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COMMUNICATION

Ester hydrogenolysis via β-C–O bond cleavage catalysed by a phenanthroline-based PNNP-cobalt(I) complex

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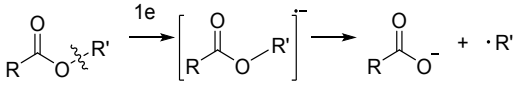
A Co(I) catalyst bearing a phenanthroline-based PNNP ligand (2,9-bis((diphenylphosphanyl)methyl)-1,10-phenanthroline) exhibits long-range metal ligand corporation behavior using a ligand backbone as a hydrogen reservoir and catalyses hydrogenolysis of benzyl benzoate derivatives *via* β-C–O cleavage with atmospheric pressure of H_2.

Transformation of esters is an important reaction in industry for the transformation of various bio-based resources. Seeds and vegetable oils, which often contain a triglyceride structure, can be transferred to fatty alcohols and other chemicals by hydrogenolysis of esters *via* α-C–O bond cleavage of ester moieties.[1] Transformation of esters *via* β-C–O bond cleavage is also important as an alternative protocol for the transformation of esters, whereas examples are still limited compared to those *via* α-C–O bond cleavage.[2,3,4,5]

Marks *et al.* reported hydrogenolysis of esters *via* β-C–O bond cleavage.[5] They used tandem catalysts of metal triflates and Pd/C, which achieves successive β-C–O bond cleavage and hydrogen activation. The strategy can be furthermore applied to various polyesters to catalytically form carboxylic acid and alkane, establishing a new methodology for polyethylene terephthalate (PET) recycling.[6]

Recently, a radical anion decomposition mechanism draws an increasing attention as a new protocol for the β-C–O bond cleavage of esters (Scheme 1).[7,8] In these radical anion decomposition reactions, ester β-C–O bond cleavage is initiated by 1e reduction of esters to form ester anion radical species, followed by radical decomposition *via* β-C–O bond cleavage to form carboxylate anion and alkyl radicals. The strategy was applied to the deoxygenation of alcohols, which was achieved by successive esterification of alcohols and β-C–O bond cleavage of esters.[7,8] The protocol can also offer the easy access for alkyl radical formation from esters, which can be applicable for the total synthesis of tricycloillicinone,[9] azadirachtin,[10] trifarienols A and B,[11] and 4-deoxy pyranosides.[12] However, the method often suffers from the use of an excess highly toxic and expensive reducing agent.[7-12]



Scheme 1 β-C–O Bond cleavage *via* radical anion decomposition mechanism.

In this study, we focused on a cobalt catalyst bearing a phenanthroline-based PNNP ligand (2,9-bis-((diphenylphosphanyl)methyl)-1,10-phenanthroline). The cationic PNNP-Co complex $[Co(PNNP)]^+$ (**1**) undergoes deprotonation of the benzylic-H atom at the ligand side-arm upon treatment of base, resulting in the formation of [Co(PNNP')] (**2**) with a dearomatized phenanthroline backbone (Scheme 2, step i). Complex **2** achieves facile H_2 activation, where H–H bond is cleaved and the two H atoms are added to the endocyclic double bond of the ligand backbone (Scheme 2, step ii).[13] As a result, the resulting complex [Co(PNNP'')] (**3**) still possesses a reactive Co(I) centre, which can further react with incoming substrates. Indeed, **3** cleaves C–X bond of aryl halides and achieves hydrodehalogenation of aryl halides.[14] Detailed mechanistic study revealed that facile electron transfer from the Co(I) centre to aryl halide to form anion radical transition state $[Co(II) + ArX\cdot^-]^‡$ facilitated the C–X bond cleavage (Scheme 2, step iii). Furthermore, the successive H-atom transfer (HAT) from the ligand backbone to the *in-situ* formed aryl radical proceeds (Scheme 2, step iv), completing the catalytic hydrodehalogenation reaction mediated *via* long-range metal ligand cooperation (MLC) using a ligand backbone. Based on these two properties of the PNNP-Co system, hydrogen activation and electron transferring property, we were inspired to challenge hydrogenolysis of esters with H_2. We expected that efficient electron transfer to esters could facilitate their β-C–O bond cleavage and successive HAT to the *in-situ* formed radical species, leading to the achievement in the hydrogenolysis of esters *via* β-C–O bond cleavage under 1 atm H_2.

