DOI: 10.1002/adsc.201000907

Efficient Iron-Catalyzed Direct β-Alkylation of Secondary Alcohols with Primary Alcohols

Jian Yang,[a,b] Xin Liu,[a] Da-Li Meng,[b] Hong-Yan Chen,[a] Zhi-Hui Zong,[a] Ting-Ting Feng,[a] and Kai Sun[a,]*

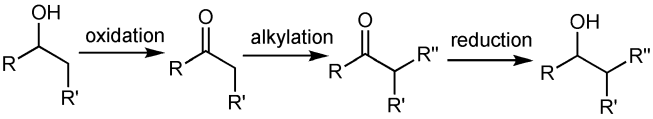
[a] School of Pharmaceutical Sciences, Jilin University, Changchun 130021, People's Republic of China
Fax: (+86)-431-8561-9803; phone: (+86)-431-8561-9152; e-mail: thomassk@jlu.edu.cn
[b] School of Traditional Medicine, Shenyang Pharmaceutical University, Shenyang 110016, People's Republic of China

Received: December 2, 2010; Revised: September 20, 2011; Published online: February 9, 2012

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201000907.

Abstract: The efficient iron-catalyzed direct β-alkylation of secondary alcohols with primary alcohols is described. In the presence of the commercially available iron catalyst (ferrocenecarboxaldehyde, **1b**) and a catalytic amount of base, the reactions give β-alkylated higher alcohols in high yields in the absence of any sacrificial agents (hydrogen acceptors or hydrogen donors) and nitrogen or phosphorus ligands. For the first time, iron is employed as an inexpensive and environmentally benign alternative with high atom efficiency to noble metal-based catalysts in this type of reaction.

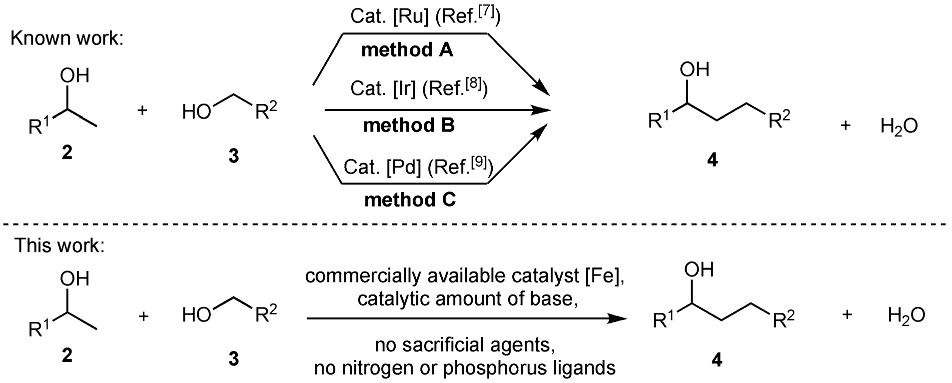
Keywords: alkylation; C–C coupling; iron; primary alcohols; secondary alcohols



Scheme 1. The classic β-alkylation of a secondary alcohol.

C–C bond formation is a pivotal method to construct complex molecules from some simple substrates, with the electrophilic alkylation of a given starting material being one of the most useful procedures.[1] Alcohols are one of the most basic and important organic materials owing to their wide variety of uses in industrial and laboratory chemistry. Although a plethora of synthetic methods of alcohols has been developed,[2] the straightforward routes to the creation of a variety of alcohols having intricate structures through alkylation of simple alcohols remain very unusual. For example, the classic β-alkylation of a secondary alcohol leading to a higher alcohol usually requires tedious processes producing a lot of waste: oxidation, alkylation and reduction (Scheme 1), which cause some disadvantages in the atom economic[3] and environmental[4] points of view. Thus any new strategy for the catalytic direct β-alkylation of secondary alcohols to create higher alcohols would be highly desirable, all the more so if it is an environmentally benign route with high atom efficiency.

On the other hand, the realm of transition metal organic chemistry has provided quite a few excellent reagents to realize the alkylation of a series of nucleophilic agents with alcohols, which has received increasing attention.[5,6] Several groups have reported some examples[7–9] of direct β-alkylation of secondary alcohols with primary alcohols as the environmentally benign electrophilic alkylating agents, which give higher alcohols along with water as a sole by-product (Scheme 2). Among them, Ru complexes are one of important classes of catalysts widely used (method A). The first successful example of such a direct β-alkylation was reported with the $RuCl_2(PPh_3)_3$/KOH system, requiring excess **3** (200.0 mol% referred to **2**), stoichiometric KOH (300.0 mol% referred to **2**), a large amount of sacrificial hydrogen acceptor (500.0 mol% of 1-dodecene referred to **2**) and hydrogen donor (dioxane solvent).[7a] Then complex $[(p\text{-cymene})RuCl_2]_2$ and Grubbs' catalyst $RuCl_2{=}CHPh(PCy_3)_2$ were mentioned to be able to realize the β-alkylation of 1-phenylethanol with benzyl alcohol, however, without any other substrate pair being studied.[7b] Although $RuCl_2(DMSO)_4$ was described as an active catalyst exhibiting high yields for this β-alkylation, the reaction was completed in 7 days with 200.0 mol% of KOH.[7c] Other Ru catalytic systems[7d–h] containing complex nitrogen or phosphor ligands have also been developed, most of which worked in the presence of a stoichiometric base with



