ORGANOMETALLICS

pubs.acs.org/Organometallics Communication

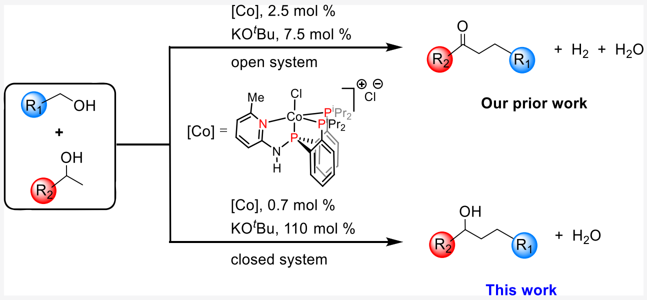
Switchable β-alkylation of Secondary Alcohols with Primary Alcohols by a Well-Defined Cobalt Catalyst

Bedraj Pandey, Shi Xu, and Keying Ding*

Cite This: *Organometallics* 2021, 40, 1207−1212 Read Online

ACCESS | Metrics & More | Article Recommendations | SI Supporting Information

ABSTRACT: β-alkylation of secondary alcohols with primary alcohols to selectively generate alcohols by a well-defined Co catalyst is presented. Remarkably, a low catalyst loading of 0.7 mol % can be employed for the reaction. More significantly, this study represents the first Co-catalyzed switchable alcohol/ketone synthesis by simply manipulating the reaction parameters. In addition, the transformation is environmentally friendly, with water as the only byproduct.



β-alkylation of secondary alcohols is one of the prominent synthetic methods for the construction of C−C bonds.[1] In the conventional β-alkylation of secondary alcohols to form alcohols or ketones, several drawbacks exist: stoichiometric oxidation, alkylation with toxic and mutagenic alkyl halides, stoichiometric reduction, and multistep processes, which inevitably generate copious wastes.[2] Therefore, it is appealing to explore new methods that are environmentally benign, are atom- and process-efficient, and utilize less toxic and abundantly available starting materials: e.g., alcohols. One such promising synthetic method is borrowing hydrogen (BH).[3,4] In a normally accepted BH process to synthesize alcohols, primary and secondary alcohols are first dehydrogenated to aldehydes and ketones, respectively, with the catalyst obtaining the hydrogen atoms. Next, a base and/or the catalyst mediates the α-C−H activation of the ketones and forms the nucleophilic carbon anions which attack the electrophilic aldehydes, leading to the formation of the α,β-unsaturated ketone intermediates with loss of water. Finally, the hydrogenated catalyst reduces the *in situ* formed ketones to the alcohol products. Alternatively, hydrogen gas can be liberated from the hydrogenated catalyst with ketones as the final products. This process is recognized as the acceptorless dehydrogenative coupling (ADC).[3,4] Both BH and ADC have recently received increasing attention in both academia and industry, as they can offer significant advantages over conventional methods in terms of sustainability.

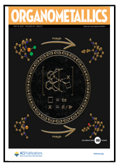
Currently, catalysts based on precious metals such as Rh,[5] Ir,[6] Ru,[7] and Pd[8] have dominated the field. It is more desirable to replace precious metal catalysts with inexpensive, less toxic, and earth-abundant base-metal surrogates, e.g. Fe,[9] Co,[10] Mn,[11] Ni,[12] and Cu,[13] due to increasing concerns regarding sustainability and economic issues.[14] To the best of our knowledge, there is only a single example of Co-catalyzed β-alkylation of secondary alcohols with primary alcohols to form alcohols via the BH process, reported by Kempe and coworkers.[10] In their pioneering work, a Co complex supported by a PN^{5}P pincer ligand was successfully employed. Nevertheless, a very high catalyst loading of 5 mol % was mandatory.

We have recently developed a new P,N mixed ^{iPr}PPPN^{H}Py^{Me} tetradentate ligand.[15] Its Co complex **A** is an efficient catalyst for dehydrogenation of secondary alcohols to ketones,[15] ADC of primary alcohols to esters,[16] and switchable alcohol amine couplings to imines or amines.[17] We recently reported the first example of Co-catalyzed β-alkylation of secondary alcohols with primary alcohols to selectively form ketones.[18]

Encouraged by the findings from our prior work, we envision that **A** could also be employed to achieve selective β-alkylated alcohol formations by manipulating the reaction parameters. Notably, the selectivity control of the products via BH or ADC, i.e., alcohol versus ketones, is critical but is also a challenge for the β-alkylation of secondary alcohols with primary alcohols.

Herein, we disclose a novel homogeneous Co catalytic system for efficient and selective β-alkylation of secondary alcohols to alcohols utilizing a significantly reduced Co catalyst loading of as low as 0.7 mol %. We also discovered that a switchable alcohol and ketone synthesis can be achieved by simply tuning the reaction parameters, such as the base loadings, with the same Co catalyst (Scheme 1), which to the

