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Reaction condition controlled nickel(II)-catalyzed C-C cross coupling of alcohols

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The challenge in the C-C cross-coupling of secondary and primary alcohols using acceptorless dehydrogenation coupling (ADC) is the difficulty of accurately controlling product selectivities. Herein we report a controlled approach to a diverse range of β-alkylated secondary alcohols, α-alkylated ketones and α,β-unsaturated ketones using ADC methodology employing a Ni(II) 4,6-dimethylpyrimidine-2-thiolate cluster catalyst under different reaction conditions. This catalyst could tolerate a wide range of substrates and displayed a high activity for the annulation reaction of secondary alcohols with 2-aminobenzyl alcohols to yield quinolines. This work is an example of precise chemoselectivity control by careful choice of reaction conditions.

Introduction

Replacing alkyl halides as substrates for C–C bond forming reactions[1] has been a goal for organic chemists for some time because of the relatively high toxicity of these electrophiles and the loss of a heavy halide ion in the substitution reaction.[2] A promising alternative is the metal-mediated utilization of stable, readily available, and less harmful alcohols as alkylating agents that generate H_2O as the byproduct.[3] In the past decade, the direct cross-coupling of secondary and primary alcohols has been developed using acceptorless dehydrogenation coupling or auto-transfer-hydrogen reactions.[4] This transformation is a multistep process that involves (i) dehydrogenation of alcohols to the corresponding aldehyde and ketone, (ii) base-mediated aldol condensation of the carbonyl product to α,β-unsaturated carbonyl derivative, and (iii) the hydrogenation of the C=C and/or C=O bonds using the borrowed hydrogen atoms from the first step.[5] Acceptorless dehydrogenative methodologies afford α,β-unsaturated ketones, α-alkylated ketones, β-alkylated secondary alcohols or unsaturated alcohols. The challenge is to control product selectivity and minimize side reactions. The most frequently used homogeneous catalysts are based on noble metals

such as Ir,[6] Ru,[7] Rh,[8] Pd[9] and they have shown high reactivity in the coupling of secondary and primary alcohols to yield α-alkylated ketones or β-alkylated secondary alcohols.

There has been much interest in developing earth-abundant metal catalysts based on Mn, Fe and Co for these oxidant-free dehydrogenative cross-couplings.[10] Co(II) chloride complexes and Mn(I) carbonyls stabilized by phosphine-based PN_5P, PNN, PNP pincer ligands catalyze the alkylation of secondary alcohols with primary alcohols[11] and the coupling of secondary and primary alcohols to ketones.[12] Nickel as the second most abundant transition metal in the Earth's crust is relatively cheap and toxicologically benign in comparison to most other transition metals. The Raney nickel-catalyzed Guerbet reaction involves self-coupling of alcohols with a strong base at high temperatures (>220 °C) and has been known for more than a century.[13] Significant recent effort has been devoted to developing modified Guerbet-type homo- and hetero-couplings to extend the utility of this reaction.[14] Ni nanoparticles and complexes have been reported to catalyze the α-alkylation of ketones,[15] β-alkylation of lactic acid[16] and esters;[17] N-alkylation of amines, amides, acylhydrazines and arylamines[18] – all with alcohols. However, the chemoselective cross-coupling of secondary alcohols with primary alcohols by a simple manipulation of reaction conditions has not been explored. Our continued interest in transfer hydrogenation reactions prompted us to investigate the possibility of using lower-cost nickel catalysts for dehydrogenative C-C formations.[19] We herein report that a Ni(II) N-heterocycle thiolate cluster chemoselectively mediates the coupling of secondary and primary alcohols to yield α,β-unsaturated ketones, α-alkylated ketones or β-alkylated

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secondary alcohols by simple manipulation of the reaction conditions.