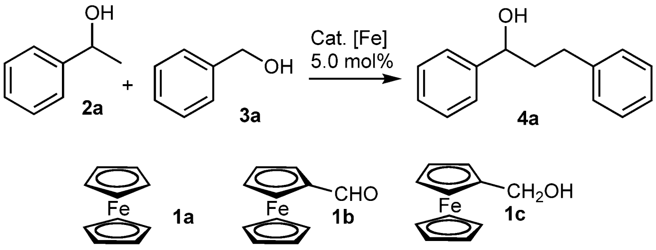
Scheme 2. Various methods of catalytic direct β-alkylation of secondary alcohols with primary alcohols to give higher alcohols.

only one exception[7g] utilizing a slight excess of **3** (120.0 mol% referred to **2**). Another class of important catalysts for this reaction is Ir complexes (method B).[8] However, they are very expensive, and in most of cases the reactions proceeded with stoichiometric base[7h,8a–c] and complex nitrogen ligands.[7f,h,8b,c]. Very recently, the first direct β-alkylation of a secondary alcohol with a primary alcohol catalyzed by a Pd complex with pincer-type N-heterocyclic carbene ligands to give a higher alcohol was published (method C).[9] Although the reaction required excess **2** (200.0 mol% referred to **3**), it could be carried out in the presence of only a catalytic amount of base. Nevertheless, so far all of the reports focus on group 8 noble metals, which are considerably expensive and precious. Therefore, it becomes a great challenge to search for more readily available, more environmentally benign and less expensive catalytic systems with higher atom efficiency for this type of β-alkylation.

As one of the most abundant metals on earth, the numerous merits of iron have made it very attractive for organic synthesis.[10] Considerable studies have been directed to iron catalysts and a variety of iron-catalyzed organic transformations, such as C–H bond oxidation,[11] Friedel–Crafts reactions,[12] cross-coupling reactions,[13] cycloaddition reactions,[14] and so on. Recently, there have also been some efforts[15] to develop C–C bond-forming reactions based on C–H functionalization, in which transition metals have traditionally played important roles.[16] To the best of our knowledge, however, the catalytic direct β-alkylation of secondary alcohols with primary alcohols based on iron to give higher alcohols has not been reported as yet. Herein, we present our preliminary experimental results – the first examples of an efficient, iron-catalyzed, direct β-alkylation of secondary alcohols with primary alcohols producing higher alcohols, which is catalyzed only by the inexpensive and commercially available iron catalyst (ferrocenecarboxaldehyde, **1b**) and a catalytic amount of base without any sacrificial agents (hydrogen acceptors or hydrogen donors) and nitrogen or phosphorus ligands (Scheme 2).

As a starting point, we initiated our research with equimolecular amounts of 1-phenylethanol (**2a**) and benzyl alcohol (**3a**) to give the corresponding higher alcohol (**4a**) under a catalytic amount of NaOH (20.0 mol%) as the reaction model from the atom economical and environmentally benign viewpoints. And the reaction was performed in *p*-xylene at 125 °C, according to the previous reports,[7–9] to screen various commercially available ferric salts (5.0 mol%,

Table 1. Selected optimization of iron catalysts for β-alkylation of 1-phenylethanol with benzyl alcohol.[a]



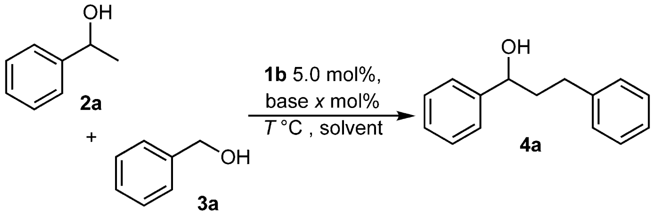
Entry	Catalyst	Yield of **4a** [%][b]
1	none[c]	3
2	$FeCl_3$	36
3	$FeCl_3{\cdot}6H_2O$	10
4	$FeCl_2$	16
5	$FeCl_2{\cdot}4H_2O$	12
6	$FeSO_4{\cdot}7H_2O$	65
7	ferrocene (**1a**)	45
8	**ferrocenecarboxaldehyde** (**1b**)	**78**
9	ferrocenemethanol (**1c**)	13

[a] *Reaction conditions:* **2a** (2.0 mmol), **3a** (2.0 mmol), iron catalyst (5.0 mol%) and NaOH powder (20.0 mol%) in *p*-xylene (2.0 mL) were refluxed at 125 °C under an argon atmosphere for 12 h.

