Rec 9/30/19

⑥

MTSU Clean Energy Initiative Project Funding Request

There are five (5) sections of the request to complete before submitting. See http://www.mtsu.edu/sga/cleanenergy.shtml for funding guidelines. Save completed form and email to cee@mtsu.edu or mail to MTSU Box 57.

1. General Information

Name of Person Submitting Request Dr. Keying Ding	
Department/Office Chemistry/SCI 3024	Phone # (Office) 615-898-2475
MTSU Box # 68	Phone # (Cell) 615-956-5990
E-mail Keying.Ding@mtsu.edu	Submittal Date 09/30/2019

2. Project Categories (Select One)

Select the category that best describes the project.

	Energy Conservation/Efficiency	X	Sustainable Design
	Alternative Fuels	X	Other Research
	Renewable Energy		

3. Project Information

a. Please provide a brief descriptive title for the project.
b. The project cost estimate is the expected cost of the project to be considered by the committee for approval, which may differ from the total project cost in the case of matching funding opportunities. **Any funding request is a 'not-to-exceed' amount. Any proposed expenditure above the requested amount will require a resubmission.**
c. List the source of project cost estimates.
d. Provide a brief explanation in response to question regarding previous funding.

3a. Project Title **Bring Green Chemistry to Campus (VII)**

3b. Project Cost Estimate $2,723

3c. Source of Estimate Chemical Vendor (Sigma Aldrich)

3d. If previous funding from this source was awarded, explain how this request differs?

This research project is in a new direction. The projects previously supported by MTSU Clean Energy Funds all contribute to green chemistry research and education. I appreciate the generous supports. As PI, I successfully secured two major National Science Foundation (NSF) grants in 2015 and 2016, totally $443,174. Another two grant applications (NIH and NSF) are currently pending. Just recently, an NSF-REU grant has been awarded to MTSU and I serve as a senior personal. ($323,940, PI Friedli) The incoming REU students will work on another green chemistry project. In addition, I am happy to report that this year so far one paper has been published on a high-impact journal (Organic Letters). MTSU Clean Energy Funds was officially acknowledged. A PDF copy of the paper is included in the application.

4. Project Description

(Completed in as much detail as possible.)

a. The scope of the work to be accomplished is a detailed description of project activities.
b. The benefit statement describes the advantages of the project as relates to the selected project category.
c. The location of the project includes the name of the building, department, and/or specific location of where the project will be conducted on campus.
d. List any departments you anticipate to be involved. Were any departments consulted in preparation of this request? Who? A listing may be attached to this form when submitted.
e. Provide specific information on anticipated student involvement or benefit.
f. Provide information for anticipated future operating and/or maintenance requirements occurring as a result of the proposed project.
g. Provide any additional comments or information that may be pertinent to approval of the project funding request.

4a. Scope: Work to be accomplished

Homogeneous transition metal-catalyzed carbon-carbon bond forming reactions are among the paramount organic synthetic methods for products of high value. One such prominent synthetic strategy is borrowing hydrogen (BH) which has recently attracted significant interests in both academia and chemical industries. In a typical BH route, a substrate (normally an alcohol) is first dehydrogenated with the catalyst "borrowing" two hydrogen atoms. The dehydrogenated intermediate is then attacked by a nucleophile (e.g., an amine), leading to an unsaturated intermediate. In the final step, the catalyst "returns" the hydrogen atoms to afford the product and the catalyst regenerates. This approach offers great advantages over conventional methods, as a) no hydrogen acceptor or oxidant is required; b) less waste is generated with water and hydrogen as the only possible byproducts; c) high atom efficiency can be achieved; and d) challenging reactants such as alcohols can be directly used. Alcohols are readily available and some alcohols are obtainable from biomass feedstocks.

Nitriles are important compounds that have found ubiquitous applications. For example, nitriles are starting materials for synthesis of carboxylic acids, ketones, amines, and other bioactive molecules (e.g., drugs). Conventional methods to synthesize nitriles employ toxic alkyl halides and stoichiometric strong bases, generating copious waste, which is unsustainable and environmentally-unfriendly. In addition, with the increasing concerns on environmental and economic problems, catalysts based on earth-abundant, inexpensive, and less toxic base transition metals are becoming more appealing, replacing the commonly used rare, toxic, and expensive noble metal analogues.