Results and discussion

Catalyst evaluation for cross-coupling of secondary and primary alcohols. Hexanuclear cluster [Ni(dmpymt)$_2$]$_6$ (**1a**, Hdmpymt = 4,6-dimethylpyrimidine-2-thione) was prepared by reaction of [Zn(dmpymt)$_2$]$_n$ with Ni(NO$_3$)$_2$·6H$_2$O in MeOH. X-ray analysis revealed that **1a** has a hexagonal wheel structure in which six Ni(II) atoms are connected by six pairs of dmpymt ligands (Fig. 1, Scheme 1). For the following catalytic performance comparison, we deliberately adapted two analogues of dmpymt, pyrimidine-2-thiol (Hpymt) and 1H-pyridine-2-thione (Hpyt), which further reacted with Ni(II) salts to give rise to two known nickel(II)/N-heterocycle thiolate complexes [Ni$_2$(pymt)$_4$]$_n$ (**1b**)[20a] and [{Ni(pyt)$_2$}$_6${Ni(MeCN)$_3$}$_2$][PF$_6$]$_4$ (**1c**),[20b] respectively (Scheme 1).
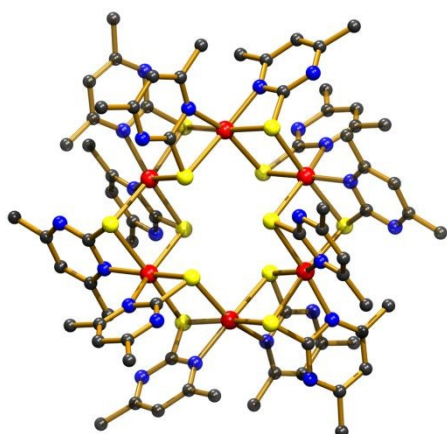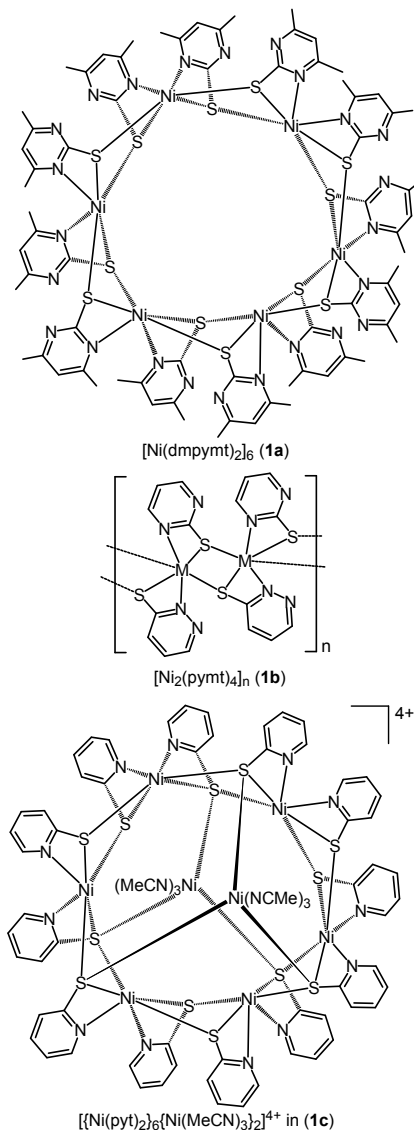

Fig. 1 View of the molecular structure of **1a**. All hydrogen atoms are omitted for clarity.Color codes: Ni (red), S (yellow), N (blue), C (black).

The catalytic activity and selectivity of these as-prepared Ni(II) complexes **1a**-**1c** were compared by using the C-C cross-coupling reaction of phenylmethanol (**2a**) and 1-phenylethan-1-ol (**3a**) as model substrates (Table 1). This reaction was performed in the presence of KOH (0.5 equiv.) and **1a** (5 mol% Ni) in toluene (3 mL) under a nitrogen flow over 24 h. 1,3-Diphenylpropan-1-one (**4aa**) was the only C-C cross-coupling product detected and was obtained in 95% yield (entry 1, Table 1). Slightly lower selectivity was observed with **1b** or **1c** as a catalyst (entries 2 and 3), facilitating 87% and 75% yields of **4aa** respectively, together with approximately 5% of 1,3-diphenylpropan-1-ol (**6aa**) and a trace of chalcone (**5aa**). NiCl$_2$/Hdmpymt also catalyzed this model reaction with high selectivity, but the yield of **4aa** was a little lower (entry 4). NiCl$_2$, NiBr$_2$, Ni(OAc)$_2$, Ni(NO$_3$)$_2$ exhibited much lower catalytic activities (entries 5-9). Complexes [NiCl$_2$(L)$_2$] (L = 2,2'-dipyridyl, 1,10-phenanthroline) displayed high activity but with lower selectivity (entries 10 and 11). Complex **1a** was therefore employed to optimize the reaction conditions of base, solvent and temperature. Of the various bases tested, KOH gave the highest yield of **4aa** and the highest selectivity (entries 1 and 12-17). Cross-coupling did not proceed in the absence of a base (entry 18). The blank reactions using 0.5-1.5 equiv. of KOH without any catalysts proceeded in a lower conversion with a lower selectivity (entries 19). Yields were

much lower in THF or 1,4-dioxane as solvent (entries 22 and 23). Cross-coupling did not proceed at all in DMSO or DMF (entries 24 and 25). Lower temperatures reduced the yield of **4aa**, but increased the yield of α,β-unsaturated ketone **5aa** (entries 27-29).

[Ni(dmpymt)$_2$]$_6$ (**1a**)

[Ni$_2$(pymt)$_4$]$_n$ (**1b**)

[{Ni(pyt)$_2$}$_6${Ni(MeCN)$_3$}$_2$]$^{4+}$ in (**1c**)

Scheme 1. Structures of **1a**, **1b** and [{Ni(pyt)$_2$}$_6${Ni(MeCN)$_3$}$_2$]$^{4+}$ in **1c**.