[b] GC yields.

[c] The control experiment without any catalysts.

Table 2. Optimization of the reaction conditions of the reaction model.[a]



Entry	Temp. [°C]	Solvent	Base (x mol%)	Yield of **4a** [%][b]
1	125	*p*-xylene	NaOH (20.0)	78
2	125	toluene	NaOH (20.0)	75
3	125	1,4-dioxane	NaOH (20.0)	31
4	125	solvent free	NaOH (20.0)	65
5	125	*p*-xylene	LiOH (20.0)	0
6	125	*p*-xylene	KOH (20.0)	72
7	125	*p*-xylene	Li_2CO_3 (20.0)	0
8	125	*p*-xylene	Na_2CO_3 (20.0)	0
9	125	*p*-xylene	K_2CO_3 (20.0)	0
10	125	*p*-xylene	NaOH (10.0)	75
11	125	*p*-xylene	NaOH (15.0)	70
12	125	*p*-xylene	NaOH (30.0)	71
13	120	*p*-xylene	NaOH (20.0)	52
14	**130**	***p*-xylene**	**NaOH (20.0)**	**99 (97)**[c]

[a] *Reaction conditions:* **2a** (2.0 mmol), **3a** (2.0 mmol), **1b** (5.0 mol%) and base were refluxed in solvent (2.0 mL) under an argon atmosphere for 12 h.

[b] GC yields.

[c] The value in parenthesis indicated the isolated yield.

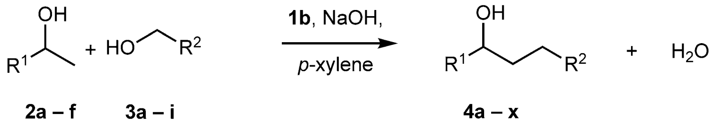
Table 1). The control experiment (entry 1), in which no catalyst was present, gave the desired product **4a** in a very low yield. We first focused on the simple inorganic ferric salts. The preliminary results showed that most of them produced **4a** in considerably low yields (entries 2–5), however, $FeSO_4 \cdot 7H_2O$ gave a moderate yield (entry 6), which indicated that some ferric salts did have considerable potential for this alkylation. This positive result pushed us to extend the catalysts to some inexpensive and commercially available ferrocene salts (**1a**–**1c**, entries 7–9). To our great delight, finally we found that **1b**, usually acting as a reagent or starting material for the synthesis of other ferrocene derivatives,[17] was the most active for this alkylation with 78% yield for the first try (entry 8).

This interesting finding promised a bright prospect and made us start to optimize other different parameters with **1b** as the catalyst (Table 2). As far as solvents were concerned, in the cases of 1, 4-dioxane and toluene, the reactions could also proceed with **1b** to give **4a** (entries 2 and 3), although the yields were lower than in the case of *p*-xylene. And it should be noted that even without any solvent, **4a** could still be formed in a slightly lower yield under the catalysis of **1b** and NaOH (entry 4), which showed us some hints for the later research. In the respect of base, only strong alkaline metal hydroxides could produce the desired product in our case, and NaOH exhibited the best result (entries 1 and 5–9). It was also found that 20.0 mol% of NaOH was the preferred amount (entries 1 and 10–12). Furthermore, we recognized that the temperature had an important effect on the yield and the reaction rate, which was consistent with the results of other groups.[6d,7c,8a] The reaction at 120 °C resulted in a considerably low yield (entry 13). However, when the temperature was raised up to 130 °C, we were very glad to observe the most satisfying result with 99% yield (entry 14).