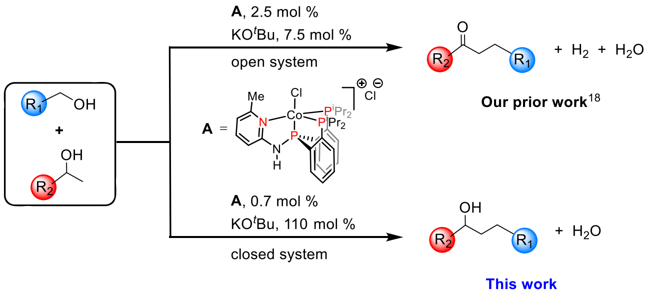
Received: March 10, 2021
Published: April 28, 2021



https://doi.org/10.1021/acs.organomet.1c00147

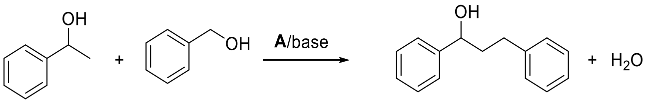
best of our knowledge, has not been reported for base-transition-metal catalysis using Co, Fe, or Mn.[19]

Scheme 1. Switchable β-Alkylation of Secondary Alcohols with Primary Alcohols Catalyzed by a Cobalt Complex



At the outset, 1-phenylethanol (**1a**) and benzyl alcohol (**2a**) were selected as the model substrates. Interestingly, it was revealed that an excess amount of base (110 mol %) was required for the selective formation of 1,3-diphenylpropan-1-ol (**3a**) (Table 1, entries 1–4), which was in stark contrast to the ketone case, where only a catalytic amount of base (7.5 mol %) was used.[18] Both **A** and base are essential for this transformation (Table 1, entries 1 and 6). Significantly, only 0.7 mol % of **A** was sufficient to mediate the alcohol-forming reaction (Table 1, entry 5). The ketone side product 3-phenylpropiophenone (**4a**) was detected with only 8% yield. To our surprise, a slightly lower yield (73%) resulted using 2.5 mol % of **A**, concurrent with the generation of unknown side products (Table 1, entry 4). Strong bases are more appropriate for the reaction (Table 1, entries 5 and 7–11). It is noteworthy that KO^{t}Bu, NaO^{t}Bu, and KHMDS led to comparable yields (Table 1, entries 5, 7, and 8). Toluene and a temperature of 110 °C proved to be more suitable (Table 1, entries 5 and 12–16). It is worth mentioning that, at a higher temperature of 120 °C, a diminished yield resulted with more unidentified side products being observed (Table 1, entry 13). Pleasingly, a very good 75% isolated yield resulted in the 1 mmol scale reaction (Table 1, entry 5[c]). A mercury test indicated a homogeneous reaction (Table 1, entry 5[d]).

Table 1. Optimization of the Reaction Conditions[a,b]



1a **2a** **3a**

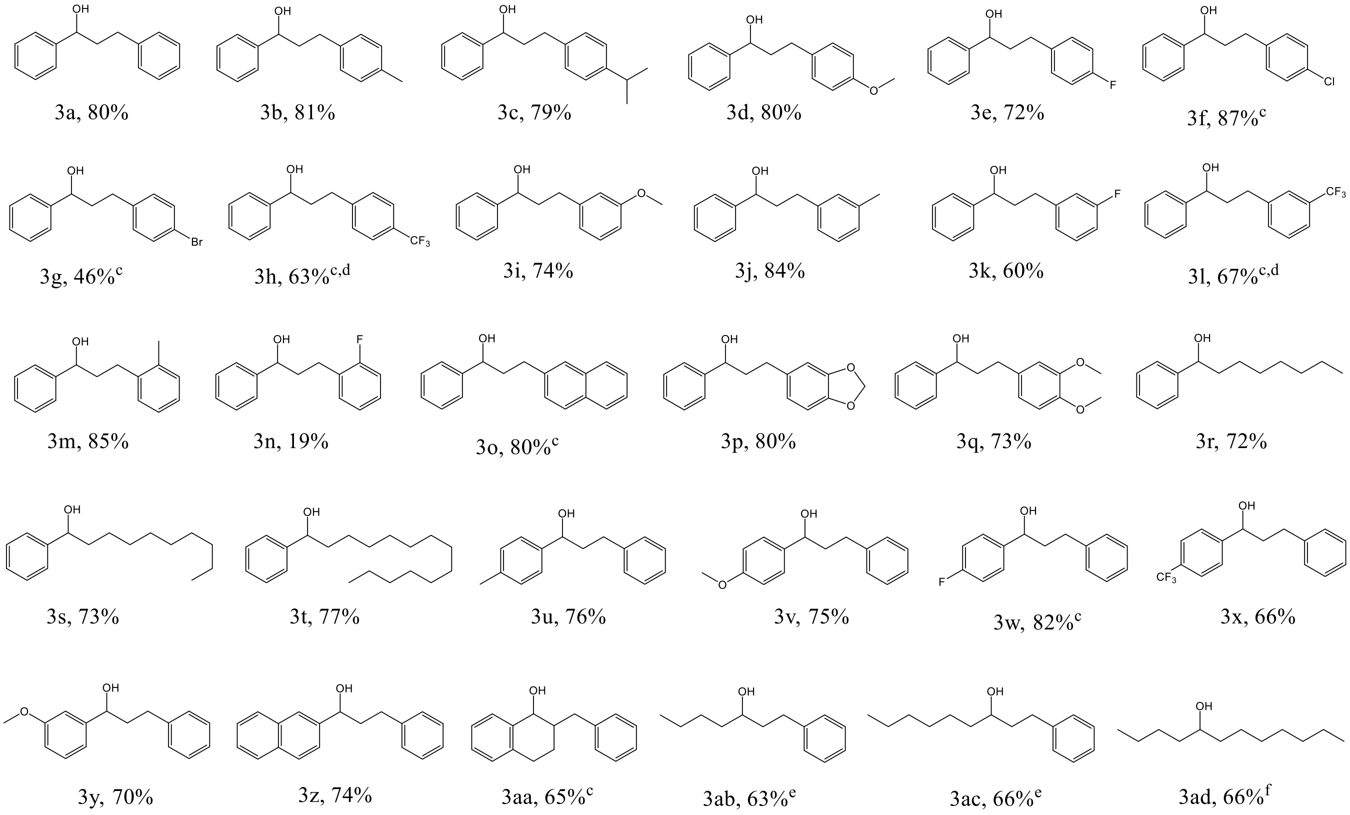
entry	base	base (mol %)	A (mol %)	solvent	yield (%)
1	KO^{t}Bu	0	2.5	toluene	0
2	KO^{t}Bu	30	2.5	toluene	31
3	KO^{t}Bu	80	2.5	toluene	53
4	KO^{t}Bu	110	2.5	toluene	73
5	KO^{t}Bu	110	0.7	toluene	80, 75,[c] 79[d]
6	KO^{t}Bu	110	0	toluene	8
7	NaO^{t}Bu	110	0.7	toluene	80
8	KHMDS	110	0.7	toluene	77
9	KOH	110	0.7	toluene	26
10	K_2CO_3	110	0.7	toluene	0
11	Cs_2CO_3	110	0.7	toluene	0
12	KO^{t}Bu	110	0.7	toluene	67[e]
13	KO^{t}Bu	110	0.7	toluene	71[f]
14	KO^{t}Bu	110	0.7	1,4-dioxane	12
15	KO^{t}Bu	110	0.7	THF	5
16	KO^{t}Bu	110	0.7	benzene	68