The addition of *t*BuOH to toluene also improved selectivity for **5aa** (entry 30). Indeed, the yield for **5aa** could be increased up to 90% using toluene/*t*BuOH in the presence of 1.0 equiv. of KOH at 70 ºC over 36 h (entry 32). **5aa** could not be hydrogenated due to the hydrogen bonding interaction of *t*BuOH with the catalytic center. When the reaction of **2a** and **3a** with **1a** and KOH in toluene was carried out in a sealed tube at 100 ºC, the selectivity for **6aa** increased to 38% (entry 33). Manipulation of reaction parameters such as substrate concentration, temperature, and amount of base could increase the percent conversion and yield of **6aa** (entries 34-43). An 88% yield of **6aa**, for example, was achieved with **1a** (2 mol% Ni), 1.5 equiv. of KOH in toluene at 120 ºC (entry 41). Thus the transfer hydrogenation of the C=O bond required the higher temperature and the higher H$_2$ pressure.

Synthesis of α-alkylated ketones. The optimized reaction conditions for the synthesis of α-alkylated ketones was thereby determined to be **1a** (5 mol% of Ni) as the catalyst, KOH (0.5 equiv.)

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as the base at 100 ºC in toluene under a slow, steady N_2 flow. We next investigated substrate scope with the reaction of various secondary alcohols and primary alcohol **2a**. Secondary aromatic alcohols (**3a**-**3p**) with electron-deficient and electron-rich groups on the phenyl rings gave the desired ketones **4aa**-**4ap** in good to excellent yields (Table 2). The yields of substrates (**3a**-**3c**, **3g**, **3i**) with electron-rich or electron-neutral groups were higher than those with electron-withdrawing groups (**3d**-**3f**, **3h**, **3j**). The reactions of aromatic substrates with substituents at the *ortho* position also gave the corresponding ketones (**4ai**-**4ak**) in good yields. Cluster **1a** also displayed a high catalytic activity toward the reaction of propiophenone or 1-phenylbutan-1-one with **2a**, giving **4ao** or **4ap** in 85% and 81% yields (Table 2). The (non-benzylic) secondary aliphatic alcohols (**3q** and **3r**) were alkylated by **2a** to give **4aq** and **4ar** in 86% and 80% yields, respectively. We next investigated the tolerance of this dehydrogenative cross-coupling to variation in the primary alcohol. Substituted benzyl alcohols bearing electron-donating and electron-withdrawing groups also reacted smoothly with **3a** to afford **4aa**-**4ka** in 60-92% yield. Reactions of ferrocenylmethanol with **3a** or α-ferrocenylethanol with **2a**

afforded the corresponding products **4an**, **4ia** in 88-90% yield. Notably, secondary and primary heteroaromatic alcohols (**3m**, **2j** and **2k**) were found to be compatible; generating the expected products (**4am**, **4ja** and **4ka**) in 73-82% yield. Additionally, following this protocol, a preparative gram scale reaction of **2a** (1.62 g, 15 mmol) and **3a** (1.22 g, 10 mmol) under the optimal conditions also proceeded smoothly to give **4aa** in 76% after 24 h. When these crossing-coupling reactions were performed in toluene at higher temperature (110 ºC), Cu(I) N-heterocycle thiolate clusters (10 mol% Cu)[19a] displayed comparable activity to that of **1a**. Cluster **1a** also displayed a high catalytic activity toward the reaction of **3o** and **2a**, giving **4ao** in 85% yield.

Exploring the mechanism. We next monitored the reaction progress of **2a** and **3a** in the presence of **1a** (5 mol% Ni) (Table 1, entry 1). As shown in Fig. 2, the dehydrogenation of primary and secondary alcohols was relatively fast with concentrations of **2a** and **3a** decreasing significantly within the first two hours. α,β-Unsaturated ketone **5aa** was produced relatively quickly and the yield reached a

