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Construction of a (NNN)Ru-Incorporated Porous Organic Polymer with High Catalytic Activity for β-Alkylation of Secondary Alcohols with Primary Alcohols

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Abstract: Solid supports functionalized with molecular metal catalysts combine many of the advantages of heterogeneous and homogeneous catalysis. A (NNN)Ru-incorporated porous organic polymer (POP-bp/bbpRuCl3) exhibited high catalytic efficiency and broad functional group tolerance in the C–C cross-coupling of secondary and primary alcohols to give β-alkylated secondary alcohols. This catalyst demonstrated excellent durability during successive recycling without leaching of Ru which is ascribed to the strong binding of the pincer ligands to the metal ions.

Keywords: heterogeneous catalysis; porous organic polymer; Ru NNN pincer complex; β-alkylation of secondary alcohols

1. Introduction

The construction of carbon–carbon bonds is fundamental to organic synthesis [1,2]. Alkyl halides were the workhorse of this transformation last century, but replacing these relatively toxic and wasteful electrophiles has been an imperative in recent years [3–5]. Transition-metal-catalyzed α- or β-alkylation of carboxyl complexes, nitriles and secondary alcohols using alcohols as alkylating agents generates only hydrogen and/or water as waste [6–8]. Metal-catalyzed heterocoupling reactions of secondary and primary alcohols proceeds through controllable dehydrogenation–condensation–hydrogenation steps, selectively affording α,β-unsaturated ketones, α-alkylated ketones or β-alkylated secondary alcohols [9–13]. Various molecular complexes based on Ru [14–17], Ir [18–21], Co [22–25], Ni [26–30], and Mn [31–36] have been developed for these transformations. However, these are homogeneous catalysts and separation and recycling is an impediment to their large-scale industrial use. Some heterogeneous catalysts, including IrO2/Fe2O3 [37], Ni/Ca,Mg,O [38], SBA-15-supported Ir/NHC complex [39], Pt–Sn/γ-Al2O3 [40], DMF-stabilized Ir nanoclusters [41] have been developed for the cross-alkylation of alcohols to give β-alkylated secondary alcohols. However, these systems suffer from the need for relatively high temperatures, and/or long catalytic reaction time, intricate formulations.

Porous organic polymers (POPs) with high stability, low skeleton density, tunable porous structures and easy synthesis are an intriguing platform for incorporating homogeneous metal/ligand molecular catalysts into heterogeneous supports [42–45]. One particular advantage of POPs is the range of possible chemical functionality within the porous framework. Phosphines, pyridines, bipyridyl/phenanthroline derivatives, porphyrins, carbenes, and salen have been introduced into the skeleton of POPs [46–49]. Functionalized POPs with metal ions or nanoparticles have demonstrated excellent catalytic performance for the Suzuki-Miyaura coupling reaction [50], Heck reaction [51], Ullmann
coupling reaction [52], CO₂ conversion into cyclic carbonates [53,54], alkyne carboxylation [55–57], photocatalytic hydrogen evolution [58], the reduction of nitroarenes [59–61] and the hydroformylation of higher olefins [62]. In the present work, we have incorporated 2,6-bis(benzimidazo-1-yl)pyridine (bbp) into a POP through a simple one-pot Scholl co-coupling polymerization with biphenyl to give NNN pincer based POP (POP-bp/bbp). RuCl₃-incorporated POP-bp/bbp (POP-bp/bbpRuCl₃) displayed high catalytic performance, selectivity and recyclability for the β-alkylation of secondary alcohols with primary alcohols.