To investigate the substrate scope, we started to examine the β-alkylation of a variety of secondary alcohols with primary alcohols (Table 3). This catalytic system could be tolerant of various functional groups. Based on the standard conditions, the most of corresponding β-alkylated higher secondary alcohols (except for entry 24) were able to be obtained in good to excellent yields with subtle tuning of the reaction conditions. The minimum loadings of catalyst and base were, respectively, 2.5 mol% (entry 16) and 15.0 mol% (entries 6–9, 22). All reactions were completed in 12–24 h. Alcohol **2a** was β-alkylated with benzyl alcohols bearing an electron-donating or electron-withdrawing substituent to produce the corresponding higher alcohols in high yields (entries 2–6). Even with the heterocyclic alcohol (entry 7), the alkylation of **2a** still proceeded efficiently. And the reactions of **3a** and 1-arylethanols could also be performed smoothly (entries 8, 12, 17 and 18). Together with the reactions of 1-arylethanols and substituted benzyl alcohols (entries 9–11 and 13–16), it was apparent that the position and the electronic nature of the substituent on the aromatic rings of **2** and **3** did not affect product yields. For the reactions of the aliphatic secondary alcohol, a higher temperature seemed to be necessary in our case. With the benzyl alcohol (entry 19), the desired product was obtained at 180 °C in excellent yield. Unfortunately, with the aliphatic primary alcohol (entry 24), this catalytic system could only offer moderate yields, although the temperature was raised up to 190 °C. It should be pointed out that the β-alkylation with aliphatic primary alcohols (entries 20–24) could be run in the absence of solvents, among which the reactions of 1-arylethanols (entries 20–23) gave the desired higher alcohols with satisfying yields, though slightly lower than the cases with benzyl alcohols.

During the parameter optimization of our reaction model, trace or small amounts of **5**–**8** (Scheme 3) were often determined in the reaction mixtures, which showed us some clues on the reaction intermediates. To obtain more information concerning the reaction mechanism, we studied the α-alkylation of ketone **5** with **3a** [Eq. (1)], the β-alkylation of **2a** with

Table 3. β-alkylation of secondary alcohols with primary alcohols catalyzed by **1b**.[a]