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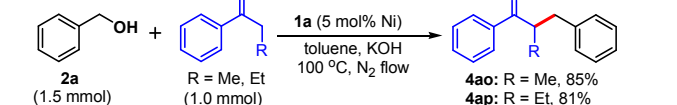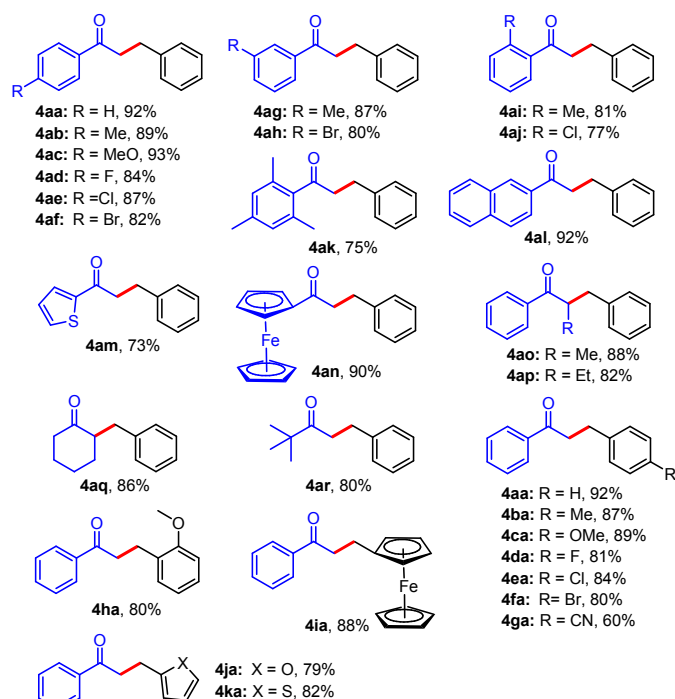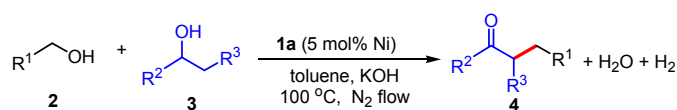**Table 1** Optimizing the acceptorless dehydrogenative cross-coupling of **2a** and **3a**
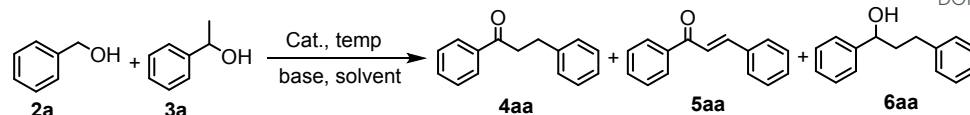
| Entry[a]	Cat.	Solvent	Base/equiv.	Temp (ºC)	Time (h)	Yield (%)[b]		
						4aa	**5aa**	**6aa**
1	**1a**	toluene	KOH/0.5	100	24	95	trace	trace
2	**1b**	toluene	KOH/0.5	100	24	87	trace	5
3	**1c**	toluene	KOH/0.5	100	24	75	trace	5
4	**1a′**[c]	toluene	KOH/0.5	100	24	91	-	trace
5	NiCl$_2$	toluene	KOH/0.5	100	24	4	trace	12
6	NiBr$_2$	toluene	KOH/0.5	100	24	3	trace	15
7	NiBr$_2$	toluene	KOH/1.0	100	24	14	9	16
8	Ni(OAc)$_2$	toluene	KOH/0.5	100	24	12	trace	19
9	Ni(NO$_3$)$_2$	toluene	KOH/0.5	100	24	8	trace	13
10	NiCl$_2$(bipy)$_2$	toluene	KOH/0.5	100	24	40	5	47
11	NiCl$_2$(phen)$_2$	toluene	KOH/0.5	100	24	51	trace	42
12	**1a**	toluene	NaOH/0.5	100	24	87	-	4
13	**1a**	toluene	Cs$_2$CO$_3$/0.5	100	24	68	5	7
14	**1a**	toluene	tBuOK/0.5	100	24	94	-	3
15	**1a**	toluene	NaOMe/0.5	100	24	82	trace	4
16	**1a**	toluene	LiOH/0.5	100	24	7	-	16
17	**1a**	toluene	K$_2$CO$_3$/0.5	100	24	trace	-	trace
18	**1a**	toluene	-	100	24	trace	trace	trace
19	-	toluene	KOH/0.5	100	24	7	3	4
20	-	toluene	KOH/1.0	100	24	9	14	7
21	-	toluene	KOH/1.5	100	24	12	21	11
22	**1a**	THF	KOH/0.5	100	24	40	trace	11
23	**1a**	1,4-dioxane	KOH/0.5	100	24	18	-	12
24	**1a**	DMF	KOH/0.5	100	24	trace	trace	trace
25	**1a**	DMSO	KOH/0.5	100	24	-	-	trace
26[d]	**1a**	toluene	KOH/0.5	100	24	77	-	trace
27	**1a**	toluene	KOH/0.5	80	24	66	15	trace
28	**1a**	toluene	KOH/0.5	70	24	46	22	trace
29	**1a**	toluene	KOH/0.5	60	24	35	12	trace
30[e]	**1a**	toluene/tBuOH	KOH/0.5	70	24	trace	74	-
31[e]	**1a**	toluene/tBuOH	KOH/0.5	70	36	trace	83	-
32[e]	**1a**	toluene/tBuOH	KOH/1.0	70	36	3	90	-
33[f]	**1a**	toluene	KOH/0.5	100	24	21	9	38
34[f]	**1a**	toluene	KOH/0.5	110	24	20	8	44
35[f]	**1a**	toluene	KOH/0.5	120	24	11	10	56
36[f]	**1a**	toluene	KOH/0.5	130	24	16	13	50
37[f,g]	**1a**	toluene	KOH/0.5	120	24	6	trace	70
38[f,g]	**1a**	toluene	KOH/1.0	120	24	5	3	75
39[f,g]	**1a**	toluene	KOH/1.5	120	24	3	4	82
40[f,g]	**1a**	toluene	KOH/2.0	120	24	11	12	74
41[d,f,g]	**1a**	toluene	KOH/1.5	120	24	trace	trace	88
42[d,f,g]	-	toluene	KOH/1.5	120	24	trace	trace	15
43[d,f,g]	-	toluene	KOH/1.5	130	24	4	3	22