This designed project will contribute to green and sustainable chemistry. In this research, we will employ our recently developed strategies to selectively synthesize nitriles by a novel cobalt-based catalyst. Preliminary results already show great promise of success of this project. In this proposed work, we will focus on optimizing reaction conditions, examining the substrate scope, and exploring the mechanism, which will serve as important preliminary data for a major external grant application. We will use the funds to purchase the necessary chemicals in this project. Students will be trained with advanced organic and inorganic synthetic skills, physical analytical methods and responsible conduct of research. This project will also be integrated with educational/outreach activities in order to disseminate the concepts of green and sustainable chemistry.

4b. Scope: Benefit Statement

Since 2013, I have initiated and established a unique "**Bring Green Chemistry on Campus**" program aiming to disseminate green and sustainable science and technology and educate the next generation of researchers within the MTSU community, throughout collaborative research, teaching and outreach. Previous and current activities have included: (1) Several research projects in green catalysis supported by MTSU Clean Energy Fee Program, which involve undergraduate and graduate participants. The students will have the opportunity of being trained and performing research and becoming skilled scientists in the future; (2) Green chemistry invitational seminars by three well-known US scientists, which are supported by MTSU Distinguished Lecture Fund and Golden Goggle Lectureship. Through these seminars, students have the opportunity to learn what's going on in these cutting-edge research areas and broaden their views. **This year, a renowned green chemistry scientist (Dr. Hairong Guan at University of Cincinnati) was invited to MTSU for a seminar and**

talked to our students in the event of Golden Goggle Lectureship. I plan to invite another green chemistry scientist to MTSU in 2020; (3) Green chemistry demos and presentations in National ACS meetings, Southeastern ACS regional meetings, Discovery Center at Murfree Spring, and university and local fairs such as Expanding Your Horizons (EYH) (participants are K-12 school girls), new Science Building events (participants are from local elementary schools) and Earth Day posters (open to the MTSU community), etc. **On the 2020 Earth Day, MTSU Chemistry Society will present a green chemistry related poster to the MTSU community**; (4) Introduction of a "Green Moments" section in General Chemistry courses (I and II). I incorporate civic engagement in teaching by advocacy of green chemistry concepts and principles. In the General Chemistry classes, I address critical sustainability problems such as global warming and ocean acidification, which are closely related to the topics of the lecture. These "Green Moments" use real-world contexts to teach more complicated concepts in General Chemistry; (5) Advocate to replace common plastic wares and cups with renewable and biodegradable PLA based ones at the MTSU Student Union food court. We drafted a letter to the President of MTSU and hope that the University can pay attention. **The MTSU Chemistry Club has won 2015 and 2016 ACS Green Chemistry Student Chapter Award.** The proposed project will greatly contribute to "Bring Green Chemistry to Campus" program that will ultimately benefit our MTSU community.

4. Project Description (continued)

4c. Location of Project (Building, etc.)

Science Building - 3021

4d. Participants and Roles

Dr. Keying Ding (PI), supervise the project

Keshav Paudel (graduate student), conduct the experiments

One undergraduate student, conduct the experiments

4e. Student participation and/or student benefit

Students will not only learn basic concepts of green and sustainable chemistry but also get hands-on research experiences in this field. Through our proposed "Bring Green Chemistry on Campus" program, more MTSU students will get involved and learn green chemistry. Most significantly, students can learn why green chemistry is so important and become interested in related research, which will benefit their future careers in the sustainable energy field.

4f. Future Operating and/or Maintenance Requirements

See 4e and 4b

4g. Additional Comments or Information Pertinent to the Proposed Project

Results from this project will be published on a peer-reviewed journal and serve as preliminary data for a major external funding application in the near future.

5. Project Performance Information

Provide information if applicable.

a. Provide information on estimated annual energy savings stated in units such as kW, kWh, Btu, gallons, etc.
b. Provide information on estimated annual energy cost savings in monetary terms.
c. Provide information on any annual operating or other cost savings in monetary terms. Be specific.
d. Provide information about any matching or supplementary funding opportunities that are available. Identify all sources and explain.

5a. Estimated Annual Energy Savings (Estimated in kW, kWh, Btu, etc.)