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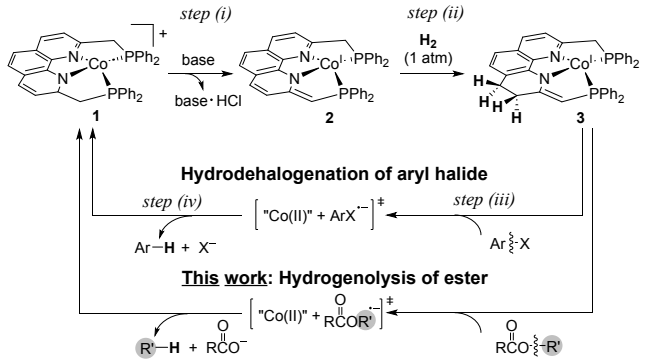
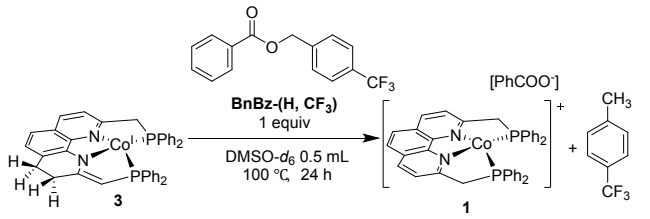
Electronic Supplementary Information (ESI) available: [Experimental details, synthesis, NMR spectra, cyclic voltammograms, and kinetic studies.]. See DOI: 10.1039/x0xx00000x



Scheme 2 Hydrodehalogenation of aryl halides and hydrogenolysis of esters via β-C–O bond cleavage catalyzed by PNNP-Co system.

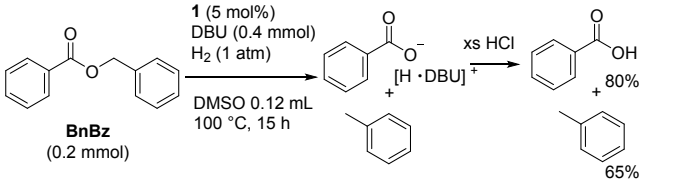
To verify the utility of the PNNP-Co system for hydrogenolysis of esters, we started with a stoichiometric reaction of **3** (0.01 mmol) with 1 equivalent of 4-trifluoromethylbenzyl benzoate (**BnBz-(H, CF_3)**) as a model substrate (Scheme 3). The reaction did not proceed at ambient temperature, however, heating at 100 °C for 24 h resulted in the formation of $[Co(PNNP)]^+$ (**1**$^+$) (26%) as well as 4-trifluoromethyl toluene (27%). Considering the stoichiometry of the reaction, the counter anion of **1**$^+$ should be a benzoate anion, although its signals were obscured in the ^{1}H NMR spectrum (Figure S1). Overall, the reaction supports that **3** facilitates hydrogenolysis of **BnBz-(H, CF_3)** *via* β-C–O bond cleavage to form corresponding alkane product. Motivated by this reaction, we next perform catalytic hydrogenolysis of benzyl benzoate (**BnBz**).



Scheme 3 Stoichiometric reaction of **3** and BnBz-(H, CF_3).

Hydrogenolysis of **BnBz** was performed under 1 atm H_2 with addition of 5 mol% **1** and 2 equivalent 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base in DMSO at 100 °C. After 15 hours, toluene was formed in 65% yield (NMR) (Scheme 4). Upon acidifying the reaction mixture with an excess of HCl, benzoic acid was quantified to be 80% yield by ^{1}H NMR spectroscopy.

Next, variations in reaction conditions were evaluated (Table S1). Reaction in toluene as a non-polar solvent resulted in the 13% benzoic formation (Table S1, entry 2). Slight increase in the polarity of the solvents did not facilitate the reaction. Thus, toluene yields remain 12% respectively in the reactions using THF (Table S1, entry 3). In a polar solvent such as acetonitrile, the yield decreased to 9% (Table S1, entry 4). The same tendency was also confirmed in the previous reported hydrodehalogenation reactions of aryl halides catalysed by **1**.[14] Both increasing the solvent volume to 0.6 mL and reduction of the reaction temperature to 80 °C led to a significant decrease in the reaction efficiency (Table S1, entries 5 and 6). Reduction in the amount of base (0.01 mmol) afforded only a trace toluene even using a stronger base NaO*t*Bu (Table S1, entries 7 and 8). It was also confirmed that both H_2 gas and **1** were essential (Table S1, entries 9 and 10).



