

Chemoselectivity Change in Catalytic Transformations –Cleavage of Less Reactive Chemical Bonds–

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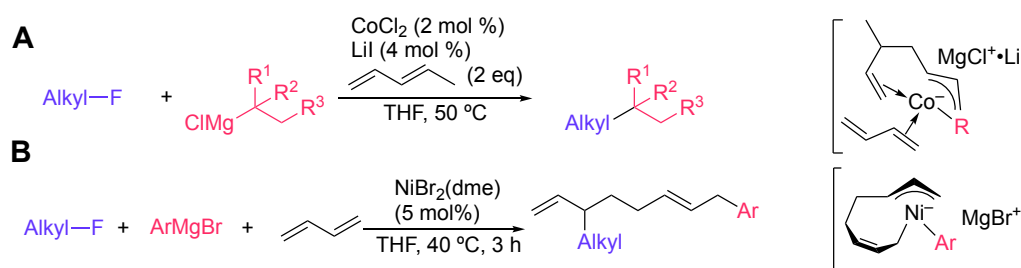
In organic synthesis, the selective bond cleavage is the fundamental issue to achieve transformation in a selective manner. While a molecule with a single reactive chemical bond can be converted into a target molecule, the selective transformation of a certain chemical bond in multifunctional molecules or a less reactive chemical bond in molecules is still highly challenging in modern organic synthesis.

To address this issue, we focus on multifunctional catalysts and enable unique chemoselective transformations. In this lecture, two topics will mainly be discussed with their brief historical background.

1. Cross- and multicomponent coupling reaction via C(sp³)–F bond cleavage

The C(sp³)–F bond is the strongest single bond in organic molecules, therefore the use of the C(sp³)–F bond as a reacting site has rarely been attempted.¹ We have developed anionic transition metal complexes generated by the reaction of transition metal complex with Grignard reagents in the presence of π -carbon ligands. When the combination of CoCl₂, LiI, and 1,3-diene was used as catalyst, the cross-coupling reaction of alkyl fluorides with tertiary alkyl Grignard reagents proceeded via C(sp³)–F bond cleavage (Scheme 1A).² It should be noted that the aromatic C–Br bond, which is good substrate in conventional cross-coupling reaction, remained intact under this Co catalysis.

A similar combination of substrates with Ni catalyst, multicomponent coupling reaction of alkyl fluorides, two molecules of 1,3-dienes, and aryl Grignard reagents afforded complex unsaturated hydrocarbon skeleton (Scheme 1B),³ where the fluorine atom acted as the best leaving group among halogen atoms.



Scheme 1. Cross- and multicomponent coupling reaction of alkyl fluorides

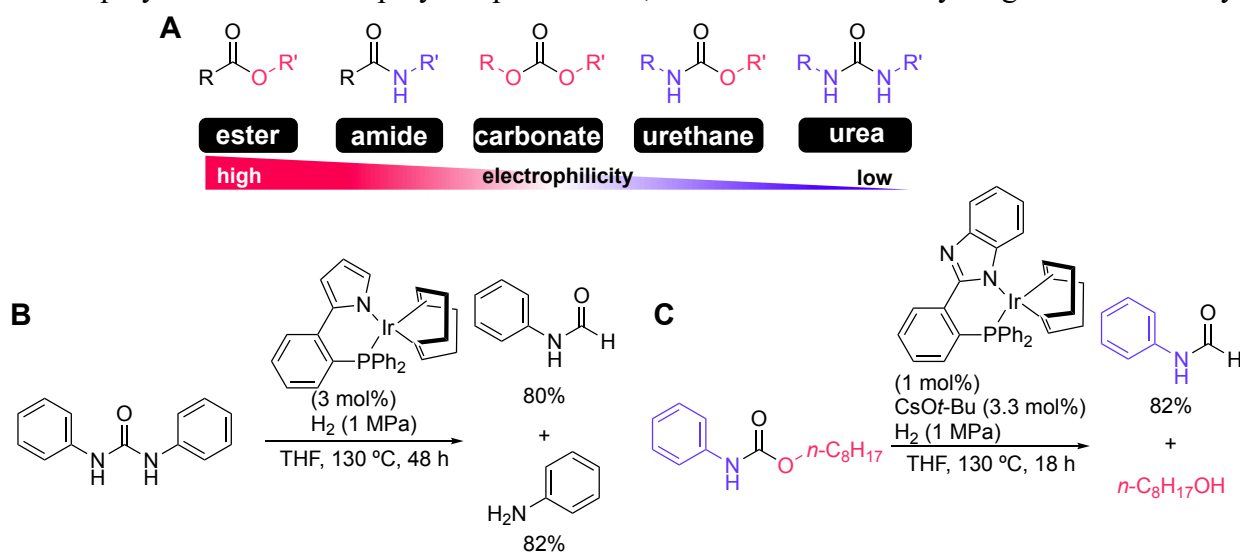
2. Chemoselective hydrogenolysis of carbonyl compounds and its application for polymer degradation

Carbonyl compounds are ubiquitous functional groups not only in organic molecules but also in polymer materials. The electrophilicity of the C=O bond is largely affected by the two substituents on the carbonyl carbon (Scheme 2A), and therefore the chemoselective transformation of the less reactive carbonyl compounds against the commonly accepted reactivity order remains an inherent issue in state-of-the-art organic synthesis.⁴ Among carbonyl compounds, ureas are the least electrophilic due to the conjugation of the carbonyl group and two N atoms. Since pioneering work by Milstein in 2011,

hydrogenolysis of urea derivatives has been achieved by late transition metal catalysts, where urea is converted into two molecules of amine and methanol due to the higher electrophilicity of expected intermediate, formamide, than ureas.

We recently reported that a novel Ir complex catalyzed hydrogenolysis of ureas to formamides and amines (Scheme 2B),⁵ showing a counterintuitive chemoselectivity against the general electrophilicity order of carbonyl compounds. In addition, the present catalyst selectively reacted with ureas over esters, amides, and urethanes.

A modified Ir catalysis enabled a similar chemoselective hydrogenolysis of urethanes to formamides and alcohols in a chemo- and regioselective manner (Scheme 2C).⁶ This catalytic hydrogenolysis can be applicable to the chemical degradation of polyurethanes, which are 6th most produced polymer in the world polymer productions, but their chemical recycling is under the way.



Scheme 2. Chemoselective hydrogenolysis of carbonyl compounds

Our mechanistic study on these catalyses enlightened us a catalyst design guideline to enable the unique chemoselectivities, being covered in the lecture.

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