[a] Reaction conditions: **2a** (1.5 mmol), **3a** (1.0 mmol), cat. (5 mol%), base (0.5 mmol), solvent (3 mL), under a slow, steady N$_2$ flow for 24 h. [b] HPLC yield. [c] Hdmpymt (10 mol%) and NiCl$_2$ (5 mol%) were used. [d] 2mol% Ni. [e] 2.5 mL toluene and 0.5 mL tBuOH as solvent. [f] The reaction was carried out in a sealed tube (0.75 mmol **2a**, 0.5 mmol **3a**). [g] 1.0 mL toluene.

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Table 2 Synthesis of α-alkylated ketones

4aa: R = H, 92%
4ab: R = Me, 89%
4ac: R = MeO, 93%
4ad: R = F, 84%
4ae: R =Cl, 87%
4af: R = Br, 82%

4ag: R = Me, 87%
4ah: R = Br, 80%

4ai: R = Me, 81%
4aj: R = Cl, 77%

4ak, 75%

4al, 92%

4am, 73%

4an, 90%

4ao: R = Me, 88%
4ap: R = Et, 82%

4aq, 86%

4ar, 80%

4aa: R = H, 92%
4ba: R = Me, 87%
4ca: R = OMe, 89%
4da: R = F, 81%
4ea: R = Cl, 84%
4fa: R= Br, 80%
4ga: R = CN, 60%

4ha, 80%

4ia, 88%

4ja: X = O, 79%
4ka: X = S, 82%

4ao: R = Me, 85%
4ap: R = Et, 81%

Reaction conditions: **2** (1.5 mmol), **3** (1.0 mmol), **1a** (5 mol% Ni), KOH (0.5 mmol), toluene (3 mL), at 100 °C under N_2 for 24 h, isolated yields.

maximum after about 1.5 h. α-Alkylated ketone **4aa** was also produced relatively quickly within the first five hours and then at a slower rate. Only a small amount of 1,3-diphenylpropan-1-ol **6aa** was produced and then subsequently consumed. At 100 °C, **1a** selectively reduced the C=C bond prior to the reduction of the C=O bond by nickel hydride species generated at the step of the dehydrogenation of alcohols.[19a,b] Therefore, we propose that **5aa** and **6aa** are intermediates in this cross-coupling reaction. In the first 15 min., the yield of **5aa** is higher than that of **4aa** (Eq. 1, Scheme 2), supporting the proposition that **4aa** is produced by the hydrogenation of **5aa**. When the transfer hydrogenation of **5aa** with **2a** (1.5 equivalents) as a hydrogen source was carried out in the presence of **1a** and KOH under N_2 flow at 100 °C for 24 h, we isolated **4aa** in 75% yield and **6aa** in 3% yield, together with some unidentified organic material (Eq. 2). The hydrogenation of **5aa** with **3a** under the same reaction conditions gave **4aa** (79% yield), together with **6aa** (7% yield) and small quantities of unidentified organic material (Eq. 3). The oxidant-free dehydrogenation of **6aa** catalyzed by **1a** at 100 °C under a N_2 flow gave **4aa** in high yield (Eq. 4). To investigate whether the benzaldehyde produced during the course of the reaction (Fig. 2) was acting as a catalyst,[21] the reaction of **2a** and **3a** with 0.5 equiv. of KOH and benzaldehyde (20 mol%)