[a] Reaction conditions unless specified otherwise: 1-phenylethan-1-ol (0.375 mmol), benzyl alcohol (0.25 mmol), **A**, base, and solvent (1.5 mL) were heated in a closed 15 mL reaction tube for 24 h under N_2. [b] NMR yield using 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yield on a 1 mmol scale. [d] Mercury (125 mg) was added to the reaction mixture. [e] 100 °C. [f] 120 °C.

With the optimized reaction conditions on hand, we then investigated the reaction scope in terms of the substrates. First, the scope of the primary alcohols was explored in the alkylation of 1-phenylethanol. To our delight, *para*-substituted benzyl alcohols with electron-donating or -withdrawing groups reacted smoothly (Table 2, **3b–h**). Notably, this method was also applicable to some challenging substrates such as those bearing −Br or $-CF_3$ functional groups (Table 2, **3g**,**h**), furnishing moderate to good yields. *Meta*-substituted substrates delivered the corresponding alcohol products in moderate to very good yields (Table 2, **3i–l**). It is noteworthy that the sterically hindered *ortho*-substituted 2-methylbenzyl alcohol afforded a very good 85% yield (Table 2, **3m**). However, 2-fluorobenzyl alcohol only resulted in a 19% yield, probably due to the coordination of the −F functionality to the catalyst, diminishing its reactivity. Aliphatic primary alcohols were amenable to this method as well (Table 2, **3r–t**). Next, a series of secondary alcohols were examined to couple benzyl alcohol. Pleasingly, for aromatic secondary alcohols, −OMe, −F, $-CF_3$, and naphthalene functional groups were well tolerated in this method (Table 2, **3u–z**). Challenging aliphatic secondary alcohols were alkylated with benzyl alcohols leading to satisfactory yields, albeit under relatively harsher conditions (Table 2, **3aa–ac**). This is likely due to the difficulty in the dehydrogenation of aliphatic secondary alcohols.[15] Notably, aliphatic secondary alcohols also coupled with aliphatic primary alcohols by this method. 2-Hexanol reacted with 1-hexanol, affording 5-dodecanol in a good 66% yield. (Table 2, **3ad**).

Next, we carried out a preliminary mechanistic study to understand the reaction and elucidate the selectivity switching. In our prior work, ketone is the major product via the ADC process.[18] It is rational to surmise that the selective alcohol formation may originate from further reduction of the *in situ* formed ketone. To examine this hypothesis, we performed the transfer hydrogenation of 3-phenylpropiophenone (**4a**) with 3 equiv of **1a** as the hydrogen source. We found that 80 mol % of KO^{t}Bu alone can efficiently reduce **4a** to **3a** to furnish a 90% yield, supporting a base-mediated Meerwein–Ponndorf–Verley (MPV) pathway.[20,21] However, a drastically lower KO^{t}Bu loading of 2.5 mol % also leads to a 71% yield of **3a**.[18] *An interesting question arises: why is excess base still required in the alcohol synthesis by the β-alkylation of secondary alcohols with primary alcohols?*We then performed the same reaction in the presence of 5 mol % of **A** and 90 mol % of KO^{t}Bu.[22] Interestingly, a lower 78% yield of **3a** was observed in comparison to that with 80 mol % KO^{t}Bu alone, suggesting that the Co species may have a negative effect on the hydrogenation of **4a** in the presence of excess base. As **A** has been recognized to be an efficient precatalyst for the dehydrogenation of secondary alcohols from our prior work,[15] the alcohol products could be dehydrogenated back to the ketones. In addition, in the β-alkylation of secondary