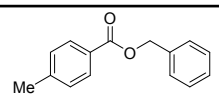
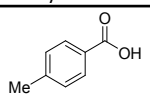
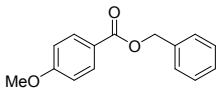
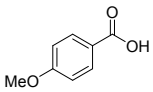
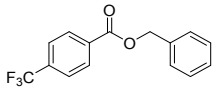
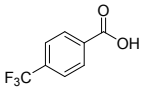
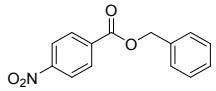
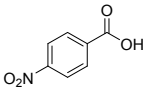
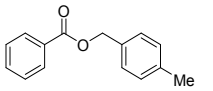
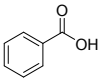
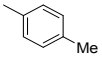
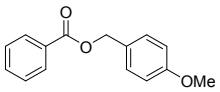
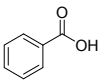
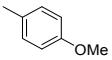
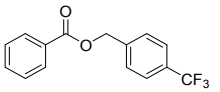
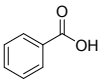
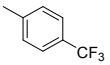
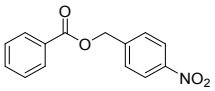
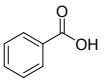
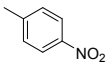
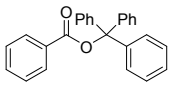
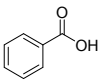
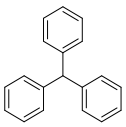
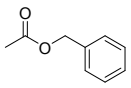
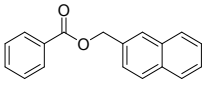
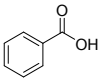
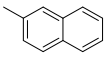
Scheme 4 Hydrogenolysis of **BnBz** catalyzed by **1**.

With the optimized reaction conditions in hands, we examined the substrate scope for this reaction (Table 1). Substrates with various substituents at benzoate moiety similarly proceeded to achieve hydrogenolysis (Table 1, entries 1–4). In hydrogenolysis of substrates having an electron-donating group, benzyl 4-methylbenzoate (**BnBz-(Me, H)**), 4-methylbenzoic acid (72%) and toluene (52%) were formed (Table 1, entry 1). The reaction of benzyl 4-methoxybenzoate (**BnBz-(OMe, H)**) afforded 4-methoxybenzoic acid (78%) and toluene (58%) (Table 1, entry 2). Substrates with electron-withdrawing groups, benzyl 4-triflormethylbenzoate (**BnBz-(CF_3,H)**) and benzyl 4-nitrobenzoate (**BnBz-(NO_2, H)**) similarly underwent the reaction to afford corresponding products in good yields (Table 1, entries 3 and 4).

Next, hydrogenolysis of **BnBz** derivatives with a substituent at the *para*-position of the benzyl moiety were investigated (Table 1, entries 5–8). The reaction of 4-methylbenzyl benzoate (**BnBz-(H, Me)**) resulted in the formation of benzoic acid (70%) and *p*-xylene (58%) (Table 1, entry 5), and the reaction of 4-methoxybenzyl benzoate (**BnBz-(H, OMe)**) resulted in the formation of benzoic acid (80%) and 4-methoxytoluene (64%) (Table 1, entry 6). In the reaction of 4-trifluoromethylbenzyl benzoate (**BnBz-(H, CF_3)**), 4-trifluoromethyl toluene was obtained in 90% yield and benzoic acid was formed in 80% yield (Table 1, entry 7). Reaction of 4-nitrobenzyl benzoate (**BnBz-(H, NO_2)**) lead to the formation of benzoic acid in 90% yield, whereas the yield of 4-nitrotoluene (30%) was significantly lower (Table 1, entry 8).[15] Hydrogenolysis of substrates bearing substituents at the methylene position of **BnBz** was also examined. Hydrogenolysis of 1-phenylethyl benzoate, benzhydryl benzoate, and 1-phenylcyclobutyl benzoate did not proceed at all due to the steric hindrance. In contrast, hydrogenolysis of bulkier trityl benzoate (**TrBz**) afforded corresponding benzoic acid and triphenylmethane almost quantitatively (Table 1, entry 9). The reaction is postulated to follow radical anion decomposition pathway (Scheme 1). Therefore, it is likely that the stability of the radical intermediate is also one of the factors to control reactivity.

