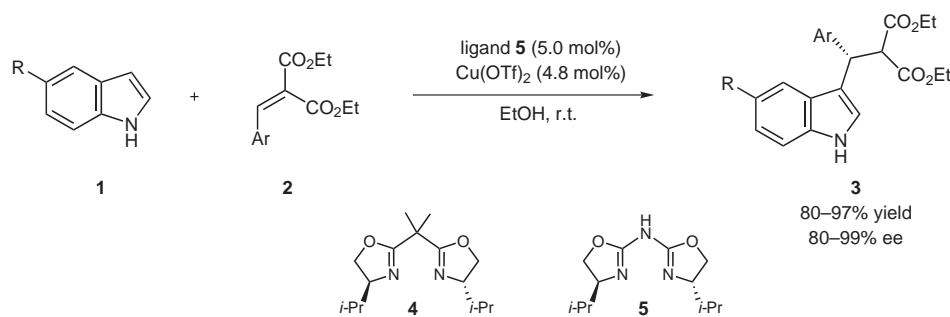


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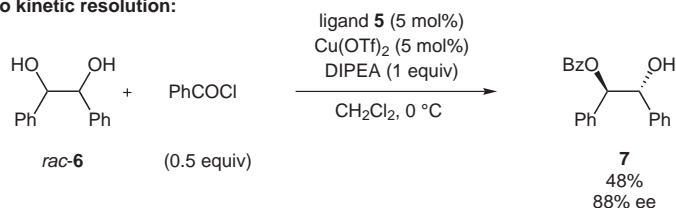
Highly Enantioselective Michael Additions of Indole to Benzylidene Malonate Using Simple Bis(oxazoline) Ligands: Importance of Metal/Ligand Ratio
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Enantioselective Michael Additions of Indole to Benzylidene Malonates



ligand ratio	1.2	1.04	1.3	1.1	1.04	1.0	0
Cu(OTf) ₂	1.0	1.0	1.0	1.0	1.0	1.0	1.0
yield	85%	89%	98%	93%	97%	90%	90%
% ee	79	99	81	85	>99	98%	0

Application to kinetic resolution:



Significance: The reported study contradicts the general trends previously observed in Cu-catalyzed reactions. Indeed, background reactions often occur faster with a ligand-free metal than with coordinated species, leading to erosion of enantioselectivity. Thus, an excess of ligand is usually used. Previous studies had concluded that BOX ligands like **4** were unsuitable for the above reaction (79% ee). It was now shown that, for the specific system presented, the BOX ligands are among the best ligands (99% ee), provided that the ligand is *not used in excess* versus the metal catalyst. The parent ligand **5** increased the reactivity, giving the desired chiral adduct **3** in 97% yield (instead of 89% with **4**).

Comment: The authors gathered evidence suggesting that excess ligand may be coordinating to the metal center in oligomeric form which prevents the organized, two-point-binding complexes from forming, thus leading to lower enantioselectivity. Most importantly, the information provided by this report suggests it may be necessary to revise some of the many Cu–BOX catalyzed processes known. The authors have also shown that ligand **5** was effective in kinetic resolution of the racemic diol **6**. When the ligand/copper ratio was varied, the enantioselectivity was not significantly affected (1.5/1.0: 85% ee, 0.67/1.0: 84% ee), but a 1/1 ratio again showed the best results (88% ee).

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