Table 2. β-Alkylation of Secondary Alcohols with Primary Alcohols to Selectively Form Alcohols[a,b]


3a, 80%
3b, 81%
3c, 79%
3d, 80%
3e, 72%
3f, 87%[c]
3g, 46%[c]
3h, 63%[c,d]
3i, 74%
3j, 84%
3k, 60%
3l, 67%[c,d]
3m, 85%
3n, 19%
3o, 80%[c]
3p, 80%
3q, 73%
3r, 72%
3s, 73%
3t, 77%
3u, 76%
3v, 75%
3w, 82%[c]
3x, 66%
3y, 70%
3z, 74%
3aa, 65%[c]
3ab, 63%[e]
3ac, 66%[e]
3ad, 66%[f]

[a] Reaction conditions unless specified otherwise: secondary alcohols (0.375 mmol), primary alcohols (0.25 mmol), **A** (0.7 mol %), KO^{t}Bu (110 mol %), and toluene (1.5 mL) were heated at 110 °C in a closed 15 mL reaction tube for 24 h under N_2. [b] NMR yield using 1,3,5-trimethoxybenzene as internal standard. [c] NaO^{t}Bu (110 mol %). [d] 48 h. [e] **A** (7.5 mol %), KO^{t}Bu (55 mol %), 125 °C. [f] **A** (7.5 mol %), 125 °C.

alcohols to form alcohols, a higher **A** loading results in a lower yield with more unidentified side products being generated (Table 1, entries 4 and 5). To counter these competitive and undesirable reactions mediated by the Co species, excess base is required to enhance the MPV process. In contrast, with regard to the selective ketone formation, a higher **A** loading (2.5 mol %), a catalytic amount of base (7.5 mol %), and an open system are more feasible to circumvent the MPV reaction and promote the dehydrogenation of alcohols. Note that the base is still needed for the Co precatalyst activation, the aldol condensation of the *in situ* formed aldehydes and ketones, and the reduction of the α,β-unsaturated ketone intermediates to the ketone products.[18] Very recently, we have presented a switchable imine and amine synthesis catalyzed by **A**, where the base loading also plays a critical role.[17] Overall, these results demonstrate the high versatility of our Co catalytic system in control of the products in these transformations.

Finally, two exemplary derivatives of **A** were investigated (Figure 1). Complex **B**, featuring a dearomatized pyridine ring, showed activity comparable to that of **A**, resulting in a 76% yield, demonstrating that **B** is also an efficient precatalyst. It is noteworthy that **C** bearing an N−Me linker rather than the N−H linker on **A** leads to a comparable yield of 74%, suggesting that metal ligand cooperativity (MLC) that could originate from the N−H linker on **A** may not play a critical role in this reaction.

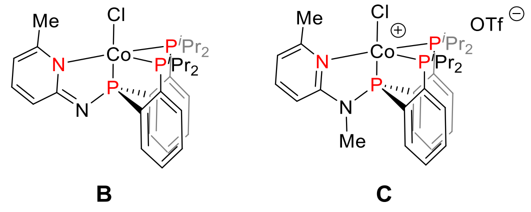
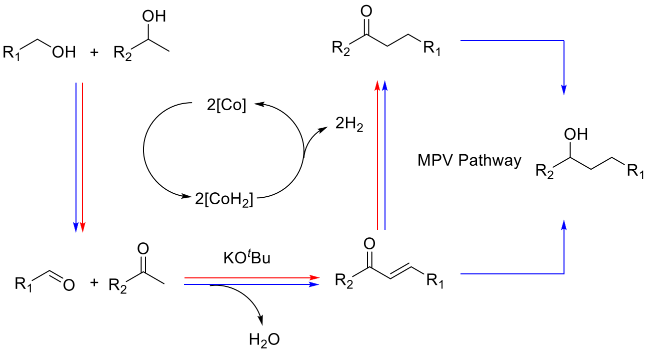


Figure 1. Complexes **B** and **C** examined.

Considering our experimental findings[18] and the literature,[3,4] we propose a plausible mechanism for the switchable alcohol/ketone formations (Scheme 2). Initially, primary and secondary alcohols are dehydrogenated by the Co catalyst to the corresponding aldehydes and ketones, respectively, which

Scheme 2. Proposed Mechanism[a]



[a] Red for the ketone formation and blue for the alcohol formation.

then undergo base-mediated condensation to generate the α,β-unsaturated ketone intermediates with the depletion of water. The Co catalyst is regenerated by releasing hydrogen gas. At low base loadings, the α,β-unsaturated ketones are reduced to the ketone products via the MPV process.[18] Alternatively, in the presence of excess amount of base, the ketones that formed are further reduced, furnishing alcohols as the final products. However, we cannot exclude the possibility that the α,β-unsaturated ketones could be directly reduced to the alcohols. It is worth noting that, in the alcohol-forming reaction, the generated hydrogen gas might go back into the reaction system.[4h,l] A comprehensive mechanistic study is currently underway in our laboratory.

In conclusion, we have presented a well-defined Co catalyst for the β-alkylation of secondary alcohols with primary alcohols to selectively form alcohols using a remarkably low catalyst loading of 0.7 mol %. Our study provides an alternative solution for the switchable synthesis of alcohols and ketones, which is environmentally benign and atom- and process-efficient. We expect this work will contribute to advanced catalyst design with base transition metals for selective and sustainable chemical transformations.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.1c00147.