Hydrogenolysis of benzyl acetate (**BnAc**) as an aliphatic ester afforded relatively lower yield of acetic acid (13%) and toluene (12%) (Table 1, entry 10). Hydrogenolysis of 2-naphthalenemethyl benzoate (**NMBz**) with an extended conjugated moiety afforded benzoic acid (94%) and

Table 1. Substrate Scope.[a]

entry	substrate	carboxylic acid yield[b]	alkane yield[b]
1	 BnBz-(Me, H)	 72%	 52%
2	 BnBz-(OMe, H)	 78%	 58%
3	 BnBz-(CF_3, H)	 85%	 55%
4	 BnBz-(NO_2, H)	 63%[c]	 60%
5	 BnBz-(H, Me)	 70%	 58%
6	 BnBz-(H, OMe)	 80%	 64%
7	 BnBz-(H, CF_3)	 80%	 90%
8	 BnBz-(H, NO_2)	 90%	 30%
9	 TrBz	 99%	 99%
10	 BnAc	 13%	 12%
11	 NMBz	 94% (87%)[d]	 83% (78%)[d]

[a] Reaction conditions: substrates (0.2 mmol), 1 (5 mol%), DBU (0.4 mmol), H_2 (1 atm), DMSO (0.12 mL), 100 °C, 15 h. [b] yields were determined by ^{1}H NMR spectroscopy using mesitylene as an internal standard. [c] 30% yield of 4-aminobenzoic acid was formed (Scheme S2, Figure S5). [d] Isolated yields of 2 mmol scale reaction.

2-methylnaphthalene (83%) (Table 1, entry 11). The reaction was performed in 2 mmol scale, confirming the isolated yields of benzoic acid (87%) and 2-methylnaphthalene (78%).

To shed light on the mechanism, the time profile of hydrogenolysis of **BnBz** by **1** was followed by means of ^{1}H NMR spectroscopy, and initial rates v_0 of toluene formation was determined at different substrate initial concentrations (Figure S8, Tables S2–S4).

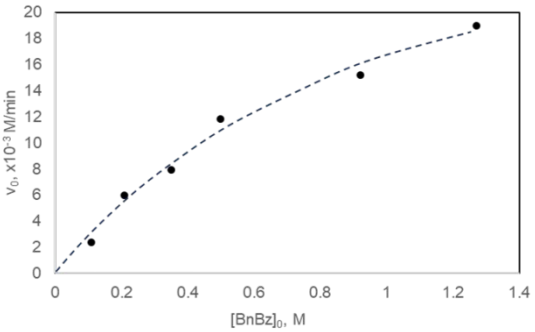


Figure 1. Initial rate of toluene formation (v_0) against concentration of **BnBz**.