was conducted in toluene (3 mL) under a nitrogen flow for 24 h to afford **4aa**, **5aa** and **6aa** in 27% yield, 10% yield and 7% yield, respectively (Eq. 5). At temperature of 70 °C, the same reaction gave 9% yield for **4aa** and 6% yield for **5aa** (Eq. 6). At 120 °C, **2a** reacted with **3a** in a sealed tube to give **4aa** in 5% yield and **6aa** in 23% yield (Eq. 7). These results indicate that benzaldehyde could slightly promote the formation of **4aa** and **6aa** but exhibited a lower catalytic activity and lower selectivity than **1a** under our optimized reaction conditions.
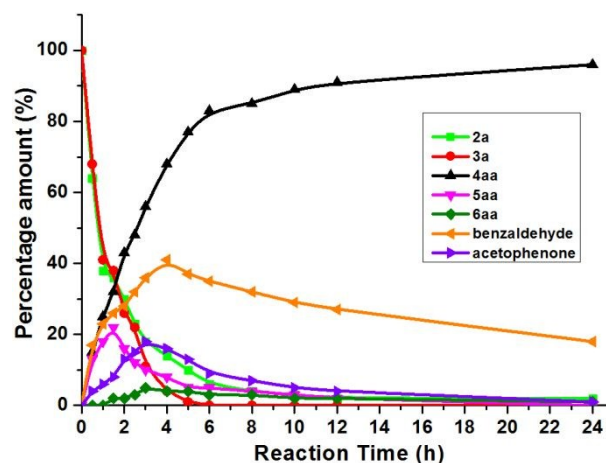
Fig. 2 Time-course monitoring of the reaction of **2a** with **3a**.
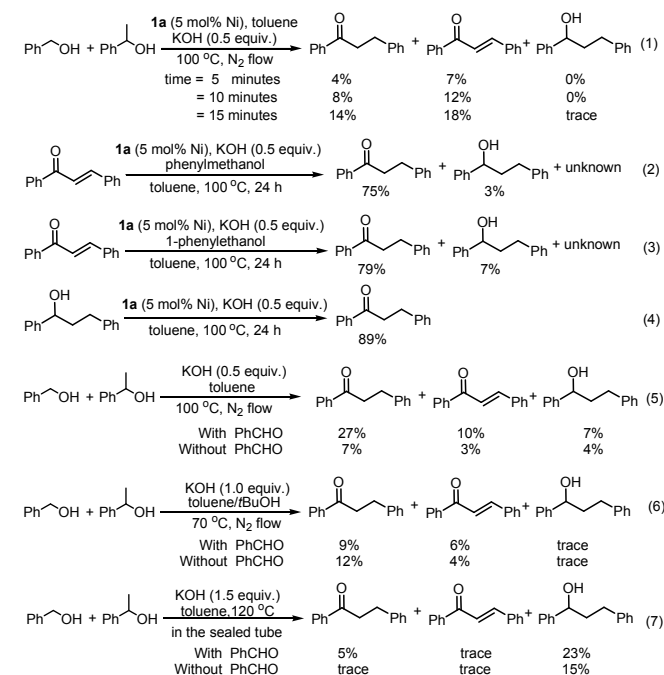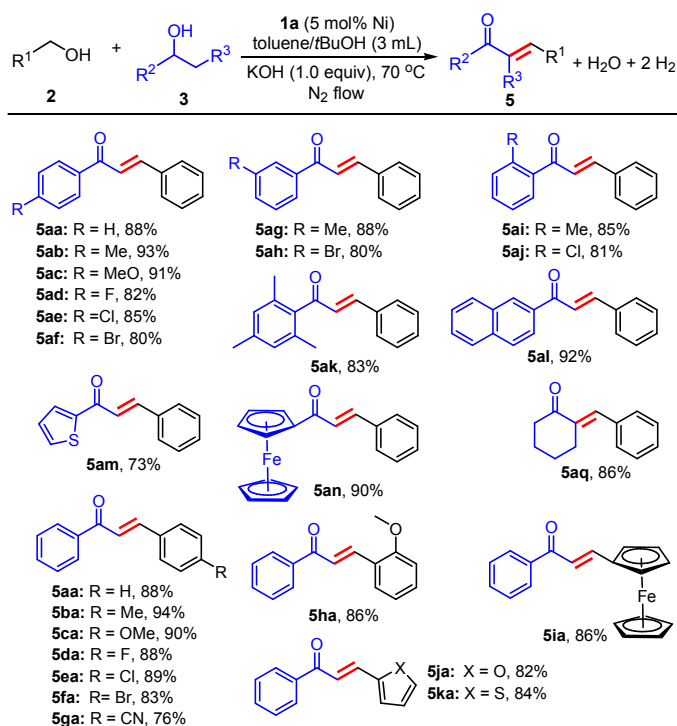

Scheme 2 Verification experiments.

On the basis of these results, a plausible pathway for this C-C hetero-coupling of secondary alcohols with primary alcohols is proposed (Scheme 3). The primary and secondary alcohols are first dehydrogenated to the corresponding aldehyde or ketone. Their base-mediated cross-aldol condensation produces an α,β-unsaturated ketone that is hydrogenated by the *in-situ* generated nickel hydride complex to an α-alkylated ketone. The latter can be

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further hydrogenated to a saturated alcohol. We can, therefore, control the product outcomes by choice of reaction conditions. The lower catalytic activity of **1a** for the hydrogenation of C=C and C=O bonds at lower temperature (70 °C) and the interaction between *t*-BuOH with the catalyst prevent the hydrogenation of α,β-unsaturated ketones. At 100 °C, **1a** displays high chemoselective transfer hydrogenation of C=C bonds in α,β-unsaturated carbonyls at 1 atm. However, because of the higher temperature (120 °C) and the higher H_2 pressure realized in a sealed tube, α-alkylated ketones can be further hydrogenated to generate β-alkylated secondary alcohols.
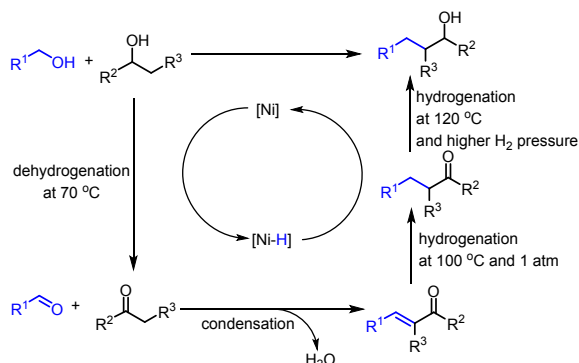
Scheme 3 Proposed mechanism for the cross-coupling of alcohols.

