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COMMUNICATION

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The Employment of Sodium Hydride as a Michael Donor in Palladium-catalyzed Reductions of α, β-Unsaturated Carbonyl Compounds

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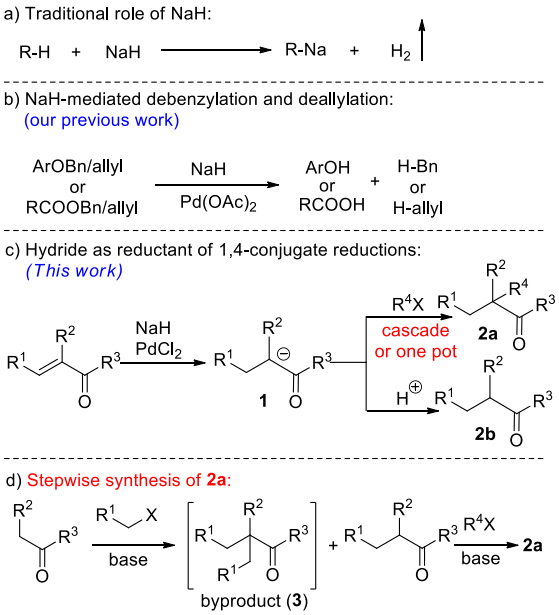
Abstract. Sodium Hydride was employed as a Michael donor under the catalysis of $PdCl_2$ for 1,4-conjugate reductions of α, β-unsaturated carbonyl compounds, which features operational simplicity, mild conditions and high atom-economy. The merits of NaH as a reductant were demonstrated by the one-pot or cascade reactions for the syntheses of complex molecules.

Keywords: sodium hydride; palladium catalysis; Michael donor; 1,4-conjugate reduction; α, β-unsaturated carbonyl compounds

As one of the most significant organic transformations, 1,4-conjugate additions provide convenient and powerful tools for the construction of C-C and C-X (X=O, N, P, S, Si, B) bonds, represented by numerous coupling reactions that use various nucleophiles as donors and electron-deficient alkenes as acceptors.[1] Among these reactions, 1,4-conjugate reductions of α, β-unsaturated carbonyl compounds have distinguished themselves as important synthetic protocols for construction of the corresponding saturated products.[2-6] Apart from the general approaches of the reduction of double-bonds through transition-metal catalysed hydrogenation using H_2 or other hydrogen sources,[2] a number of hydride reagents such as $NaBH_4$,[3] $[(Ph_3P)CuH]_6$ (Stryker's reagent),[4] R_xSiH_{4-x}[5] and Hantzsch ester (1,4-dihydropyridine ester)[6] also work well for this purpose. However, these well-established methods frequently suffer from either the use of hazardous hydrogen gas or the lack of atom economy for the hydride reagents. In this context, it's highly desirable to develop a more convenient, safer and atom-economic method for these transformations.



Scheme 1. NaH was used as a base or reductant.

Compared with the other widely utilized strong bases, structurally simple sodium hydride (NaH) seems to be special because of the release of hydrogen gas *via* deprotonation of substrates (Scheme 1a). It should be noted that this process is accompanied by energy loss along with some