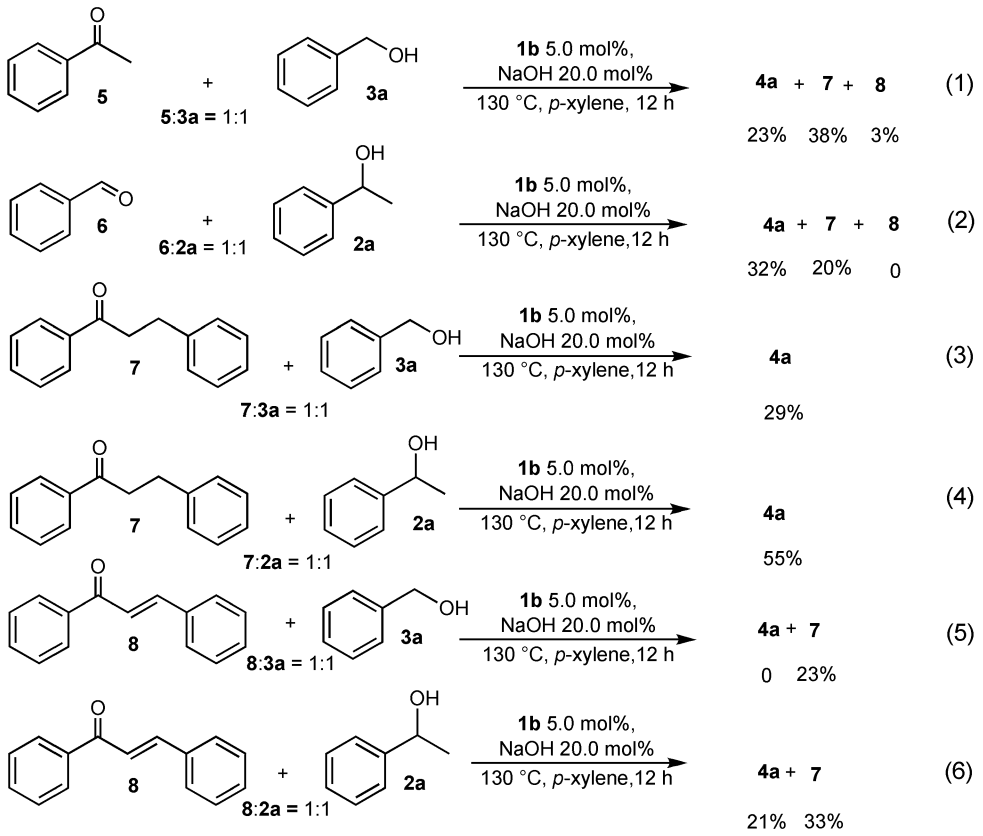


Entry	R^1	R^2	**1b** loading [mol%]	Temp. [°C]	NaOH [mol%]	Time [h]	Product	Yield [%][b]
1	**2a**: R^1=Ph	**3a**: R^2=Ph	5.0	130	20.0	12	**4a**	97
2	**2a**	**3b**: R^2=4-MeC$_6$H$_4$	5.0	130	20.0	24	**4b**	82
3	**2a**	**3c**: R^2=4-ClC$_6$H$_4$	5.0	135	20.0	12	**4c**	77
4	**2a**	**3d**: R^2=4-MeOC$_6$H$_4$	5.0	130	20.0	24	**4d**	81
5	**2a**	**3e**: R^2=3-ClC$_6$H$_4$	5.0	130	30.0	12	**4e**	81
6	**2a**	**3f**: R^2=3,4-(MeO)$_2$C$_6$H$_3$	5.0	130	15.0	12	**4f**	87
7[c]	**2a**	**3g**: R^2=2-furyl	5.0	130	15.0	12	**4g**	81
8	**2b**: R^1=4-MeC$_6$H$_4$	**3a**	5.0	130	15.0	12	**4h**	80
9	**2b**	**3b**	5.0	135	15.0	24	**4i**	83
10	**2b**	**3c**	5.0	130	20.0	24	**4j**	87
11	**2b**	**3d**	5.0	130	20.0	12	**4k**	82
12	**2c**: R^1=4-ClC$_6$H$_4$	**3a**	7.5	130	30.0	12	**4l**	81
13	**2c**	**3b**	5.0	130	20.0	24	**4m**	86
14	**2c**	**3c**	5.0	130	20.0	12	**4n**	80
15	**2c**	**3d**	5.0	130	20.0	12	**4o**	72
16	**2c**	**3e**	2.5	140	20.0	12	**4p**	92
17[d]	**2d**: R^1=2-MeC$_6$H$_4$	**3a**	7.5	130	20.0	12	**4q**	95
18[d]	**2e**: R^1=4-FC$_6$H$_4$	**3a**	7.5	130	37.5	12	**4r**	72
19[e]	**2f**: R^1=phenethyl	**3a**	7.5	180	30.0	12	**4s**	94
20[f]	**2a**	**3h**: R^2=*n*-Pr	7.5	135	30.0	12	**4t**	72
21[g]	**2b**	**3h**	5.0	140	40.0	12	**4u**	75
22[h]	**2c**	**3h**	5.0	140	15.0	12	**4v**	70
23[i]	**2a**	**3i**: R^2=*t*-Bu	7.5	150	30.0	12	**4w**	78
24[i]	**2f**	**3i**	7.5	190	30.0	12	**4x**	54

[a] *Reaction conditions:* **2** (2.0 mmol), **3** (2.0 mmol), NaOH powder (referred to **3**) and **1b** (referred to **3**) were refluxed in *p*-xylene (2.0 mL) under an argon atmosphere, unless other stated.
[b] The isolated yields.
[c] **2** (1.0 mmol) and **3** (1.0 mmol) were used with *p*-xylene (1.0 mL).
[d] With *p*-xylene (0.5 mL).
[e] **2** (1.0 mmol) and **3** (1.0 mmol) were used with *p*-xylene (0.25 mL).
[f] **2** (10.0 mmol) were used without any solvent.
[g] **2** (3.5 mmol) were used without any solvent.
[h] **2** (4.0 mmol) were used without any solvent.
[i] **2** (1.0 mmol), **3** (2.0 mmol), NaOH powder (referred to **2**) and **1b** (referred to **2**) were used without any solvent.

aldehyde **6** [Eq. (2)], and the transfer hydrogenation of ketone **7** [Eqs. (3) and (4)] and α,β-unsaturated ketone **8** [Eqs. (5) and (6)], respectively, with alcohols **2a** and **3a** under the standard conditions. These experiments exhibited that it was possible for **5–8** to produce the desired higher alcohol **4a** with our catalytic system, which indicated the possibility for **5–8** to be the intermediates in this catalytic reaction, although other pathways could not be fully ruled out at this stage.

Based on these results, a simplified plausible mechanism for the **1b**-catalyzed, direct β-alkylation of secondary alcohols with primary alcohols was formulated as described in Scheme 4. At first, the reaction involves the nucleophilic attack of alkoxy anions to the aldehyde group of **1b** under the basic conditions, which results in the hydride abstraction by iron cation of **1b** to generate an iron hydride species with the oxidation of primary and secondary alcohols to the corresponding aldehyde and ketone. And then base-mediated cross-aldol condensation occurs to produce an α,β-unsaturated ketone, which undergoes transfer hydrogenation of C=O and C=C double bonds with that iron hydride species to give the desired product and regenerate the catalyst. The hydride species generated at the stage of the oxidation of alcohols are consumed at the stage of the final reduction, which follows the reported "hydrogen autotransfer process" or "borrowing hydrogen" process.[5] So the sacrificial agents are not required for our catalytic system.



Scheme 3. Results obtained in the study on the intermediates of **1b**-catalyzed β-alkylation of secondary alcohols with primary alcohols.