Table 3 Synthesis of α,β-unsaturated ketones

5aa: R = H, 88%
5ab: R = Me, 93%
5ac: R = MeO, 91%
5ad: R = F, 82%
5ae: R =Cl, 85%
5af: R = Br, 80%

5ag: R = Me, 88%
5ah: R = Br, 80%

5ai: R = Me, 85%
5aj: R = Cl, 81%

5ak, 83%

5al, 92%

5am, 73%

5an, 90%

5aq, 86%

5aa: R = H, 88%
5ba: R = Me, 94%
5ca: R = OMe, 90%
5da: R = F, 88%
5ea: R = Cl, 89%
5fa: R= Br, 83%
5ga: R = CN, 76%

5ha, 86%
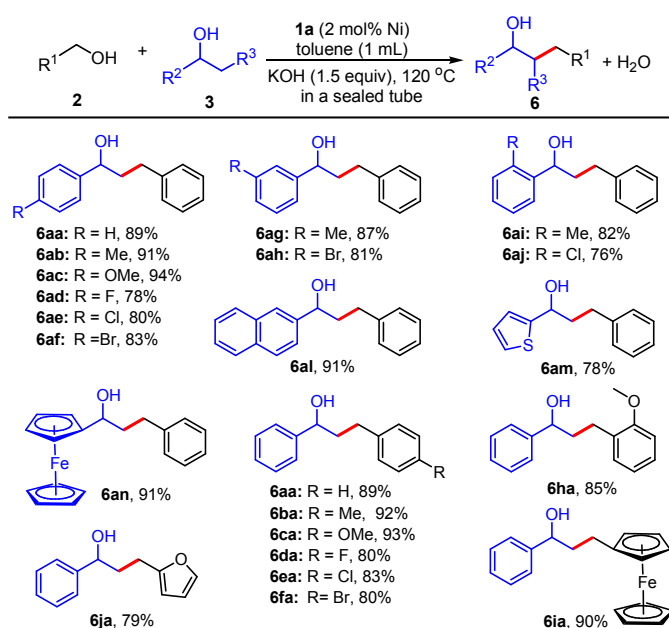
5ia, 86%

5ja: X = O, 82%
5ka: X = S, 84%

Reaction conditions: **2** (1.5 mmol), **3** (1.0 mmol), **1a** (5 mol% Ni), KOH (1.0 mmol), toluene (2.5 mL), *t*BuOH (0.5 mL), at 70 °C under a N_2 flow for 36 h, isolated yield.

Synthesis of α,β-Unsaturated Ketones. α,β-Unsaturated ketones are widely employed in the biological, agrochemical, and pharmaceutical industries. They are generally made by the aldol condensation of ketones and aldehydes,[22] or by the aerobic

oxidative cross-coupling of secondary and primary alcohols.[23] The dehydrogenative C-C cross-coupling reaction of primary and secondary alcohols to α,β-unsaturated ketones is less well known. We have been able to selectively obtain α,β-unsaturated ketones using **1a** (5 mol %) as the catalyst, KOH (1 equiv.) as the base in toluene/*t*BuOH under N_2 at 70 ºC. A variety of secondary alcohols with electron-rich, -neutral, and -withdrawing groups were investigated for this conversion and gave the desired products in high yields (Table 3). The nature of the substituents had a similar influence on product yields as previously observed for the corresponding synthesis of α-alkylated ketones. Moderate to excellent yields (76–94%) of the α,β-unsaturated ketones (**5aa**-**5ka**) were obtained from 1-phenylethanol **3a** and various substituted benzyl alcohols, including electron-donating, electron-withdrawing, sterically hindered, and heteroaromatic examples.

Table 4 Substrate scope for the β-alkylation of secondary alcohols

6aa: R = H, 89%
6ab: R = Me, 91%
6ac: R = OMe, 94%
6ad: R = F, 78%
6ae: R = Cl, 80%
6af: R =Br, 83%

6ag: R = Me, 87%
6ah: R = Br, 81%

6ai: R = Me, 82%
6aj: R = Cl, 76%

6al, 91%

6am, 78%

6an, 91%

6aa: R = H, 89%
6ba: R = Me, 92%
6ca: R = OMe, 93%
6da: R = F, 80%
6ea: R = Cl, 83%
6fa: R= Br, 80%

6ha, 85%

6ja, 79%

6ia, 90%

Reaction conditions: **2** (0.75 mmol), **3** (0.5 mmol), **1a** (2 mol% Ni), KOH (0.75 mmol), toluene (1 mL), at 120 °C in a sealed tube for 24 h, isolated yields.