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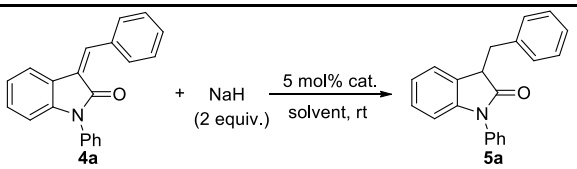
potential dangers in experiments. In contrast, the employment of NaH as a reducing reagent by incorporating hydride into the products could significantly improve its versatility and atom economy. Although NaH was documented as a reductant a long time ago,[7] it was not until recently this underdeveloped chemistry received considerable interest again from synthetic communities.[8-11] For example, Chiba et al. discovered that NaH-iodide composites could be endowed with unprecedented hydride donor reactivity for several transformations, such as hydrodecyanation, the reduction of amides to aldehydes, the dearylation of arylphosphine oxides, hydrodehalogenation, amide-directed C-H sodiation and nucleophilic amination of methoxy arenes.[9] Studer group reported a similar radical hydrodehalogenation using NaH as a reagent.[10] Very recently, we demonstrated that NaH could be switched to a nucleophilic reductant with the addition of $Pd(OAc)_2$ as a promoter, the reactivity of which was engineered into a reductive debenzylation and deallylation of aryl ethers and esters (Scheme 1b).[11] In further studies, we found that the reductive system could also be applied to the 1,4-conjugate reductions of α, β-unsaturated carbonyl compounds (Scheme 1c). To the best of our knowledge, this is the first example of using a simple alkali metal hydride as a nucleophile in Michael-type reactions. It is particularly noteworthy that the 1,4-conjugate adduct **1** is a reactive carbanionic intermediate, which allows further reaction with electrophiles to furnish product **2a** in a cascade or one-pot fashion, or directly give **2b** by treatment with acid. In contrast, the traditional step-by-step synthesis of **2a** not only requires at least two equivalents of base but also suffers from potential contamination by the side product **3** (Scheme 1d). Generally, our protocol has the advantages of atom-economy and environmental benignity over the traditional reduction methods[2-6] since the latter usually cannot be involved into the cascade process,[4,12] or need to deal with the waste issues generated from the hydride source used. Herein, we would like to report our new discovery of the reduction of α, β-unsaturated carbonyl compounds by the NaH/[Pd] system and the relevant one-pot or cascade reactions that provide an efficient method for the preparation of useful synthetic building blocks.

Initially, the feasibility of 1,4-conjugate reductions of α, β-unsaturated carbonyl compounds using NaH as a reductant was investigated with 3-benzylidene-1-phenylindolin-2-one **4a** as the model substrate. At the outset, the addition reaction was conducted in the absence of catalyst, and no conversion was observed (Table 1, Entry 1). When $Pd(OAc)_2$ was added as a promoter, the desired product **5a** was rapidly generated in 84% yield (Table 1, Entry 2). Encouraged by this result, a series of other palladium catalysts were then evaluated (Table 1, Entries 3-9), and $PdCl_2$ was identified as the optimal one (Table 1, Entry 3). The other transition metallic catalysts, such as rhodium and ruthenium salts, were also screened as catalysts, which only led to lower yield (Table 1, Entry 10), or even no conversion (Table 1, Entry 11). Next, the optimization of catalyst loading indicated that neither increasing nor decreasing the amount of $PdCl_2$ could improve the yields (Table 1, Entries 12 and 13). Similarly, attempts to optimize the reaction by adjusting the NaH loading failed to achieve superior results (Table 1, Entries 14 and 15). Finally, the reaction media was examined (Table 1, Entries 16-21), and DMA was shown to be the solvent of choice, delivering **5a** in 94% yield (Table 1, Entry 20).

Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst	Solvent	Time	Yield (%)[b]
1	-	DMF	10 h	0
2	$Pd(OAc)_2$	DMF	50 min	84
3	$PdCl_2$	DMF	30 min	88
4	$Pd(TFA)_2$	DMF	25 min	87
5	Pd/C	DMF	10 h	8
6	$[(\eta^3\text{-}C_3H_5)PdCl]_2$	DMF	40 min	75
7	$Pd(MeCN)_2Cl_2$	DMF	30 min	62
8	$Pd_2(dba)_3$	DMF	50 min	76
9	$Pd(PPh_3)_4$	DMF	10 h	7
10	$RhCl_3 \cdot 3H_2O$	DMF	10 h	36
11	$RuCl_3 \cdot nH_2O$	DMF	10 h	NR
12[c]	$PdCl_2$	DMF	50 min	82
13[d]	$PdCl_2$	DMF	40 min	88
14[e]	$PdCl_2$	DMF	40 min	80
15[f]	$PdCl_2$	DMF	30 min	88
16	$PdCl_2$	$CHCl_3$	10 h	NR
17	$PdCl_2$	THF	2 h	59
18	$PdCl_2$	dioxane	4 h	30
19	$PdCl_2$	CH_3CN	8 h	8
20	**$PdCl_2$**	**DMA**	**40 min**	**94**
21	$PdCl_2$	toluene	2 h	42
22[g]	$PdCl_2$	DMA	10 h	0