Experimental details and NMR spectral data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Keying Ding − *Department of Chemistry, Middle Tennessee State University, Murfreesboro, Tennessee 37132, United States; Molecular Biosciences Program, Middle Tennessee State University, Murfreesboro, Tennessee 37132, United States;* orcid.org/0000-0002-7367-129X;
Email: Keying.Ding@mtsu.edu

Authors

Bedraj Pandey − *Department of Chemistry, Middle Tennessee State University, Murfreesboro, Tennessee 37132, United States*

Shi Xu − *Department of Chemistry, Middle Tennessee State University, Murfreesboro, Tennessee 37132, United States*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.organomet.1c00147

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge support from the National Science Foundation (CHE-1465051 and MRI CHE-1626549). We also thank FRCAC, URECA, and the Clean Energy Fee Funds of MTSU for support.

■ REFERENCES

(1) (a) Obora, Y. Recent Advances in α-Alkylation Reactions using Alcohols with Hydrogen Borrowing Methodologies. *ACS Catal.* **2014**, *4*, 3972−3981. (b) Chelucci, G. Ruthenium and Osmium Complexes in C-C Bond-Forming Reactions by Borrowing Hydrogen Catalysis. *Coord. Chem. Rev.* **2017**, *331*, 1−36.

(2) (a) Sawatari, K.; Nakanishi, Y.; Matsushima, T. Relationships between chemical structures and mutagenicity: a preliminary survey for a database of mutagenicity test results of new work place chemicals. *Ind. Health* **2001**, *39*, 341−345. (b) Trost, B. M.; Fleming, I. *Comprehensive organic synthesis: selectivity, strategy, and efficiency in modern organic chemistry;* Pergamon Press: Oxford, New York, 1991. (c) Otera, J. *Modern Carbonyl Chemistry*; Wiley-VCH: Weinheim, Germany, 2000.

(3) For selected recent reviews and articles within, see: (a) Filonenko, G. A.; van Putten, R.; Hensen, E. J. M.; Pidko, E. A. Catalytic (de)hydrogenation promoted by non-precious metals − Co, Fe and Mn: recent advances in an emerging field. *Chem. Soc. Rev.* **2018**, *47*, 1459−1483. (b) Mukherjee, A.; Milstein, D. Homogeneous Catalysis by Cobalt and Manganese Pincer Complexes. *ACS Catal.* **2018**, *8*, 11435−11469. (c) Kallmeier, F.; Kempe, R. Manganese Complexes for (De)Hydrogenation Catalysis: A Comparison to Cobalt and Iron Catalysts. *Angew. Chem., Int. Ed.* **2018**, *57*, 46−60. (d) Gorgas, N.; Kirchner, K. Isoelectronic Manganese and Iron Hydrogenation/Dehydrogenation Catalysts: Similarities and Divergences. *Acc. Chem. Res.* **2018**, *51*, 1558−1569. (e) Alig, L.; Fritz, M.; Schneider, S. First-Row Transition Metal (De)Hydrogenation Catalysis Based On Functional Pincer Ligands. *Chem. Rev.* **2019**, *119*, 2681−2751. (f) Irrgang, T.; Kempe, R. 3d-Metal Catalyzed N- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer. *Chem. Rev.* **2019**, *119*, 2524−2549. (g) Ai, W.; Zhong, R.; Liu, X.; Liu, Q. Hydride Transfer Reactions Catalyzed by Cobalt Complexes. *Chem. Rev.* **2019**, *119*, 2876−2953. (h) Junge, K.; Papa, V.; Beller, M. Cobalt−Pincer Complexes in Catalysis. *Chem. - Eur. J.* **2019**, *25*, 122−143.

