For any metal complexes containing bidentate cyclometalated ligands, a change in the ligand coordination mode may occur if the ligand bears an additional neighbouring functionality,” says Xiao. “And as in the case in question, such variation may bring about dramatic effects on catalysis, such as activity and selectivity.”

Andrew Bissette, Associate Editor,  
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**ORIGINAL ARTICLE** Zhou, G. et al. N,O- vs N,C-chelation in half-sandwich iridium complexes: a dramatic effect on enantioselectivity in asymmetric transfer hydrogenation of ketones. *ACS Catal.* **8**, 8020–8026 (2018)



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