2. Materials and Methods

2.1. Materials

2,6-Bis(benzimidazo-1-yl)pyridine (bbp) was prepared according to a published procedure [63]. All chemicals were commercially available and used as received without further purification. Biphenyl, 2,6-pyridinedicarboxylic acid, o-phenylenediamine, phenylmethanol, (4-chlorophenyl)methanol, (4-(trifluoromethyl)phenyl)methanol, p-tolylmethanol, (4-methoxyphenyl) methanol, (4-(tert-butyl)phenyl)methanol, o-tolylmethanol, (2-methoxyphenyl) methanol, (3-methoxyphenyl)methanol, m-tolylmethanol, (3-chlorophenyl) methanol, naphthalen-1-ylmethanol, benzo[d][1,3]dioxol-5-ylmethanol, thiophen-2-ylmethanol, 1-phenylethan-1-ol, 1-(4-chlorophenyl)ethan-1-ol, 1-(4-bromophenyl)ethan-1-ol, 1-(p-tolyl)ethan-1-ol, 1-(4-methoxyphenyl)ethan-1-ol, 1-(2-chlorophenyl)ethan-1-ol, 1-(2-methoxyphenyl)ethan-1-ol, 1-(o-tolyl)ethan-1-ol, 1-(3-methoxyphenyl)ethan-1-ol, 1-(m-tolyl)ethan-1-ol, 1-(naphthalen-2-yl)ethan-1-ol, RuCl₃·xH₂O, CDCI₃ were purchased from J&K. Toluene, chloroform, methanol, tetrahydrofuran, N,N-dimethylformamide, dimethyl sulfoxide, petroleum ether, and ethyl acetate were from Shanghai Titan Technology Co., Ltd. (Shanghai, China). Orthophosphoric acid, hydrochloric acid, aluminum chloride, potassium hydroxide, potassium tert-butoxide, cesium carbonate, sodium hydroxide, cesium hydroxide got from Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China).

2.2. Synthesis of Porous Organic Polymer (POP)-bp/bbp

Under a N₂ atmosphere, 2,6-bis(benzimidazo-1-yl)pyridine (bbp) (0.311 g, 1 mmol) and biphenyl (0.154 g, 1 mmol) were dissolved in anhydrous chloroform (20 mL), followed by the addition of anhydrous aluminum chloride (10 mmol, 1.33 g) with vigorous stirring at 58 °C. After 24 h, the reaction mixture was cooled to ambient temperature, filtered and the solid product was washed with methanol, HCl-H₂O (v/v = 1:1), H₂O, CH₂Cl₂ and EtOH, followed by washing with methanol in a Soxhlet thimble for 72 h. The polymer was then dried in a vacuum oven at 100 °C for 24 h to give a brown solid. Yield: 0.418 g (90%). Elemental analysis: calculated: C, 82.66; H, 4.95; N, 15.05. Found: C, 73.86; H, 4.19; N, 13.42.

2.3. Synthesis of POP-bp/bbpRuCl₃

Under a N₂ atmosphere, a mixture of POP-bp/bbp (0.2 g), RuCl₃·xH₂O (0.017 g), and anhydrous ethanol (25 mL) was introduced into a round-bottom flask (100 mL). The resulting mixture was refluxed for 12 h. After this period, the brown solid POP-bp/bbpRuCl₃ was separated by centrifugation, washed sequentially with ethanol and ethyl ether, and then dried under vacuum.

2.4. Typical Procedure for Syntheses of β-Alkylated Secondary Alcohols

Under an N₂ atmosphere, a mixture of secondary alcohol (1 mmol), primary alcohol (1.2 mmol), POP-bp/bbpRuCl₃ (20 mg, 0.6 mol% Ru), KOH (0.5 mmol) and toluene (2 mL) was added into a 15 mL sealed tube equipped with a stirring bar. The reaction mixture was heated to 130 °C for 12 h. After cooling to ambient temperature, the catalyst was separated by centrifugation and washed with ethanol and diethyl ether. The catalyst was then dried in a vacuum at 60 °C for 2 h to give recycled catalyst for the next run. The organic layers were combined and dried over anhydrous Na₂SO₄ and concentrated under
reduced pressure. The crude product was purified by flash column chromatography using petroleum ether and ethyl acetate as the eluent.