N/A

5b. Annual Energy COST Savings ($)

N/A

5c. Annual Operating or Other Cost Savings. Specify. ($)

N/A

5d.Matching or Supplementary Funding (Identify and Explain)

N/A

SIGMA-ALDRICH

Order Preview(This order has not been submitted)

Web Copy

Order Date:2019-09-30
Purchase Order:
Payment Term: Prepaid - 1 day net

Email order confirmations to:

Subtotal:2,684.30 USD
Ice/Special Packaging Charges:38.00 USD
Order Total:2,722.30 USD

Line	Product Number	Description	Qty	Your Reference	Your Price	Net Price
000010	157791-250G	PHOSPHORUS TRICHLORIDE, REAGENTPLUS, 99%	1		57.40	57.40
		1 : Estimated to ship on 11/28/19				
000020	481408-5G	CHLORODICYCLOHEXYLPHOSPHINE, 97%	1		231.00	231.00
		1 In Stock from MILWAUKEE 09/30/19				
000030	D71984-500G	DICHLOROPHENYLPHOSPHINE, 97%	1		130.00	130.00
		1 In Stock from MILWAUKEE 09/30/19				
000040	116025-50G	MANDELONITRILE, TECH.	1		42.40	42.40
		1 In Stock from MILWAUKEE 09/30/19				
000050	D77001-100ML	ADIPONITRILE, 99%	1		19.50	19.50
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		1 In Stock from MILWAUKEE 09/30/19				
000070	D139505-25G	4-(DIMETHYLAMINO)BENZONITRILE, 98%	1		106.00	106.00
		1 In Stock from Alternate Warehouse 10/01/19				
000080	115959-25G	BENZOYL CYANIDE, 98%	1		49.20	49.20
		1 In Stock from MILWAUKEE 09/30/19				
000090	U1605-25G	UNDECYL CYANIDE, 99%	1		68.40	68.40
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000100	89660-250ML	O-TOLUNITRILE, >=97.0%	1		57.40	57.40
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000110	132330-25G	PARA-TOLUNITRILE, 98%	1		25.80	25.80
		1 In Stock from MILWAUKEE 09/30/19				
000120	185590-5ML	PROPIONITRILE, 99%	1		36.30	36.30
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000130	159263-25G	(1-ETHOXYETHYLIDENE)-MALONONITRILE, 98%	1		114.00	114.00
		1 In Stock from MILWAUKEE 09/30/19				
000140	126349-100G	(3,4-DIMETHOXYPHENYL)ACETONITRILE, 98%	1		56.20	56.20
		1 In Stock from MILWAUKEE 09/30/19				
000150	591149-1G	(3,5-DIMETHOXYPHENYL)ACETONITRILE, 97%	1		54.20	54.20
		1 In Stock from MILWAUKEE 09/30/19				
000160	C27808-25G	3-CHLOROBENZYL CYANIDE, 99%	1		57.10	57.10
		1 In Stock from MILWAUKEE 09/30/19				
000170	C28006-100G	4-CHLOROBENZYL CYANIDE, 96%	1		24.80	24.80
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000180	228540-25G	(DIMETHYLAMINO)ACETONITRILE, 97%	1		54.60	54.60