(4) For selected examples, see: (a) Zhang, G.; Hanson, S. K. Cobalt-Catalyzed Acceptorless Alcohol Dehydrogenation: Synthesis of Imines from Alcohols and Amines. *Org. Lett.* **2013**, *15*, 650−653. (b) Bala, M.; Verma, P. K.; Kumar, N.; Sharma, U.; Singh, B. Highly efficient iron phthalocyanine catalyzed oxidative synthesis of imines from alcohols and amines. *Can. J. Chem.* **2013**, *91*, 732−737. (c) Yan, T.; Feringa, B. L.; Barta, K. Iron catalysed direct alkylation of amines with alcohols. *Nat. Commun.* **2014**, *5*, 5602. (d) Saha, B.; Wahidur Rahaman, S. M.; Daw, P.; Sengupta, G.; Bera, J. K. Metal−Ligand Cooperation on a Diruthenium Platform: Selective Imine Formation through Acceptorless Dehydrogenative Coupling of Alcohols with Amines. *Chem. - Eur. J.* **2014**, *20*, 6542−6551. (e) Rösler, S.; Ertl, M.; Irrgang, T.; Kempe, R. Cobalt-Catalyzed Alkylation of Aromatic Amines by Alcohols. *Angew. Chem., Int. Ed.* **2015**, *54*, 15046−15050. (f) Mukherjee, A.; Nerush, A.; Leitus, G.; Shimon, L. J. W.; Ben-David, Y.; Espinosa Jalapa, N. A.; Milstein, D. Manganese-Catalyzed Environmentally Benign Dehydrogenative Coupling of Alcohols and Amines to Form Aldimines and H2: A Catalytic and Mechanistic Study. *J. Am. Chem. Soc.* **2016**, *138*, 4298−4301. (g) Elangovan, S.; Neumann, J.; Sortais, J.-B.; Junge, K.; Darcel, C.; Beller, M. Efficient and selective N-alkylation of amines with alcohols catalysed by manganese pincer complexes. *Nat. Commun.* **2016**, *7*, 12641. (h) Mastalir, M.; Glatz, M.; Gorgas, N.; Stöger, B.; Pittenauer, E.; Allmaier, G.; Veiros, L. F.; Kirchner, K. Divergent Coupling of Alcohols and Amines Catalyzed by Isoelectronic Hydride Mn^{I} and Fe^{II} PNP Pincer Complexes. *Chem. - Eur. J.* **2016**, *22*, 12316−12320. (i) Zhang, G.; Yin, Z.; Zheng, S. Cobalt-Catalyzed N-Alkylation of Amines with Alcohols. *Org. Lett.* **2016**, *18*, 300−303. (j) Mastalir, M.; Tomsu, G.; Pittenauer, E.; Allmaier, G.; Kirchner, K. Co(II) PCP Pincer Complexes as Catalysts for the Alkylation of Aromatic Amines with Primary Alcohols. *Org. Lett.* **2016**, *18*, 3462−3465. (k) Yan, T.; Feringa, B. L.; Barta, K. Benzylamines via Iron-Catalyzed Direct Amination of Benzyl Alcohols. *ACS Catal.* **2016**, *6*, 381−388. (l) Mastalir, M.; Stöger, B.; Pittenauer, E.; Puchberger, M.; Allmaier, G.; Kirchner, K. Air Stable Iron(II) PNP Pincer Complexes as Efficient Catalysts for the Selective Alkylation of Amines with Alcohols. *Adv. Synth. Catal.* **2016**, *358*, 3824−3831. (m) Deibl, N.; Kempe, R. Manganese-Catalyzed Multicomponent Synthesis of Pyrimidines from Alcohols and Amidines. *Angew. Chem., Int. Ed.* **2017**, *56*, 1663−1666. (n) Neumann, J.; Elangovan, S.; Spannenberg,

A.; Junge, K.; Beller, M. Improved and General Manganese-Catalyzed N-Methylation of Aromatic Amines Using Methanol. *Chem. - Eur. J.* **2017**, *23*, 5410−5413. (o) Bruneau-Voisine, A.; Wang, D.; Dorcet, V.; Roisnel, T.; Darcel, C.; Sortais, J.-B. Mono-N-methylation of anilines with methanol catalyzed by a manganese pincer-complex. *J. Catal.* **2017**, *347*, 57−62. (p) Midya, S.; Mondal, A.; Begum, A.; Balaraman, E. A. A Simple Cobalt(II) Chloride Catalyzed N-Alkylation of Amines with Alcohols. *Synthesis* **2017**, *49*, 3957−3961. (q) Liu, Z.; Yang, Z.; Yu, X.; Zhang, H.; Yu, B.; Zhao, Y.; Liu, Z. Efficient Cobalt-Catalyzed Methylation of Amines Using Methanol. *Adv. Synth. Catal.* **2017**, *359*, 4278−4283. (r) Brown, T. J.; Cumbes, M.; Diorazio, L. J.; Clarkson, G. J.; Wills, M. Use of (Cyclopentadienone)iron Tricarbonyl Complexes for C−N Bond Formation Reactions between Amines and Alcohols. *J. Org. Chem.* **2017**, *82*, 10489−10503. (s) Fertig, R.; Irrgang, T.; Freitag, F.; Zander, J.; Kempe, R. Manganese-Catalyzed and Base-Switchable Synthesis of Amines or Imines via Borrowing Hydrogen or Dehydrogenative Condensation. *ACS Catal.* **2018**, *8*, 8525−8530. (t) Midya, S. P.; Pitchaimani, J.; Landge, V. G.; Madhu, V.; Balaraman, E. Direct access to N-alkylated amines and imines via acceptorless dehydrogenative coupling catalyzed by a cobalt(ii)-NNN pincer complex. *Catal. Sci. Technol.* **2018**, *8*, 3469−3473. (u) Samuelsen, S.; Santilli, C.; Ahlquist, M. S. G.; Madsen, R. Development and mechanistic investigation of the manganese(iii) salen-catalyzed dehydrogenation of alcohols. *Chem. Sci.* **2019**, *10*, 1150−1157. (v) Das, K.; Mondal, A.; Pal, D.; Srivastava, H. K.; Srimani, D. Phosphine-Free Well-Defined Mn(I) Complex-Catalyzed Synthesis of Amine, Imine, and 2,3-Dihydro-1*H*-perimidine via Hydrogen Autotransfer or Acceptorless Dehydrogenative Coupling of Amine and Alcohol. *Organometallics* **2019**, *38*, 1815−1825.

(5) Satyanarayana, P.; Maheswaran, H.; Reddy, G. M.; Kantam, M. L. Tris(acetylacetonato)rhodium(III)-Catalyzed α-Alkylation of Ketones, β-Alkylation of Secondary Alcohols and Alkylation of Amines with Primary Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 1859−1867.