[a]Reaction conditions unless specified: **4a** (0.2 mmol), NaH (0.4 mmol) and catalyst (0.01 mmol) in solvent (1.5 ml) at room temperature under N_2 atmosphere. [b]Isolated yield. [c]1 mol% $PdCl_2$. [d]10 mol% $PdCl_2$. [e]1.5 equiv of NaH. [f]2.5 equiv of NaH. [g]LiH instead of NaH was used.

With the optimal reaction conditions in hand, the generality of the hydride addition reaction was then investigated with a variety of 2-indolinone-based substrates bearing electronically and sterically diverse substituents subjected to this reduction. To our delight, all the substrates were tolerant of the NaH/$PdCl_2$ system, furnishing the desired products **5** in good to excellent yields (Table 2). Remarkably, the electronic nature of aromatic groups R^1 (Table 2, Entries 1-10) had a trivial impact on the process,

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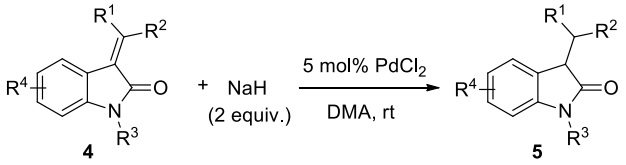
although the phenyl group bearing *m*-CF_3 exhibited a slightly detrimental effect on the conversion (Table 2, Entry 10). In addition, the substrates incorporating hetero-aromatic groups, such as 3-pyridyl, 2-thienyl and 2-furyl as well as 4-quinolyl were also examined, wherein electron-poor heterocycles were found to be favourable to the reaction (Table 2, Entries 14 and 17). Remarkably, the conjugate reductions also proceeded smoothly when R^1 was replaced by aliphatic groups, providing the desired products **5r**-**5t** in moderate to good yields (Table 2, Entries 18-20). At last, the high tolerance of this transformation was further proved by altering the R^1, R^2, R^3 and R^4 groups on the substrates, with all cases providing **5u**-**x** in good yields (Table 2, Entries 21-24).

Table 2. Substrate scope of oxindole-based alkenes.[a]