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000200	171719-100G	1,2-DICYANOBENZENE, 98%	1		22.80	22.80
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000220	P23709-5G	1,3-PHENYLENEDIACETONITRILE, 98%	1		30.70	30.70
		1 In Stock from MILWAUKEE 09/30/19				
000230	D76722-25G	1,4-DICYANOBENZENE, 98%	1		27.40	27.40
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000240	P23806-10G	1,4-PHENYLENEDIACETONITRILE, 99%	1		91.80	91.80
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000250	C92804-25G	1-CYANONAPHTHALENE, 98%	1		80.90	80.90
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000260	C103403-10G	1-CYCLOHEXENYLACETONITRILE, 92%, REMAIN&	1		45.00	45.00
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000270	677760-1G	2,4-DIMETHOXY-6-METHYLBENZONITRILE	1		79.70	79.70
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000280	527823-5G	2,4,5-TRIMETHYLBENZONITRILE, 97%	1		83.70	83.70
		1 : Estimated to ship on 10/28/19				
000290	264490-5G	2,4-DIFLUOROPHENYLACETONITRILE, 97%	1		92.50	92.50
		1 In Stock from MILWAUKEE 09/30/19				
000300	154415-10G	2,4-DIMETHOXYBENZONITRILE, 99%	1		57.30	57.30
		1 In Stock from MILWAUKEE 09/30/19				
000310	527696-1G	2,4-DINITROBENZONITRILE, 97%	1		38.90	38.90
		1 In Stock from MILWAUKEE 09/30/19				
000320	594776-5G	2,5-DIMETHOXYBENZONITRILE, 97%	1		86.50	86.50
		1 In Stock from MILWAUKEE 09/30/19				
000330	D57558-25G	2,6-DICHLOROBENZONITRILE, 97%	1		54.10	54.10
		1 In Stock from MILWAUKEE 09/30/19				
000340	264512-5G	2,6-DIFLUOROPHENYLACETONITRILE, 96%	1		104.00	104.00
		1 In Stock from MILWAUKEE 09/30/19				
000350	49157-5G-F	2-(2-CYANETHYL)CYCLOHEXANONE, >=97.0%	1		70.80	70.80
		1 : Estimated to ship on 12/27/19				
000360	232955-5G	2-(TRIFLUOROMETHYL)PHENYLACETONITRILE, &	1		56.10	56.10
		1 In Stock from MILWAUKEE 09/30/19				
000370	A89901-25G	ANTHRANILONITRILE, 98%	1		40.20	40.20
		1 In Stock from MILWAUKEE 09/30/19				
000380	B58008-1G	2-BROMOBENZONITRILE, 99%	1		26.00	26.00
		1 In Stock from MILWAUKEE 09/30/19				
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		1 In Stock from MILWAUKEE 09/30/19				
000400	218146-5G	2-CHLORO-6-FLUOROPHENYLACETONITRILE, 98%	1		26.30	26.30
		1 : Estimated to ship on 12/26/19				
000410	C24795-100G	2-CHLOROBENZONITRILE, 98%	1		35.70	35.70
		1 : Estimated to ship on 10/11/19				
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000440	141038-5G	2-CYANOPHENOL, 99%	1		48.40	48.40
		1 In Stock from MILWAUKEE 09/30/19				

OL Organic Letters
Letter
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pubs.acs.org/OrgLett

Selective Ketone Formations via Cobalt-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols

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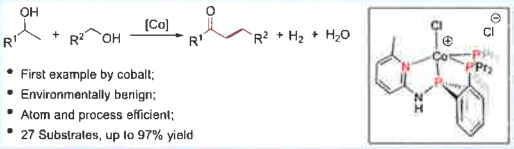
Supporting Information

ABSTRACT: A homogeneous cobalt-catalyzed β-alkylation of secondary alcohols with primary alcohols to selectively synthesize ketones via acceptorless dehydrogenative coupling is reported for the first time. Notably, this transformation is environmentally benign and atom economical with water and hydrogen gas as the only byproducts.



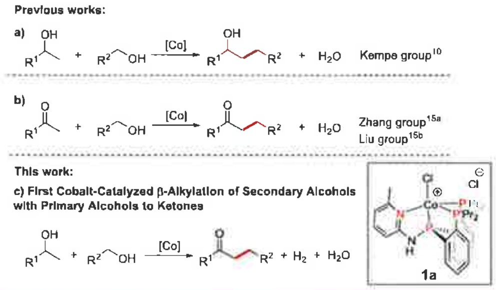
- First example by cobalt;
- Environmentally benign;
- Atom and process efficient;
- 27 Substrates, up to 97% yield

Homogeneous transition-metal-catalyzed carbon−carbon bond formations are among the paramount methods for value-added products.[1] In the conventional β-alkylation of secondary alcohols to synthesize ketones or alcohols, a multistep process is required, e.g., stoichiometric oxidation and alkylation with toxic and mutagenic alkyl halides, generating copious wastes.[2] Thus, it is highly desirable to develop alternative methods that are environmentally friendly and atom and process efficient, using readily available and less toxic substrates, e.g., alcohols. One such prominent synthetic strategy is acceptorless dehydrogenative coupling (ADC).[3,4] In a typical ADC pathway to ketones, primary and secondary alcohols are first dehydrogenated to aldehydes and ketones, respectively, with the catalyst taking the hydrogen atoms. The electrophilic aldehydes are attacked by the enolates formed via removal of the α-C−H of the ketones by a base, leading to the ketone products with loss of water. Finally, hydrogen gas is liberated from the hydrogenated catalyst. Alternatively, the hydrogenated catalyst can reduce the formed ketones, affording the alcohol products. This process is known as borrowing hydrogen (BH).[3,4] Offering great advantages over conventional methods, ADC and BH have recently attracted enormous interests.