2.5. Characterizations

The analytical instruments employed in this work are as described in our previous article [57,64,65], unless otherwise noted. $^1$H and $^{13}$C NMR spectra were recorded at ambient temperature on a Varian UNITY plus-400 spectrometer. Solid-state cross-polarization magic angle spinning $^{13}$C NMR measurements were carried out on Bruker Avance III/WB solid-state NMR spectrometer operating at 400 MHz equipped with a standard 4 mm magic angle spinning double resonance probe head. Powder X-ray diffraction patterns were collected on a PANalytical Aeris diffractometer (Cu-Kα). Infrared spectra were recorded on a Varian Scamiter-1000 spectrometer. The thermal stability of materials was evaluated using thermogravimetric analysis (Perkin-Elmer Pyrisl) under a nitrogen atmosphere. Scanning electron microscopy (SEM) images and energy dispersive X-ray spectroscopy spectra were obtained using a HITACHI S-4700 cold field-emission SEM. Transmission electron microscopy (TEM) was performed on a FEI Tecnai G20 electron microscope operating at 200 kV. Annular dark-field scanning TEM (ADF-STEM) was performed on a FEI Tecnai F20 electron microscope operating at 200 kV, equipped with Genesis EDS detector. X-ray photoelectron spectra were recorded on an X-ray photoelectron spectrometer (AXIS Ultra DLD) and binding energies were referenced to C 1s at 284.7 eV from hydrocarbon to compensate for possible charging effects.

3. Results and Discussion

3.1. Subsection Synthesis and Characterization of POP-bp/bbpRuCl$_3$

POP-bp/bbp was synthesized by the AlCl$_3$-promoted Scholl reaction of bbp and biphenyl (bp) in CHCl$_3$ at 58 °C (Scheme 1). The resulting brown polymer was insoluble in common organic solvents such as tetrahydrofuran (THF), methanol (MeOH), N,N-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). Thermogravimetric analysis (TGA) showed that POP-bp/bbp was stable at temperatures up to 300 °C (Figure S1). The $^{13}$C NMR solid-state spectrum of POP-bp/bbp contained signals at δ = 148, 140 and 138 ppm ascribed to the carbons on pyridine and imidazole rings, and a broad signal at δ = 125 ppm assigned to the other aromatic carbons (Figure S2). Scanning electron microscopy (SEM) (Figure S3) and transmission electron microscopy (TEM) (Figure S4) images showed that the as-prepared polymer POP-bp/bbp was amorphous with particles of irregular shape and size. The energy-dispersive X-ray (EDX) elemental mapping images (Figure S5) indicated the homogenous distribution of C and N, indicating homogeneous distribution of bbp monomer. The FT-IR spectrum (Figure 1a) contained absorptions at 1600, 1573, and 1460 cm$^{-1}$ attributed to the C−C, C=N and C−N stretching vibrations, respectively. In addition, the band at 3185 cm$^{-1}$ were assigned to the −NH, originating from the imidazole moiety.

Scheme 1. Synthesis of porous organic polymer (POP)-bp/bbp and POP-bp/bbpRuCl$_3$. 

### Notes
- Subsection Synthesis and Characterization of POP-bp/bbpRuCl$_3$
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### References
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The N 1s XPS profile of POP-bp/bbp was deconvoluted into two peaks centered at
approximately 398.84 and 400.47 eV, which are assigned to pyridinic N and imidazolic N,
respectively (Figure 1c). After the loading of RuCl₃, a new N 1s XPS peak was observed at 399.71 eV,
corresponding to Ru-bound N species [66].

The binding energy of Ru 3p of RuCl₃ was 463.35 eV, indicating that the Ru species maintained its original oxidation state of Ru³⁺ in POP-bp/bbpRuCl₃ [67]. Compared with the reported binding energy of Ru 3p of RuCl₃ (464.1 eV), the down-shift (0.75 eV) of coordinated Ru³⁺ can be attributed to additional electron density from the strongly electron-donating ligands [68].

High-resolution transmission electron microscopy (HR-TEM) (Figure 1e) did not reveal the presence of Ru nanoparticles. EDX elemental mapping confirmed that the Ru was distributed evenly throughout the POP-bp/bbpRuCl₃ (Figure 1f). The C, N and Ru contents of the as-synthesized POP-bp/bbpRuCl₃ were 80.5 wt %, 14.6 wt %, and 4.8 wt %, respectively (Figure S11). The Ru content obtained by EDX element mapping analysis is higher than that calculated by the
ICP-OES analysis, which is attributed to the fact that Ru is mainly loaded on the surface of bp/bbp material.