In summary, we have developed a novel iron-catalyzed, direct, β-alkylation of secondary alcohols with primary alcohols to produce higher alcohols with high atom efficiency. It should be noted that this reaction system only required inexpensive and commercially available **1b** and a catalytic amount of NaOH without any sacrificial agents (hydrogen acceptors or hydrogen donors) and complex nitrogen or phosphorus ligands. It is the first time for iron to be employed as an inexpensive and environmentally benign alternative to noble metal-based catalysts in this β-alkylation of secondary alcohols with primary alcohols giving higher alcohols. Based on the theoretical calculations, the exploration of the details on the mechanistic aspects for this reaction is underway, and other reactions catalyzed by inexpensive metals, especially iron catalysts, to activate alcohols as electrophilic alkylating agents are also currently being pursued in our laboratory. When we were preparing this report, an very interesting alkaline metal base-promoted direct β-alkylation of secondary alcohols with primary alcohols in air, based on Oppenauer oxidation and Meerwein–Ponndorf–Verley reduction, was published.[18] Unfortunately, It was not a catalytic reaction, and stoichiometric base (100.0 mol% of KOH or NaOH) was required.

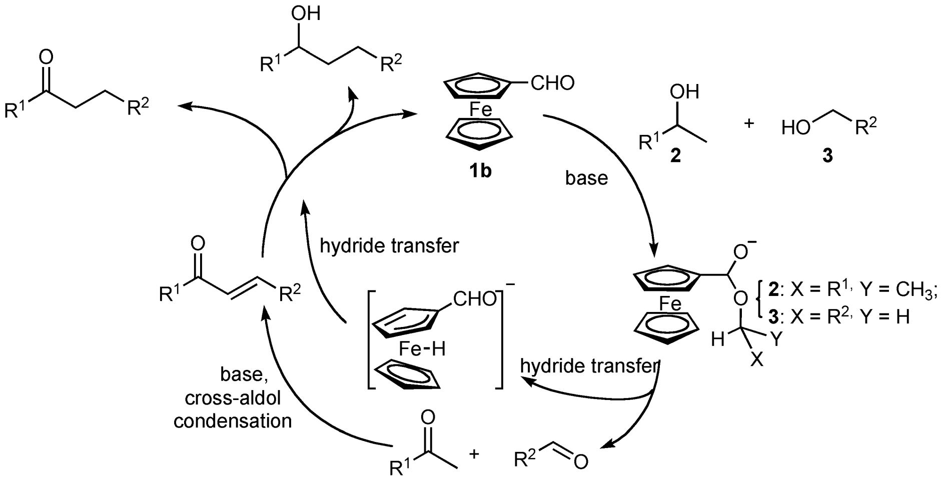
Experimental Section

General Procedure A for the β-Alkylation of Various Secondary Alcohols with Benzyl Alcohols and Heterocyclic Alcohols

β-Alkylation of 2a with 3a as an example: Under an atmosphere of argon in a heavy-walled glass reactor, **2a** (2.0 mmol), **3a** (2.0 mmol), **1b** (5.0 mol%), NaOH powder (20.0 mol%), *p*-xylene (2.0 mL) and a Teflon-coated stirring bar were placed. The reactor was sealed, and the mixture was magnetically stirred at 130 °C for 12 h in a silicon oil bath. It was cooled down to room temperature and directly purified by column chromatography on silica gel (*n*-hexane/ethyl acetate = from 100/1 to 30/1) to give **4a**; yield: 411.6 mg (1.94 mmol, 97%).

General Procedure B for the β-Alkylation of Various Secondary Alcohols with Aliphatic Primary Alcohols

β-Alkylation of 2a with 3h as an example: Under an atmosphere of argon in a heavy-walled glass reactor, **2a** (10.0 mmol), **3h** (2.0 mmol), **1b** (7.5 mol% referred to **3h**), NaOH powder (30.0 mol%, referred to **3h**) and a Teflon-coated stirring bar were placed. The reactor was sealed, and the mixture was magnetically stirred at 135 °C for 12 h in a silicon oil bath. It was cooled down to room temperature and directly purified by column chromatography on silica



Scheme 4. The simplified plausible mechanism for β-alkylation of secondary alcohols with primary alcohols catalyzed by **1b**.

gel (*n*-hexane/ethyl acetate = from 100/1 to 40/1) to give **4t**; yield: 256.8 mg (1.44 mmol, 72% referred to **3h**).

Compounds **4b**–**4s** were synthesized in a similar way to general procedure **A**, and compounds **4u**–**4x** were obtained in a similar way to general procedure **B**. All the compounds were characterized by MS and NMR (^{1}H and ^{13}C). Data are given in the Supporting Information.