Currently, precious metal catalysts based on Rh,[5] Ir,[6] Ru,[7] and Pd[8] dominate the β-alkylation of secondary alcohols with primary alcohols. With increasing concerns on sustainability and environment, less toxic and earth-abundant base metal analogues such as Fe,[9] Co,[10] Mn,[11] Ni,[12] and Cu[13] are becoming more appealing and have witnessed rapid recent developments. However, examples of homogeneous base metal catalyzed such transformations for ketone synthesis are rare.

In the Cu case, high catalyst and base loadings of 10% and 50% were mandatory, respectively.[13b] In the Mn version, unfortunately, very limited substrates were reported with moderate to good yields.[11c] Transition-metal-free examples are also available.[14] To the best of our knowledge, no homogeneous Co catalyst has been reported for β-alkylation of secondary alcohols with primary alcohols for selective ketone synthesis to date. Instead, there is just one example of alcohol formations via the BH process by a PNP−Co catalyst[10] (Scheme 1a). Methods for Co-catalyzed α-alkylation of ketones with primary alcohols to generate ketones are also known[15] (Scheme 1b). As the ketone reactants are normally obtained from stoichiometric oxidation of the secondary alcohols, it is more desirable to directly utilize secondary alcohols for the ketone formations (Scheme 1c). However, as H_2 is one of the byproducts, the formed ketones could be further hydrogenated to alcohols, imposing a challenge in product selectivity.[10] Herein, we report the first systematic study of homogeneous Co-catalyzed β-alkylation of secondary alcohols with primary alcohols to selectively synthesize ketones via ADC. Notably, this reaction is environmentally benign and atom efficient with water and hydrogen gas as the only byproducts.

Scheme 1. Cobalt-Catalyzed Couplings of Secondary Alcohols or Ketones with Primary Alcohols



We have recently developed a new family of base transition-metal complexes supported by a ^{iPr}PPPN^{H}Py^{Me} tetradentate

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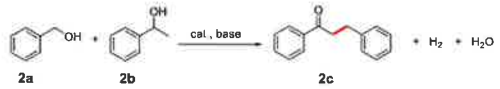
ligand.[16] The Co complex **1a** is an efficient catalyst for dehydrogenation of secondary alcohols to ketones[16] and dehydrogenative coupling of primary alcohols to esters.[17] We speculate that **1a** is a potentially efficient catalyst to mediate the β-alkylation of secondary alcohols with primary alcohols to synthesize ketones.

Initially, benzyl alcohol **2a** and 1-phenylethanol **2b** were chosen as the standard substrates. Different base additives were examined, and KO^{t}Bu turned out to be more suitable. Other reaction parameters were also optimized. Gratifyingly, the optimal results with 90% yield of 3-phenylpropiophenone **2c** were obtained using 2.5 mol % of **1a** and 7.5 mol % of KO^{t}Bu in toluene at 125 °C for 24 h under argon flow (Table 1, entry 2). It is noteworthy that the selectivity is excellent with a **2c**/1,3-diphenylpropanol **2d** ratio of 100:0, despite the fact that **2d** is known as the major side product of such transformation in the literature.[7e,12b,13b] Interestingly, when 5 mol % of KO^{t}Bu was utilized, which was exactly the amount of base used for activation of 2.5 mol % of **1a**, no **2c** product was observed, indicating the crucial role of base besides precatalyst activation (Table 1, entry 4). Further, control experiments showed both **1a** and base were essential for this reaction (Table 1, entries 5 and 6). Mercury tests demonstrated a homogeneous catalytic process. H_2 was confirmed by GC from the gas phase, suggesting an ADC pathway (see the SI).