### 3.2. Catalytic β-Alkylation of Secondary Alcohols

We next determined the performance of as-prepared POP-bp/bbpRuCl₃ as a catalyst for the catalytic acceptorless dehydrogenation coupling of alcohols. The reaction of 1-phenylethanol (mol %) with benzyl alcohol (2a) was conducted in toluene with KOH under a nitrogen atmosphere (Table 1). A standard workup produced 1-[(1,1′-biphenyl)-4-yl]ethan-1-one (3aa) in 68% yield with a trace of 1,3-diphenylpropan-1-one (4aa) as determined by high-performance liquid chromatography (HPLC). The screening of different bases (entries 1–5) revealed that CsOH was more selective than KOtBu, Cs₂CO₃ or NaOH, but that KOH facilitated the highest yield. Lowering the reaction temperature to 100 °C or 120 °C reduced the yield of 3aa significantly, while raising it slightly (140 °C) had a modest impact (entries 6–9). The optimal amount of KOH was 0.5 equivalents (entries 10–13). The yield of 3aa could be increased up to 93% by extending the reaction time to 12 h (entries 15). Interestingly, neither of the individual components of the catalyst (i.e., POP-bp/bbp or RuCl₃) facilitated more than a very modest amount of product under these conditions (entries 16 and 17).

**Table 1. Optimization of the reaction conditions.**

| Entry  | Catalyst          | Base (equiv.) | Temperature (°C) | Time (h) | Yield (%) 3aa | Yield (%) 4aa |
|--------|-------------------|---------------|------------------|----------|---------------|---------------|
| 1      | POP-bp/bbpRuCl₃  | KOH/1.0       | 130              | 4        | 68            | <5            |
| 2      | POP-bp/bbpRuCl₃  | KOtBu/1.0     | 130              | 4        | 33            | trace         |
| 3      | POP-bp/bbpRuCl₃  | Cs₂CO₃/1.0    | 130              | 4        | 32            | <5            |
| 4      | POP-bp/bbpRuCl₃  | NaOH/1.0      | 130              | 4        | 11            | trace         |
| 5      | POP-bp/bbpRuCl₃  | CsOH/1.0      | 130              | 4        | 45            | <5            |
| 6      | POP-bp/bbpRuCl₃  | KOH/1.0       | 100              | 4        | 7             | 25            |
| 7      | POP-bp/bbpRuCl₃  | KOH/1.0       | 110              | 4        | 20            | 14            |
| 8      | POP-bp/bbpRuCl₃  | KOH/1.0       | 120              | 4        | 49            | 20            |
| 9      | POP-bp/bbpRuCl₃  | KOH/1.0       | 140              | 4        | 70            | trace         |
| 10     | POP-bp/bbpRuCl₃  | KOH/0.3       | 130              | 4        | 60            | 12            |
| 11     | POP-bp/bbpRuCl₃  | KOH/0.5       | 130              | 4        | 76            | 8             |
| 12     | POP-bp/bbpRuCl₃  | KOH/0.7       | 130              | 4        | 75            | 6             |
| 13     | POP-bp/bbpRuCl₃  | KOH/1.5       | 130              | 4        | 69            | <5            |
| 14     | POP-bp/bbpRuCl₃  | KOH/1.0       | 130              | 8        | 82            | <5            |
| 15     | POP-bp/bbpRuCl₃  | KOH/0.5       | 130              | 12       | 93            | trace         |
| 16     | POP-bp/bbpRuCl₃  | KOH/0.5       | 130              | 12       | 0             | trace         |
| 17     | POP-bp/bbpRuCl₃  | KOH/0.5       | 130              | 12       | 18            | trace         |

* 130 Reaction conditions: 1a (1 mmol), 2a (1.2 mmol), cat. (20 mg, 0.6 mol% Ru), base (eq.), toluene (2 mL) in a 15 mL sealed tube, at 130 °C for 4 h, high-performance liquid chromatography (HPLC) yield using biphenyl as the internal standard.