Acknowledgements

This work was financially supported by Foundation of Sci-tech Development Project of Jilin Province (Scientific Research Foundation for Youth Scholars, No. 20100135) and Basic Professional Foundation for Scientific Research of Jilin University (No. 200903351). K. Sun greatly thanks Prof. C.-J. Li (Tulane University & McGill University) for his valuable suggestions on the plausible mechanism of this reaction.

References

[1] a) D. Seebach, *Angew. Chem.* **1990**, *102*, 1363–1409; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1320–1367; b) S. L. Schreiber, *Science* **2000**, *287*, 1964–1969.

[2] a) S. G. Wilkinson, in: *Comprehensive Organic Chemistry*, Vol. 1, (Eds.: D. Barton, W. D. Ollis), Pergamon, Oxford, **1979**, pp 579–706; b) O. Mitsunobu, in: *Comprehensive Organic Synthesis*, Vol. 6, (Ed.: E. Winterfeldt), Pergamon, Oxford, **1991**, pp 1–31; c) J. B. Sweeney, in: *Comprehensive Organic Functional Group Transformations*, Vol. 2, (Eds.: A. R. Katritzky, O. Meth-Cohn, C. W. Rees), Pergamon, Oxford, **1995**, pp 37–88.

[3] a) B. M. Trost, *Science* **1991**, *254*, 1471–1477; b) R. A. Sheldon, *Pure Appl. Chem.* **2000**, *72*, 1233–1246; c) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695–705.

[4] a) J. F. Jenck, F. Agterberg, M. J. Droescher, *Green Chem.* **2004**, *6*, 544–556; b) J. O. Metzger, M. Eissen, *C. R. Chim.* **2004**, *7*, 569–581; c) G. Parthasarathy, R. Hart, E. Jamro, L. Miner, *Clean Technol. Environ. Policy* **2005**, *7*, 219–229; d) J. M. Thomas, R. Raja, *Annu. Rev. Mater. Res.* **2005**, *35*, 315–350.

[5] For selected reviews, see: a) G. Guillena, D. J. Ramón, M. Yus, *Angew. Chem.* **2007**, *119*, 2410–2416; *Angew. Chem. Int. Ed.* **2007**, *46*, 2358–2364; b) M. H. S. A. Hamid, P. A. Slatford, J. M. J. Williams, *Adv. Synth. Catal.* **2007**, *349*, 1555–1575.

[6] Selected recent examples: a) M. G. Capdevila, F. Benfatti, L. Zoli, M. Stenta, P. G. Cozzi, *Chem. Eur. J.* **2010**, *16*, 11237–11241; b) A. Martinez-Asencio, D. J. Ramon, M. Yus, *Tetrahedron Lett.* **2010**, *51*, 325–327; c) F. Alonso, P. Riente, M. Yus, *Eur. J. Org. Chem.* **2009**, *2009*, 6034–6042; d) K. Shimizu, R. Sato, A. Satsuma, *Angew. Chem.* **2009**, *121*, 4042–4046; *Angew. Chem. Int. Ed.* **2009**, *48*, 3982–3986.

[7] For Ru catalysts, see: a) C. S. Cho, B. T. Kim, H.-S. Kim, T.-J. Kim, S. C. Shim, *Organometallics* **2003**, *22*, 3608–3610; b) G. R. A. Adair, J. M. J. Williams, *Tetrahedron Lett.* **2005**, *46*, 8233–8235; c) R. Martínez, D. J. Ramón, M. Yus, *Tetrahedron* **2006**, *62*, 8982–8987; d) M. Viciano, M. Sanaú, E. Peris, *Organometallics* **2007**, *26*, 6050–6054; e) A. Prades, M. Viciano, M. Sanaú, E. Peris, *Organometallics* **2008**, *27*, 4254–4259; f) D. Gnanamgari, C. H. Leung, N. D. Schley, S. T. Hilton, R. H. Crabtree, *Org. Biomol. Chem.* **2008**, *6*, 4442–4445; g) H. W. Cheung, T. Y. Lee, H. Y. Lui, C. H. Yeung, C. P. Laua, *Adv. Synth. Catal.* **2008**, *350*, 2975–2983; h) D. Gnanamgari, E. L. O. Sauer, N. D. Schley, C. Butler, C. D. Incarvito, R. H. Crabtree, *Organometallics* **2009**, *28*, 321–325.

[8] For Ir catalysts, see: a) K. Fujita, C. Asai, T. Yamaguchi, F. Hanasaka, R. Yamaguchi, *Org. Lett.* **2005**, *7*, 4017–4019; b) A. P. da Costa, M. Viciano, M. Sanaú, S. Merino, J. Tejeda, E. Peris, B. Royo, *Organometallics* **2008**, *27*, 1305–1309; c) A. P. da Costa, M. Sanaú, E. Peris, B. Royo, *Dalton Trans.* **2009**, 6960–6966; see also refs.[7f,7h]

[9] For Pd catalysts, see: O. Kose, S. Saito, *Org. Biomol. Chem.* **2010**, *8*, 896–900.