(6) For selected examples, see: (a) Fujita, K.-i.; Asai, C.; Yamaguchi, T.; Hanasaka, F.; Yamaguchi, R. Direct β-Alkylation of Secondary Alcohols with Primary Alcohols Catalyzed by a Cp*Ir Complex. *Org. Lett.* **2005**, *7*, 4017−4019. (b) Ruiz-Botella, S.; Peris, E. Unveiling the Importance of π-Stacking in Borrowing-Hydrogen Processes Catalysed by Iridium Complexes with Pyrene Tags. *Chem. - Eur. J.* **2015**, *21*, 15263−15271. (c) Jiménez, M. V.; Fernandez-Tornos, J.; Modrego, F. J.; Perez-Torrente, J. J.; Oro, L. A. Oxidation and β-Alkylation of Alcohols Catalysed by Iridium(I) Complexes with Functionalised N-Heterocyclic Carbene Ligands. *Chem. - Eur. J.* **2015**, *21*, 17877−17889. (d) Wang, R.; Ma, J.; Li, F. Synthesis of a-Alkylated Ketones via Tandem Acceptorless Dehydrogenation/a-Alkylation from Secondary and Primary Alcohols Catalyzed by Metal−Ligand Bifunctional Iridium Complex [Cp*Ir(2,2′-bpyO)(H$_2$O)]. *J. Org. Chem.* **2015**, *80*, 10769−10776. (e) Genç, S.; Günnaz, S.; Çetinkaya, B.; Gülcemal, S.; Gülcemal, D. Iridium(I)-Catalyzed Alkylation Reactions To Form α-Alkylated Ketones. *J. Org. Chem.* **2018**, *83*, 2875−2881. (f) Genç, S.; Arslan, B.; Gülcemal, S.; Günnaz, S.; Çetinkaya, B.; Gülcemal, D. Iridium(I)-Catalyzed C−C and C−N Bond Formation Reactions via the Borrowing Hydrogen Strategy. *J. Org. Chem.* **2019**, *84*, 6286−6297.

(7) For selected examples, see: (a) Gnanamgari, D.; Leung, C. H.; Schley, N. D.; Hilton, S. T.; Crabtree, R. H. Alcohol cross-coupling reactions catalyzed by Ru and Ir terpyridine complexes. *Org. Biomol. Chem.* **2008**, *6*, 4442−4445. (b) Cheung, H. W.; Lee, T. Y.; Lui, H. Y.; Yeung, C. H.; Lau, C. P. Ruthenium-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols. *Adv. Synth. Catal.* **2008**, *350*, 2975−2983. (c) Wang, Q.; Wu, K.; Yu, Z. Ruthenium(III)-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols. *Organometallics* **2016**, *35*, 1251−1256. (d) Roy, B. C.; Chakrabarti, K.; Shee, S.; Paul, S.; Kundu, S. Bifunctional Ru$^{\text{II}}$-Complex-Catalysed Tandem C−C Bond Formation: Efficient and Atom Economical Strategy for the Utilisation of Alcohols as Alkylating Agents. *Chem. - Eur. J.* **2016**, *22*, 18147−18155. (e) Sahoo, A. R.; Lalitha, G.; Murugesh, V.; Bruneau, C.; Sharma, G. V. M.; Suresh, S.; Achard, M. Ruthenium Phosphine−Pyridone Catalyzed Cross-Coupling of Alcohols To form α-Alkylated Ketones. *J. Org. Chem.* **2017**, *82*, 10727−10731. (f) Zhang, C.; Zhao, J.-P.; Hu, B.; Shi, J.; Chen, D. Ruthenium-Catalyzed β-Alkylation of Secondary Alcohols and α-Alkylation of Ketones via Borrowing Hydrogen: Dramatic Influence of the Pendant N-Heterocycle. *Organometallics* **2019**, *38*, 654−664.

(8) (a) Kose, O.; Saito, S. Cross-coupling reaction of alcohols for carbon−carbon bond formation using pincer-type NHC/palladium catalysts. *Org. Biomol. Chem.* **2010**, *8*, 896−900. (b) For a review, see: Muzart, J. Pd-Catalyzed Hydrogen-Transfer Reactions from Alcohols to C = C, C = O, and C = N Bonds. *Eur. J. Org. Chem.* **2015**, *2015*, 5693−5707.

(9) Yang, J.; Liu, X.; Meng, D.-L.; Chen, H.-Y.; Zong, Z.-H.; Feng, T.-T.; Sun, K. Efficient Iron-Catalyzed Direct β-Alkylation of Secondary Alcohols with Primary Alcohols. *Adv. Synth. Catal.* **2012**, *354*, 328−334.

(10) Freitag, F.; Irrgang, T.; Kempe, R. Cobalt-Catalyzed Alkylation of Secondary Alcohols with Primary Alcohols via Borrowing Hydrogen/Hydrogen Autotransfer. *Chem. - Eur. J.* **2017**, *23*, 12110−12113.