Substrate scope was investigated with a variety of secondary and primary alcohols under the optimized conditions (Table 2). Good to high yields of β-alkylation were obtained with a variety of primary alcohols as the cross-coupling partner. The reaction of 1-phenylethanol with benzyl alcohols bearing both electron-donating and electron-withdrawing groups at the para-position resulted in products 3ab-3af in good yields (73–87%). Substrates bearing ortho- and meta-methoxy, methyl or chloro also delivered the expected products 3ag-3ak in good yields (79–89%). Likewise, 1-naphthylmethanol and 3,4-methylenedioxybenzyl alcohol reacted with 1a to form 3al and 3am in yields of 88% and 80%, respectively. Heterocyclic 2-thiophenemethanol 2n reacted with 1-phenylethanol less efficiently, giving 3an in 59% yield.
Next, the generality of this catalytic alkylation was investigated with various secondary alcohols (Table 3). The reaction of benzyl alcohol with 1-phenylethanol less efficiently, giving 3an in 59% yield. Substrates bearing ortho- and para-substituted 1-phenylethanol gave the desired secondary alcohols 3fa-3af in good yields (73–87%). No obvious substituent effect was observed. Chloro, methyl and methoxy groups afforded the desired β-alkylated secondary alcohols 3ba-3ea in excellent yields (80–89%).

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### Table 2. β-Alkylation of 1-phenylethanol with various primary alcohols.

| Entry | Primary Alcohol | Product | Yield (%) |
|-------|-----------------|---------|-----------|
| 1     | 2a              | 3aa     | 88        |
| 2     | 2b              | 3ab     | 85        |
| 3     | 2c              | 3ac     | 73        |
| 4     | 2d              | 3ad     | 85        |
| 5     | 2e              | 3ae     | 87        |
| 6     | 2f              | 3af     | 87        |
| 7     | 2g              | 3ag     | 89        |
| 8     | 2h              | 3ah     | 79        |
| 9     | 2i              | 3ai     | 86        |
| 10    | 2j              | 3aj     | 81        |
| 11    | 2k              | 3ak     | 85        |
| 12    | 2l              | 3al     | 88        |
| 13    | 2m              | 3am     | 80        |
| 14    | 2n              | 3an     | 59        |

* Reaction condition: 1a (1 mmol), primary alcohol (1.2 mmol), POP-bp/bbpRuCl₃ (20 mg, 0.6 mol % Ru), KOH (0.5 equiv.), toluene (2 mL), 130 °C, 12 h, isolated yields.
Next, the generality of this catalytic alkylation was investigated with various secondary alcohols (Table 3). The reaction of benzyl alcohol with para-substituted 1-phenylethanol bearing either electron withdrawing (-Cl, -Br) or electron-donating (-Me, -OMe) groups afforded the desired β-alkylated secondary alcohols 3ba-3ea in excellent yields (80–89%). No obvious substituent effect was observed. Chloro, methyl and methoxy groups at the ortho position of 1-phenylethanol gave the desired secondary alcohols 3fa-3ga in lower yields (53–79%) probably due to steric hindrance. Substrates with methoxy and methyl groups at the meta-position gave 3ia and 3ja in good yields (85 and 88%). 1-(Naphthalen-2-yl)ethanol was successfully converted to the coupled product 3ka (90%).

**Table 3. β-Alkylation of various secondary alcohols with benzyl alcohol.**

| Entry | Secondary Alcohol | Product | Yield (%) |
|-------|-------------------|---------|-----------|
| 1     | 1                 | 1a      | 3aa       |
| 2     | 2                 | 1b      | 3ba       |
| 3     | 3                 | 1c      | 3ca       |
| 4     | 4                 | 1d      | 3da       |
| 5     | 5                 | 1e      | 3ea       |
| 6     | 6                 | 1f      | 3fa       |
| 7     | 7                 | 1g      | 3ga       |
| 8     | 8                 | 1h      | 3ha       |
| 9     | 9                 | 1i      | 3ia       |
| 10    | 10                | 1j      | 3ja       |
| 11    | 11                | 1k      | 3ka       |