[10] a) C. Bolm, J. Legros, J. Le Paih, L. Zani, *Chem. Rev.* **2004**, *104*, 6217–6254; b) A. Fürstner, K. Majima, R. Martin, H. Krause, E. Kattnig, R. Goddard, C. W. Lehmann, *J. Am. Chem. Soc.* **2008**, *130*, 1992–2004; c) *Iron Catalysis in Organic Synthesis*, (Ed.: B. Plietker), Wiley-VCH, Weinheim, **2008**.

[11] a) M. Christmann, *Angew. Chem.* **2008**, *120*, 2780–2783; *Angew. Chem. Int. Ed.* **2008**, *47*, 2740–2742; b) M. S. Chen, M. C. White, *Science* **2007**, *318*, 783–787; c) M. P. Sibi, M. Hasegawa, *J. Am. Chem. Soc.* **2007**, *129*, 4124–4125.

[12] *Lewis Acids in Organic Synthesis*, Vols. 1 and 2, (Ed.: H. Yamamoto), Wiley-VCH, Weinheim, **2000**.

[13] a) M. Mayer, W. M. Czaplik, A. J. V. Wangelin, *Adv. Synth. Catal.* **2010**, *352*, 2147–2152; b) X. Xie, X.-B. Xu, H.-F. Li, X.-L. Xu, J.-Y. Yang, Y.-Z. Li, *Adv. Synth. Catal.* **2009**, *351*, 1263–1267; c) D. Bézier, C. Darcel, *Adv. Synth. Catal.* **2009**, *351*, 1732–1736; d) U. Jana, S. Biswas, S. Maiti, *Tetrahedron Lett.* **2007**, *48*, 4065–4069; e) T. Hatakeyama, M. Nakamura, *J. Am. Chem. Soc.* **2007**, *129*, 9844–9845; f) A. Guérinot, S. Reymond, J. Cossy, *Angew. Chem.* **2007**, *119*, 6641–6644; *Angew. Chem. Int. Ed.* **2007**, *46*, 6521–6524; g) J. Kischel, K. Mertins, D. Michalik, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2007**, *349*, 865–870.

[14] a) G. Hilt, P. Bolze, K. Harms, *Chem. Eur. J.* **2007**, *13*, 4312–4325; b) D. Necas, P. Drabina, M. Sedlak, M. Kotora, *Tetrahedron Lett.* **2007**, *48*, 4539–4541; c) A. Fürstner, R. Martin, K. Majima, *J. Am. Chem. Soc.* **2005**, *127*, 12236–12237.

[15] a) S.-Y. Zhang, Y.-Q. Tu, C.-A. Fan, F.-M. Zhang, L. Shi, *Angew. Chem.* **2009**, *121*, 8917–8921; *Angew. Chem. Int. Ed.* **2009**, *48*, 8761–8765; b) Z. Li, R. Yu, H. Li, *Angew. Chem.* **2008**, *120*, 7607–7610; *Angew. Chem. Int. Ed.* **2008**, *47*, 7497–7500; c) Z. Li, L. Cao, C.-J. Li, *Angew. Chem.* **2007**, *119*, 6625–6627; *Angew. Chem. Int. Ed.* **2007**, *46*, 6505–6507; d) Y. Zhang, C.-J. Li, *Eur. J. Org. Chem.* **2007**, *2007*, 4654–4657.

[16] a) K. Godula, D. Sames, *Science* **2006**, *312*, 67–72; b) *Handbook of C–H Transformations*, (Ed.: D. Dyker), Wiley-VCH, Weinheim, **2005**.

[17] a) B. V. Silva, N. M. Ribeiro, M. D. Vargas, M. Lanznaster, J. W. de M. Carneiro, R. Krogh, A. D. Andricopulo, L. C. Dias, A. C. Pinto, *Dalton Trans.* **2010**, *39*, 7338–7344; b) V. Mamane, *Tetrahedron: Asymmetry* **2010**, *21*, 1019–1029; c) L.-C. Feng, Y.-W. Sun, W.-J. Tang, L.-J. Xu, K.-L. Lam, Z.-Y. Zhou, A. S. C. Chan, *Green Chem.* **2010**, *12*, 949–952; d) G. G. A. Balavoine, J.-C. Daran, G. Iftime, E. Manoury, C. Moreau-Bossuet, *J. Organomet. Chem.* **1998**, *567*, 191–198.

[18] L. J. Allen, R. H. Crabtree, *Green Chem.* **2010**, *12*, 1362–1364.