Table 1. Optimization of Reaction Conditions[a]

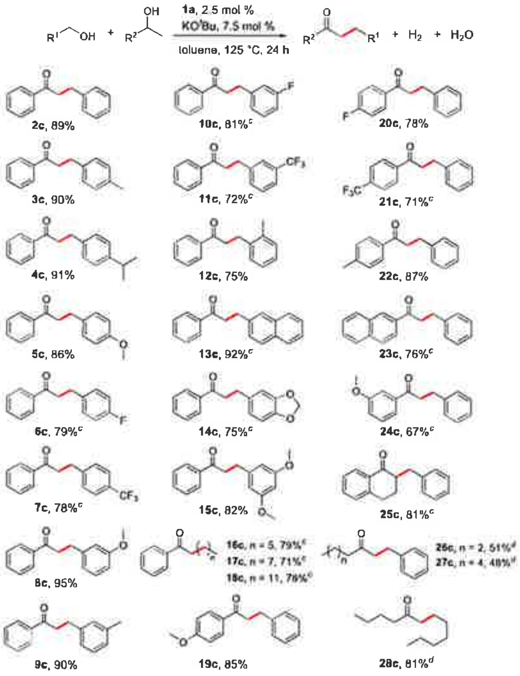


entry	cat.	base	solvent	temp (°C)	yield[b] (%)
1	**1a**	KO^{t}Bu	toluene	105	31
2	**1a**	KO^{t}Bu	toluene	125	90 (86)[c]
3	**1a**	KO^{t}Bu	toluene	140	84
4[d]	**1a**	KO^{t}Bu	toluene	125	0
5		KO^{t}Bu	toluene	125	<1
6	**1a**		toluene	125	0
7	**1a**	KO^{t}Bu	1,4-dioxane	125	0
8	**1a**	NaO^{t}Bu	toluene	125	78
9	**1a**	KHMDS	toluene	125	59
10	**1a**	KOH	toluene	125	<1
11	**1a**	K_2CO_3	toluene	125	0

[a] General conditions: catalyst (2.5 mol %), base (7.5 mol %), **2a** (0.25 mmol), **2b** (0.3 mmol), and solvent (1.5 mL) for 24 h under an argon flow atmosphere. [b] Yields were determined by ^1H NMR with 1,3,5-trimethoxybenzene as an internal standard. [c] 1 mmol scale, isolated yield. [d] KO^{t}Bu (5 mol %) was used.

Having established the optimized reactions, we next explored the substrate scope and efficiency of the reaction. We first investigated the scope of primary alcohols. Aromatic primary alcohols with electron-donating groups like −Me, −iPr, and −OMe at the *para* position furnished the corresponding ketones in excellent 90−93% yields (Table 2, **3c**−**5c**). Primary alcohols with electron-withdrawing groups at the *para* position also reacted smoothly (Table 2, **6c**, **7c**). Notably, *meta*-substituted substrates were transformed to the corresponding ketones as well (Table 2, **8c**−**11c**). Sterically hindered 2-methyl benzyl alcohol **12a** also proceeded in a good yield (Table 2, **12c**). Aliphatic primary alcohols afforded the desired ketones in 73−80% yields (Table 2, **16c**−**18c**).

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



[a] General conditions: **1a** (2.5 mol %), KO^{t}Bu (7.5 mol %), **2a** (0.25 mmol), **2b** (0.3 mmol), and toluene (1.5 mL) for 24 h under an argon flow atmosphere. [b] Isolated yield. [c] **1a** (5 mol %) and KO^{t}Bu (15 mol %) were used. [d] **1a** (5 mol %) and KO^{t}Bu (60 mol %) were used.

Next, we investigated the scope of secondary alcohols. *Para*-substituted aromatic secondary alcohols reacted with **2a** delivering the corresponding ketones in good to excellent yields (Table 2, **19c**−**22c**). *Meta*-substituted 1-(3-methoxyphenyl)ethanol **24b** showed a diminished activity (Table 2, **24c**). Aliphatic secondary alcohols were also amenable to this method, albeit under harsher conditions (Table 2, **26c**, **27c**). It is noteworthy that the reaction of *n*-hexanol **28a** and 2-hexanol **28b** proceeded smoothly, giving an 80% yield (Table 2, **28c**). To the best of our knowledge, β-alkylation of aliphatic secondary alcohols with primary alcohols to ketones mediated by homogeneous base transition-metal catalyst has not been disclosed before. Unfortunately, heterocyclic substrates were not tolerated. Couplings of different secondary alcohols, e.g., **2b** and cyclohexanol **29b**, were incompatible with this method.