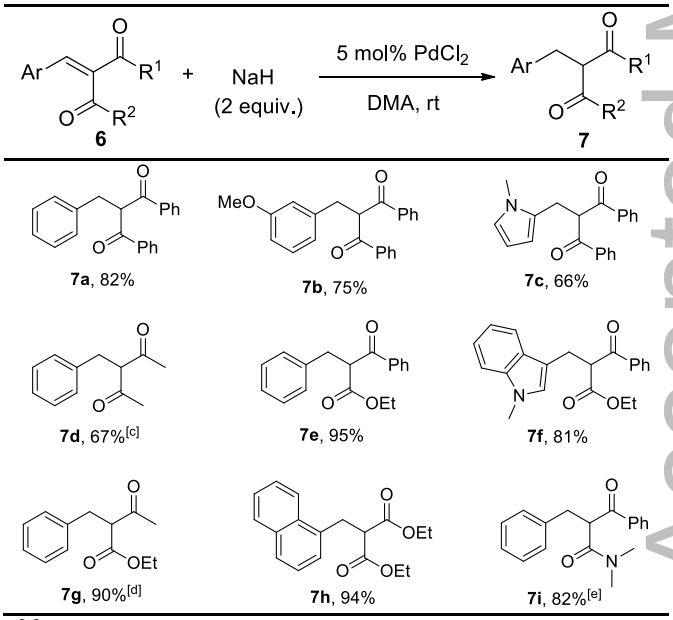
Entry	5	R^1	R^2	R^3	R^4	Yield (%)[b]
1	**5a**	Ph	H	Ph	H	94
2	**5b**	4-MeC_6H_4	H	Ph	H	93
3	**5c**	2-$MeOC_6H_4$	H	Ph	H	90
4	**5d**	3-$MeOC_6H_4$	H	Ph	H	92
5	**5e**	4-$MeOC_6H_4$	H	Ph	H	89
6	**5f**	4-$F_3COC_6H_4$	H	Ph	H	86
7	**5g**	2-FC_6H_4	H	Ph	H	91
8	**5h**	4-FC_6H_4	H	Ph	H	81
9	**5i**	4-$MeO_2CC_6H_4$	H	Ph	H	88
10	**5j**	3-$F_3CC_6H_4$	H	Ph	H	76
11	**5k**	2-Naphthyl	H	Ph	H	90
12	**5l**	1-Naphthyl	H	Ph	H	89
13[c]	**5m**	9-Anthracenyl	H	Ph	H	76
14	**5n**	3-Pyridyl	H	Ph	H	86
15	**5o**	2-Thienyl	H	Ph	H	84
16	**5p**	2-Furyl	H	Ph	H	75
17	**5q**	4-quinolyl	H	Ph	H	98
18	**5r**	Cyclohexyl	H	Ph	H	85
19	**5s**	Isopropyl	H	Ph	H	72
20	**5t**	Phenylpropyl	H	Ph	H	81
21[c]	**5u**	Ph	H	Me	6-CF_3	83
22[c]	**5v**	Ph	H	Me	5-Ph	87
23[c,d]	**5w**	Ph	Me	Ph	H	96[e]
24[f]	**5x**	Me	Me	Ph	H	95

[a]Reaction conditions unless specified: **4** (0.2 mmol), NaH (0.4 mmol) and $PdCl_2$ (0.01 mmol) in DMA (1.5 ml) at room temperature under N_2 atmosphere. [b]Isolated yield. [c]Stirred at 60 °C. [d]15 mol % $PdCl_2$. [e]A mixture of separable diastereomers is formed in a ratio of 58:42. [f]Stirred at 45 °C.

Subsequently, the generality of this method were further investigated (Table 3). A number of 2-benzylidene-substituted propane-1,3-dicarbonyl compounds were subjected to the NaH/$PdCl_2$-mediated conjugate reduction, providing the desired products **7a-i** in good to high yields. As it's known that NaH is a hard metal hydride reagent containing ionic metal-H bonds,[13] which should favour the 1,2-reduction[7g] over 1,4-reduction in the case of α, β-enone. However, in our examples, no 1,2-reduction product was observed when ketone group was present in the substrates, demonstrating the robustness and chemospecificity of our protocol.

Having established the efficient 1,4-conjugate reductions of α, β-unsaturated carbonyl compounds, we next focused our studies on one-pot reactions to further improve the atom-economy of our method. As shown in Scheme 2, the sodium salt **5a-Na** generated *in situ* from **4a** could react with various electrophiles to provide the pharmaceutically interesting 3,3'-disubstituted oxindole derivatives. A number of alkylating reagents, such as (bromomethyl)cyclopropane, MeI and BnBr, were employed to deliver products **8-10** bearing all-carbon quaternary stereocenter in high yields. Similarly, **5a-Na** could also serve as a Michael donor, exampled by the reaction using methyl acrylate to construct oxindole **11** in moderate yield. Additionally, the hydroxyl group was installed readily at the C3-position of the oxindole *via* oxidation with H_2O_2 as an oxidant to furnish the desired product **12** in good yield, which further highlighted the synthetic applicability of our protocol.