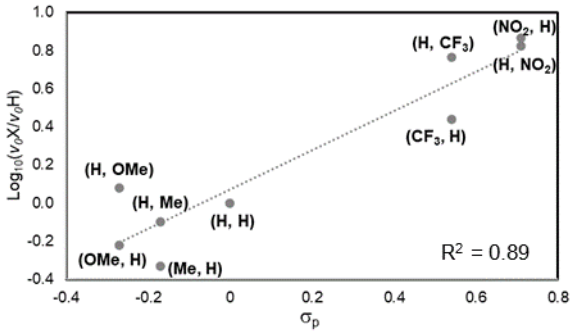


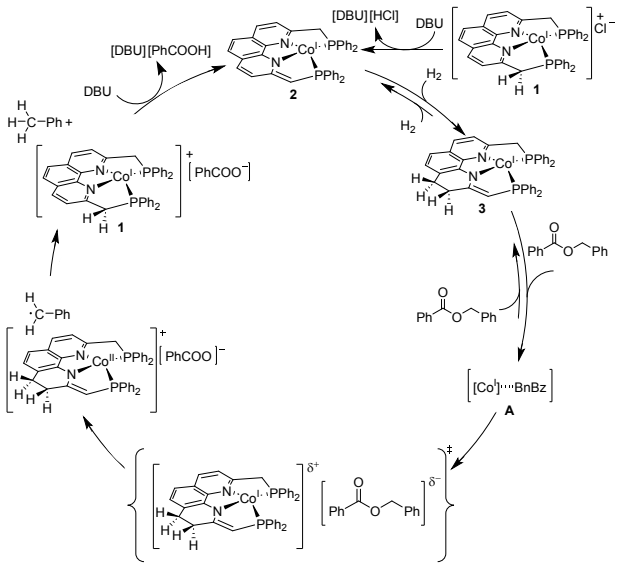
Figure 2 A Hammett plot for the rate constants (v_0) of 1-catalyzed hydrogenolysis of **BnBz** derivatives against the σ_P values of para substituents on the Ar groups. log(v_0/ v_{0H}) = 1.0σ_P−0063 (R^2= 0.89).

Figure 1 includes the plot of v_0 against different **BnBz** concentrations, showing a saturation behavior of v_0 against the concentration of **BnBz**. Based on the curve-fitting analysis using Michaelis-Menten-type equation, V_{max} and Michaelis constant (K_M) were determined to be 3.6 × 10^{-3} M/min and 1.1 M, respectively. Thus, a pre-equilibrium process between **1** and substrate was supported.[16]

The v_0 of **BnBz** derivatives with various substituents were similarly determined and revealed that v_0 increased as the electron-withdrawing ability of the substituents increased. Each kinetic parameter showed a modest linear correlation with the Hammett parameter (σ_p)[17] of substituents at the *para* positions (Figure 2). The ρ value was calculated to be +1.0. Therefore, the partially negatively charged substrates, which could be stabilized by electron-withdrawing substrates, should be included at the transition state of this reaction.[18] It was also confirmed that the plot of log(v_0) also represents a linear free energy relationship with regard to the 1st cathodic reduction potential ($E_{p,c}$) of various **BnBz** derivatives with different substituents (Figure S14). Although the slope value (+2.3) was smaller than those expected value for free energy single electron transfer process,[19] the rate-determining step of hydrogenolysis of esters catalyzed by **1** should be somewhat dependent on the electron donation from the Co(I) center to the substrate.

A possible reaction mechanism is proposed in Scheme 5. Complex **1** is deprotonated by DBU to afford **2**. Complex **2** achieves H–H bond cleavage to form **3**. Complex **3** reacts with

substrate to form an adduct intermediate **A**. This aggregation process should be under equilibrium as suggested by the kinetics. Upon formation of the transition state, electron donation from the Co centre to the substrate proceeds so that the adducted substrate exhibits partial negative charge (δ^-). After the transition state, β-C–O bond cleavage proceeded to form a benzyl radical, which furthermore undergoes HAT from the ligand backbone of the concomitantly formed Co(II) species to form toluene and $\mathbf{1}^+$ with benzoate counter anion.[20] Such the intramolecular HAT process *via in-situ* formed radical species was evidenced in our previous hydrodehalogenation of aryl radical process based on a radical clock experiment.[14] Finally, $\mathbf{1}^+$ with a benzoate anion as counter anion is deprotonated again to finish the catalytic cycle.



Scheme 5. Plausible mechanism of hydrogenolysis of esters *via* β-C–O bond cleavage catalysed by **1**.

Conclusions

Hydrogenolysis of esters *via* β-C–O bond cleavage was achieved under 1 atm H_2. The reaction was facilitated by a long-range MLC of the PNNP-Co system, where the ligand backbone behaves as a hydrogen reservoir. The reaction was applicable to various benzyl benzoate derivatives with both electron-withdrawing and -donating substituents. Kinetic study revealed the involvement of pre-equilibrium process in the reaction path. Combined with electrochemical study, it was also revealed that the rate-limiting step is dependent on the electron transfer from the Co(I) centre to the substrate. Overall, the present catalytic reaction was achieved by precisely designed PNNP-Co reaction platform, and thus the study demonstrates the novel concept of catalyst design to achieve ester hydrogenolysis *via* β-C–O bond cleavage as a new ester transformation method.

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