We then sought a mechanistic understanding of this reaction. First, two derivatives of **1a** (**1b** and **1c**, Figure 1) were investigated. Compound **1b** bearing a dearomatized pyridine arm shows comparable activity to **1a** in an 81% yield, indicating **1b** is also a precatalyst. To test if metal ligand cooperativity (MLC) from the N−H linker plays a role, a ^{iPr}PPPN^{Me}Py^{Me} complex **1c** was tested as the precatalyst. A 66% yield of **2c** and 22% yield of **2d**, a further hydrogenated product from **2c**, were recorded, suggesting MLC may not have a crucial effect.

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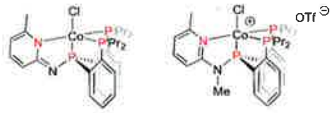
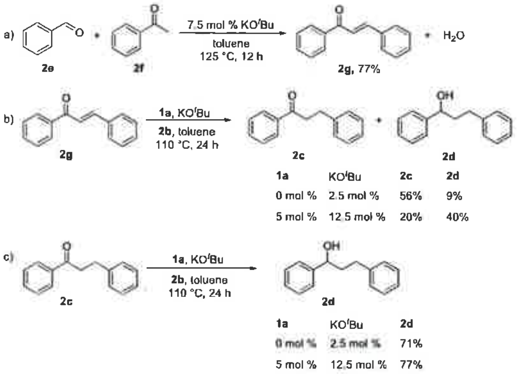


1b **1c**

Figure 1. Derivatives **1b** and **1c** of compound **1a** examined.

Our prior work showed that **1a** was capable of mediating dehydrogenation of primary and secondary alcohols to esters (via aldehydes)[17] and ketones,[16] respectively. In the current study, when benzaldehyde **2e** reacted with acetophenone **2f** in the presence of 7.5 mol % of KO^{t}Bu (Scheme 2a), a 77% yield of chalcone **2g** was observed, which suggested that the *α*,*β*-unsaturated ketone is likely one of the intermediates in the alkylation of secondary alcohols with primary alcohols. Interestingly, in a transfer hydrogenation experiment employing **2b** as the hydrogen source in a sealed reaction vessel, **2g** can be hydrogenated to **2c** (56% yield) and **2d** (9% yield) by 2.5 mol % of KO^{t}Bu alone (Scheme 2b). This suggests a base-mediated Meerwein–Ponndorf–Verley (MPV) type reduction pathway.[14,18] Alternatively, with 5 mol % of **1a** and 12.5 mol % of KO^{t}Bu,[19] a 20% yield of **2c** and a 40% yield of **2d** were observed, suggesting that **1a** may favor alcohol formations under these conditions. To further testify this proposal, we explored the transfer hydrogenation of **2c** with **2b** in a seal reaction vessel (Scheme 2c). Using 2.5 mol % of KO^{t}Bu alone, a 71% yield of **2d** was obtained, advocating an operational MPV reduction. Notably, in the presence of 12.5 mol % of KO^{t}Bu and 5 mol % of **1a**,[19] a slight increase in **2d** yield (77%) was observed. In addition, when the standard reaction (Table 1, entry 2) was carried out in a sealed reaction vessel, only a 34% yield of **2c** resulted together with a 26% yield of **2d**, suggesting the essential role of utilizing open systems for the selective ketone synthesis, in which extrusion of hydrogen gas could efficiently suppress the formation of the alcohol side-products.

Scheme 2. Control Experiments



1a	KO^{t}Bu	2c	2d
0 mol %	2.5 mol %	56%	9%
5 mol %	12.5 mol %	20%	40%

1a	KO^{t}Bu	2d
0 mol %	2.5 mol %	71%
5 mol %	12.5 mol %	77%

In summary, we reported the first homogeneous cobalt-catalyzed *β*-alkylation of secondary alcohols with primary alcohols to form ketones. Remarkably, this is an environmentally benign and atom-efficient process, which contributes to sustainable synthesis by base transition-metal catalysts.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b02727.

Experimental details, additional figures, and other results (PDF)

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Notes

The authors declare no competing financial interest.

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