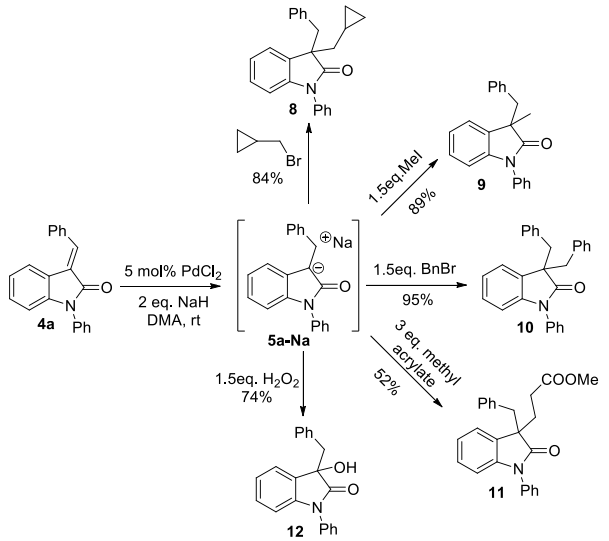
Table 3. 1,4-Conjugate reduction of 2-benzylidene-substituted propane-1,3-dicarbonyl compounds.[a,b]



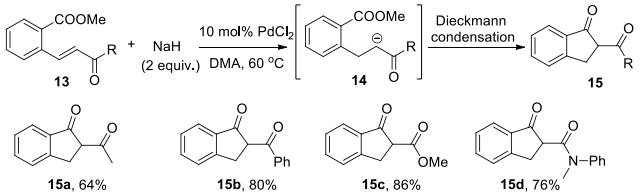
[a]Reaction conditions unless specified: **6** (0.2 mmol), NaH (0.4 mmol) and $PdCl_2$ (0.01 mmol) in DMA (1.5 ml) at room temperature under N_2 atmosphere. [b]Isolated yield. [c]Stirred at 50 °C. [d]50 mol % $PdCl_2$. [e]10 mol % $PdCl_2$.

Cascade reactions have been intensively studied as versatile strategies for the construction of complex molecular architectures due to their high efficiency. Thus, ester group was introduced in the ortho position

of chalcone or cinnamate to capture the *in-situ* generated carbanion of **14** in the pattern of Dieckmann condensation (Scheme 3). To our delight, the desired 1,3-dicarbonyl products **15a** and **15b** were generated efficiently. Similarly, the relatively less reactive α, β-unsaturated esters and amide could also undergo the sequential Michael addition/Dieckmann condensation to afford the desired products **15c** and **15d** in good yields.



Scheme 2. One-pot synthesis of oxindole derivatives.



Scheme 3. The Michael-Dieckmann cascade reaction.

In summary, we discovered that sodium hydride could act as a Michael donor for 1,4-conjugate reduction of various α, β-unsaturated carbonyl compounds under the catalysis of palladium, which could be elegantly combined with alkylation, Michael addition, oxidation or Dieckmann condensation in one-pot or cascade fashion to expediently provide more complex compounds. This protocol features operational simplicity, mild conditions, high atom-economy and chemospecificity as well as wide substrate scope, which offers synthetic chemists an attractive and powerful alternative for hydrogenation of polarized alkenes.

Experimental Section

General procedure for preparation of compound 5

A mixture of $PdCl_2$ (1.8 mg, 0.01 mmol, 5 mol%) and sodium hydride (60% in oil) (16 mg, 0.4 mmol, 2 equiv) in DMA (1.0 mL) was stirred at room temperature under N_2 for 5 min until the mixture turned black. Compound **4** (0.2 mmol) in DMA (0.5 mL) was added through syringe, then the reaction was stirred at rt. After the reaction was completed monitored by TLC, a saturated aqueous NH_4Cl solution was added to quench the reaction. The resulting mixture was extracted with EtOAc, and the combined organic layers were washed with water and brine and dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by column chromatography to give desired prouct **5**.