(11) (a) Liu, T.; Wang, L.; Wu, K.; Yu, Z. Manganese-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols under Phosphine-Free Conditions. *ACS Catal.* **2018**, *8*, 7201−7207. (b) Chakraborty, S.; Daw, P.; David, Y. B.; Milstein, D. Manganese-Catalyzed α-Alkylation of Ketones, Esters, and Amides Using Alcohols. *ACS Catal.* **2018**, *8*, 10300−10305. (c) Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega* **2019**, *4*, 10741−10754. (d) El-Sepelgy, O.; Matador, E.; Brzozowska, A.; Rueping, M. C-Alkylation of Secondary Alcohols by Primary Alcohols through Manganese-Catalyzed Double Hydrogen Autotransfer. *ChemSusChem* **2019**, *12*, 3099−3102.

(12) Tang, G.; Cheng, C.-H. Synthesis of α-Hydroxy Carboxylic Acids via a Nickel(II)- Catalyzed Hydrogen Transfer Process. *Adv. Synth. Catal.* **2011**, *353*, 1918−1922.

(13) (a) Liao, S.; Yu, K.; Li, Q.; Tian, H.; Zhang, Z.; Yu, X.; Xu, Q. Copper-catalyzed C-alkylation of secondary alcohols and methyl ketones with alcohols employing the aerobic relay race methodology. *Org. Biomol. Chem.* **2012**, *10*, 2973−2978. (b) Tan, D.-W.; Li, H.-X.; Zhu, D.-L.; Li, H.-Y.; Young, D. J.; Yao, J.-L.; Lang, J.-P. Ligand-Controlled Copper(I)-Catalyzed Cross-Coupling of Secondary and Primary Alcohols to α-Alkylated Ketones, Pyridines, and Quinolines. *Org. Lett.* **2018**, *20*, 608−611.

(14) Bullock, R. M. *Catalysis without Precious Metals*; Wiley-VCH: 2010.

(15) Xu, S.; Alhthlol, L. M.; Paudel, K.; Reinheimer, E.; Tyer, D. L.; Taylor, D. K.; Smith, A. M.; Holzmann, J.; Lozano, E.; Ding, K. Tripodal N, P Mixed-Donor Ligands and Their Cobalt Complexes: Efficient Catalysts for Acceptorless Dehydrogenation of Secondary Alcohols. *Inorg. Chem.* **2018**, *57*, 2394−2397.

(16) Paudel, K.; Pandey, B.; Xu, S.; Taylor, D. K.; Tyer, D. L.; Torres, C. L.; Gallagher, S.; Kong, L.; Ding, K. Cobalt-Catalyzed Acceptorless Dehydrogenative Coupling of Primary Alcohols to Esters. *Org. Lett.* **2018**, *20*, 4478−4481.

(17) Paudel, K.; Xu, S.; Hietsoi, O.; Pandey, B.; Onuh, C.; Ding, K. Switchable Imine and Amine Synthesis Catalyzed by a Well-Defined Cobalt Complex. *Organometallics* **2021**, *40*, 418−426.

(18) Pandey, B.; Xu, S.; Ding, K. Selective Ketone Formations via Cobalt-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols. *Org. Lett.* **2019**, *21*, 7420−7423.

(19) For a recent case mediated by a Ni cluster, see: Zhang, M.-J.; Li, H.-X.; Young, D. J.; Lia, H.-Y.; Lang, J.-P. Reaction condition controlled nickel(II)-catalyzed C−C cross-coupling of alcohols. *Org. Biomol. Chem.* **2019**, *17*, 3567−3574.

(20) For selected examples, see: (a) Walling, C.; Bollyky, L. Homogeneous Hydrogenation in the Absence of Transition-Metal Catalysts. *J. Am. Chem. Soc.* **1964**, *86*, 3750−3752. (b) Berkessel, A.; Schubert, T. J. S.; Müller, T. N. Hydrogenation without a Transition-Metal Catalyst: On the Mechanism of the Base-Catalyzed Hydro-

genation of Ketones. *J. Am. Chem. Soc.* **2002**, *124*, 8693−8698. (c) Polshettiwar, V.; Varma, R. S. Revisiting the Meerwein−Ponndorf−Verley reduction: a sustainable protocol for transfer hydrogenation of aldehydes and ketones. *Green Chem.* **2009**, *11*, 1313−1316. (d) Ouali, A.; Majoral, J.-P.; Caminade, A.-M.; Taillefer, M. NaOH-Promoted Hydrogen Transfer: Does NaOH or Traces of Transition Metals Catalyze the Reaction? *ChemCatChem* **2009**, *1*, 504−509. (e) Bauer, H.; Alonso, M.; Färber, C.; Elsen, H.; Pahl, J.; Causero, A.; Ballmann, G.; Proft, F. D.; Harder, S. Imine hydrogenation with simple alkaline earth metal catalysts. *Nat. Catal.* **2018**, *1*, 40−47.

(21) For alcohol synthesis under aerobic conditions, see: (a) Xu, Q.; Chen, J.; Liu, Q. Aldehyde-Catalyzed Transition Metal-Free Dehydrative *β*-Alkylation of Methyl Carbinols with Alcohols. *Adv. Synth. Catal.* **2013**, *355*, 697−704. (b) Allen, L. J.; Crabtree, R. H. Green alcohol couplings without transition metal catalysts: base-mediated *β*-alkylation of alcohols in aerobic conditions. *Green Chem.* **2010**, *12*, 1362−1364.

(22) As 1 equiv of **1a** depletes 2 equiv of KO^{t}Bu in the activation process, 5 mol % of **1a** and 90 mol % of KO^{t}Bu were employed to result in a net KO^{t}Bu amount of 80 mol %.