* Reaction condition: secondary alcohol (1 mmol), 2a (1.2 mmol), POP-bp/bbpRuCl₃ (20 mg, 0.6 mol%Ru), KOH (0.5 equiv.), toluene (2 mL), 130 °C, 12 h, isolated yields.
The recycling of POP-bp/bbpRuCl$_3$ was examined under optimized reaction conditions. No significant loss of catalytic activity was observed after four cycles (Figure 2a) and ICP analysis indicated that 96% of Ru remained. Ru nanoparticles were not observed in the subsequent TEM images (Figure 2b). EDX analysis revealed the homogeneous distribution of Ru components throughout the polymer POP-bp/bbp (Figure S12). The FT-IR spectrum of the recovered catalyst did not change noticeably (Figure 2c), except for a new peak at 1960 cm$^{-1}$ which we assign to a Ru-H species [69] generated during the catalytic cycle. XPS measurements indicated that the Cl 2p peak had disappeared in the recovered catalyst indicating ligand substitution (Figure S13). The binding energies of Ru 3p$_{3/2}$ and Ru 3d$_{5/2}$ for the catalyst were 463.15 eV and 281.4 eV, respectively (Figure 2d and Figure S14). The slight decrease in binding energies compared to that of fresh catalyst may be due to the substitution of hydride, which has a greater electron donating ability than chloride [69]. To verify whether the observed catalysis was due to the heterogeneous catalyst POP-bp/bbpRuCl$_3$ or due to leached ruthenium species, a reaction was performed between 1a and 2a under standard conditions. The yield of 3aa was 42% accompanied by 7% 4aa after 2h. The reaction was then filtered. No catalytic function was observed in the filtered solution over 24 h and negligible Ru content was detected by ICP. These results indicate that the POP-bp/bbpRuCl$_3$ catalyst is stable, which we ascribe to the strong binding of pincer ligand to metal centers.

A probable mechanism of this reaction was determined by investigating each step individually. The POP-bp/bbpRuCl$_3$-catalysed dehydrogenation of phenylmethanol and 1-phenylethanol for 4 h afforded benzaldehyde in 90% yield and acetophenone in 73% yield, respectively (Scheme 2(a,b)). The condensation of benzaldehyde with acetophenone, facilitated by KOH afforded chalcone in good yield (Scheme 2(c)). reduction of chalcone with 1a under the standard reaction conditions achieved 31% of the corresponding secondary
alcohol, as shown in Scheme 2, hydrogenation of chalcone with 2a under the same reaction conditions also gave the same reduced product in a similar 27% yield (Scheme 2(d)).

Scheme 2. Mechanism elucidation experiments.

In light of these results, and of previous literature reports [14–17], a catalytic mechanism is proposed (Scheme 3). Primary and secondary alcohols are dehydrogenated by the Ru catalyst to form the corresponding aldehyde, ketone and a ruthenium hydride complex. Base-catalysed aldol condensation of the resulting ketone and aldehyde give the α,β-unsaturated ketone intermediate which is reduced by the ruthenium hydride to generate β-alkylated secondary alcohol.

Scheme 3. Proposed mechanism.
4. Conclusions

A novel porous organic polymer incorporating a NNN pincer ligand possessed excellent thermal durability and high surface area. This acceptorless dehydrogenation, cross-coupling catalyst exhibited good activity, broad substrate scope and good recycling ability. We believe this work provides a green, convenient and scalable method for constructing C–C bonds, combining many of the advantages of homogeneous and heterogeneous catalysis.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/polym14020231/s1, Figure S1: TGA curve. Figure S2: 13C CP-MAS NMR spectrum. Figure S3: SEM image. Figure S4: TEM image. Figure S5: EDS elemental mapping. Figure S6: FT-IR spectrum. Figure S7: Pore-size distribution. Figure S8: PXRD patterns. Figure S9: XPS survey scan spectrum. Figure S10: XPS spectra. Figures S11 and S12: EDX spectroscopy elemental mapping. Figures S13 and S14: XPS survey scan spectra. Figures S15–S38: NMR data of products. References [12,31,70–73] are cited in the supplementary materials.

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