Acknowledgements

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References

[1] a) K. Zheng, X. Liu, X. Feng, *Chem. Rev.* **2018**, *118*, 7586; b) M. H. Majid, D. Mahzad, Z. Vahideh, *Tetrahedron: Asymmetry* **2016**, *27*, 513; c) P. Mukund, M. Shankar, *Tetrahedron* **2000**, *56*, 8033; d) J. Yang, C Qiu, J. Jiang, Y. Hu, S. Chen, S. Zhang, Y. Zhang, *Adv. Synth. Catal*. **2017**, *359*, 2184; e) Y. Zhu, P. Qian, J. Yang, S. Chen, Y. Hu, P. Wu, W. Wang, W. Zhang, S. Zhang, *Org. Biomol. Chem.* **2015**, *13*, 4769.

[2] a) H. Choi, S. Ham, E. Cha, Y. Shin, H. Kim, J. K. Bang, S. H. Son, H. D. Park, Y. Byun, *J. Med. Chem.* **2017**, *60*, 9821; b) R. A. Ward, C. Brassington, A. L. Breeze, *J. Med. Chem.* **2012**, *55*, 3285; c) G. M. O. Amomboa, T. Kramera, F. L. Montea, S. Göring, M. Fach, S. Smith, S. Kolb, R. Schubenel, K. Baumann, B. Schmidt, *Bioorg. Med. Chem. Lett.* **2012**, *22*, 7634; d) H. Chen, J. P. Luzy, C. Garbay, *Tetrahedron Lett.* **2005**, *46*, 3319; e) T. Liu, Y. Zeng, H. Zhang, T. Wei, X. Wu, N. Li, *Tetrahedron Lett*. **2016**, *57*, 4845; (f) O. Verho, A. Nagendiran, E. V. Johnston, C. Tai, J. Bckvall, *ChemCatChem* **2013**, *5*, 612; g) C. Batarseh, Z. Nairoukh, I. Volovych, M. Schwarze, R. Schomäcker, M. Fanuna, J. Blum, *J. Mol. Catal. A Chem.* **2013**, *366*, 210.

[3] a) T. Pillaiyar, M. Köse, K. Sylvester, H. Weighardt, D. Thimm, G. Borges, I. Förster, I. V. Kügelgen, C. E.Müller, *J. Med. Chem.* **2017**, *60*, 3636; b) B. T. Kim, H. S. Kim, W. S. Moon, K. J. Hwang, *Tetrahedron* **2009**, *65*, 4625; c) A. T. Russo, K. L. Amezcua, V. A. Huynh, Z. M. Rousslang, D. B. Cordes, *Tetrahedron Lett*. **2011**, *52*, 6823.

[4] a) C. Deutsch, N. Kraus, *Chem. Rev*. **2008**, *108*, 2916; b) T. M. Koenig, J. F. Daeuble, D. M. Brestensky, J. M. Stryker, *Tetrahedron Lett*. **1990**, *31*, 3237; c) D. C. Sass, V. C. G. Heleno, S. Cavalcante, J. D. S. Barbosa, A. C. F. Soares, M. G. Constantino, *J. Org. Chem*. **2012**, *77*, 9374; d) D. C. Sass, E. C. D. L. Jr, J. D. S. Barbosa, K. T. D. Oliveira, M. G. Constantino, *Tetrahedron Lett.* **2011**, *52*, 5371; e) T. M. Kamenecka, L. E. Overman, S. K. Ly Sakata, *Org. Lett*. **2002**, *4*, 79; f) P. Chiu, C. P. Szeto, Z. Geng, K. F. Cheng, *Org. Lett*. **2001**, *3*, 1901; g) B. H. Lipshutz, W. Chrisman, K. Noson, P. Papa, J. A. Sclafani, R. W. Vivian, J. M. Keith, *Tetrahedron* **2000**, *56*, 2779.