The β-alkylation of secondary alcohols. In a sealed tube, **1a** (2 mol% Ni) effectively catalyzed the β-alkylation of secondary alcohols with primary alcohols, giving the desired β-alkylated secondary alcohols in good to excellent isolated yields at 120 °C (Table 4). This catalytic system was tolerant of substrates with various functional groups. Electron-rich or electron-deficient 1-arylethanols (**3a**-**3j**, **3l**) were effectively alkylated to give the desired β-alkylated secondary alcohols (**6aa**–**6aj**, **6al**) in high isolated yields. Benzylic alcohols(**2b**−**2f**, and **2h**) bearing an electron-donating methyl, methoxy, or an electron-deficient fluoro, chloro, bromo substituent reacted with **3a** to form the corresponding products **6ba**−**6fa**, and **6ha** in 80–93% yield. The reaction of α-ferrocenylethanol (**3n**) with **2a** or **3a** with ferrocenemethanol (**2i**) formed the desired products **6an** and **6ia** in 91% and 90%, respectively. This catalytical system was also applicable to the conversion of heterocyclic alcohols. Reactions of 1-(thiophen-2-yl)ethan-1-ol (**3m**) with **2a**, or **3a** with furan-2-ylmethanol (**2j**) gave

the desired products **6am** and **6ja** in good yields. Catalyst **1a** showed higher catalytic activity for the β-alkylation of **3a** with **2a** than Ni(OAc)$_2$(H$_2$O)$_4$/bis(diphenylphosphanyl)methane (dppm) at 115 °C. The latter facilitated an 85% yield of **6aa** after 30 h.[16]

Synthesis of quinoline. Our Ni(II) catalytic system also displayed high activity for dehydrogenative cyclization of 2-aminobenzyl alcohol with secondary alcohols to yield industrially useful quinolines (Table 5). Various secondary alcohols gave the corresponding products in 50-71% yield using **1a** (5 mol % Ni) as the catalyst, KOH (0.5 equiv.) as the base in toluene at 110 °C, under a steady N$_2$ flow for 24 h. Secondary alcohols (**3a**, **3b**, **3c**, **3h**) with electron-rich groups provided slightly higher yields than those with electron-deficient substituents (**3d**-**3g**). Heteroatom-containing alcohols such as 1-(pyridin-3-yl)ethan-1-ol, 1-(thiophen-2-yl)ethan-1-ol reacted in moderate yield (**8k** in 65% yield and **8l** in 61% yield).

Table 5 Synthesis of quinoline derivatives
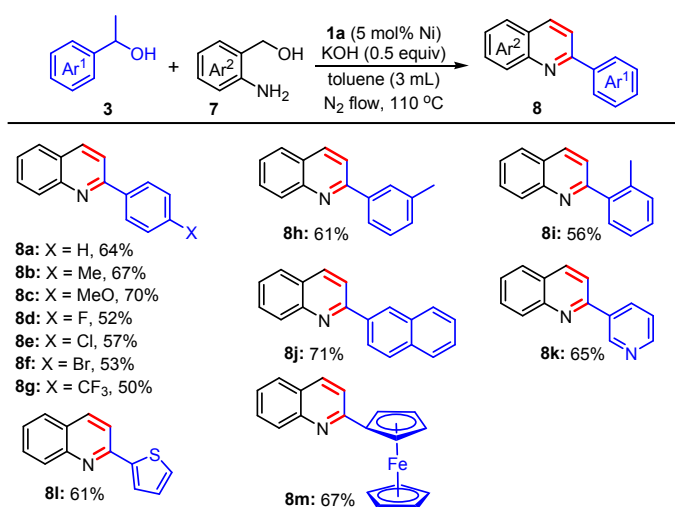
Reaction conditions: **3** (1.2 mmol), **7** (1.0 mmol), **1a** (5 mol% Ni), KOH (0.5 mmol), toluene (3 mL), at 110 ºC under a N$_2$ flow for 24 h, isolated yield.

Conclusions

In the work reported here, we have developed a well-defined Ni(II)/thiolate cluster catalyst **1a** for the efficient and chemoselective C-C cross-coupling of secondary and primary alcohols to generate α,β-unsaturated ketones, α-alkylated ketones or β-alkylated secondary alcohols, just through simply controlling reaction temperature, catalyst loading, reaction vessel closeness, etc.. Diverse secondary and primary alcohols were well-tolerated to furnish the corresponding products in good to excellent yields. This catalytic system also displayed high activity for cross-coupling annulation of 2-aminobenzyl alcohols with secondary alcohols to yield quinolines under mild conditions. This methodology offers a simple road to precisely control the multiple chemoselectivities of the hydrogen-autotransfer catalysis and other complex systems by carefully modifying reaction conditions.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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