[5] a) X. Bai, L. Xu, L. Zheng, J. Jiang, G. Lai, J. Shang, *Chem. Eur. J.* **2012**, *18*, 8174; b) A. A. Poeylaut-Palena, S. A. Testero, E. G. Mata, *Chem. Commun.* **2011**, *47*, 1565; c) A. Zheng, F. Shan, Z. Li, Z. Li, L. Jiang, *Chem. Pap.* **2013**, *67*, 1271.

[6] a) J. Che, Y. Lam, *Adv. Synth. Catal.* **2010**, *352*, 1752; b) J. Che, Y. Lam, *Synlett* **2010**, *16*, 2415; c) D. B. Ramachary, M. Kishor, *Org. Biomol. Chem.* **2008**, *6*, 4176.

[7] a) R. J. P. Corriu, C. Guerin, *J. Chem. Soc. Chem. Commun.* **1980**, 168; b) L. H. Krull, H. Friedman, *Biochem. Biophys. Res. Commun.* **1967**, *29*, 373; c) Y. J. Lee, W. D. Closson, *Tetrahedron Lett.* **1974**, *15*, 381; d) R. B. Nelson, G. W. Gribble, *J. Org. Chem.* **1974**, *39*, 1425; e) P. Caubere, J. Moreau, *Tetrahedron* **1969**, *25*, 2469; f) M. Natsume, S. Kumadaki, Y. Kanda, K. Kiuchi, *Tetrahedron Lett.* **1973**, *14*, 2335. g) F. W. Swamer, C. R. Hauser, *J. Am. Chem. Soc.* **1946**, *68*, 2647.

[8] D. Hesek, M. Lee, B. C. Noll, J. F. Fisher, S. Mobashery, *J. Org. Chem.* **2009**, *74*, 2567.

[9] a) P. C. Too, G. H. Chan, Y. L. Tnay, H. Hirao, S. Chiba, *Angew. Chem. Int. Ed.* **2016**, *55*, 3719; b) G. H. Chan, D. Y. Ong, S. Chiba, *Org. Synth.* **2018**, *95*, 240; c) G. H. Chan, D. Y. Ong, Z. Yen, S. Chiba, *Helv. Chim. Acta*. **2018**, *101*, e1800049; d) Z. Hong, D. Y. Ong, S. K. Muduli, P. C. Too, G. H. Chan, Y. L. Tnay, S. Chiba, Y. Nishiyama, H. Hirao, H. S. Soo, *Chem. Eur. J.* **2016**, *22*, 7108; e) C. Tejo, J. H. Pang, D. Y. Ong, M. Oi, M. Uchiyama, R. Takita, S. Chiba, *Chem. Commun.* **2018**, *54*, 1782; f) D. Y. Ong, C. Tejo, K. Xu, H. Hirao, S. Chiba, *Angew. Chem. Int. Ed.* **2017**, *56*, 1840; g) Y. Huang, G. H. Chan, S. Chiba, *Angew. Chem. Int. Ed.* **2017**, *56*, 6544; h) A. Kaga, H. Hayashi, H. Hakamata, M. Oi, M. Uchiyama, R. Takita, S. Chiba, *Angew. Chem. Int. Ed*. **2017**, *56*, 11807; i) J. H. Pang, A. Kaga, S. Chiba, *Chem. Commun.* **2018**, *54*, 10324.

[10] T. Hokamp, A. Dewanji, M. Lübbesmeyer, C. Mück-Lichtenfeld, E. Würthwein, A. Studer, *Angew. Chem. Int. Ed.* **2017,** *56*, 13275.

[11] Y. Mao, Y. Liu, Y. Hu, L. Wang, S. Zhang, W. Wang, *ACS catal.* **2018**, *8*, 3016.

[12] $[(Ph_3P)CuH]_6$ (Stryker's reagent) could also promote cascade reactions, but this reagent is expensive and not readily available.

[13] L. Kürti, B. Czakó, *Strategic Applications of Named Reactions in Organic Synthesis, Background and Detailed Mechanisms;* Elsevier Inc.: **2005**; pp 268.

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