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Iridium(I)-Catalyzed C–C and C–N Bond Formation Reactions via Borrowing Hydrogen Strategy

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KEYWORDS: *iridium*, *N-heterocyclic carbene*, *alcohols*, *quinolines*, *alkylation*, *borrowing hydrogen*

ABSTRACT

Iridium(I) complexes having an imidazol-2-ylidene ligand with benzylic wingtips efficiently catalyzed the β-alkylation of secondary alcohols with primary alcohols and acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohol with ketones through a borrowing hydrogen pathway. The β-alkylated alcohols, including cholesterol derivatives, and substituted quinolines were obtained in good yields by using a minute amount of catalyst with a catalytic amount of NaOH or KOH under air atmosphere liberating water (and H_2 in the case of quinoline synthesis) as the sole-byproduct. Notably, this system demonstrated TONs of 940000 (for β-alkylation of secondary alcohols with primary alcohols by using down to 0.0001 mol% = 1 ppm of catalyst) and 9200 (acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohol with ketones).

INTRODUCTION

The borrowing hydrogen (BH) or hydrogen autotransfer (HA) methodology has become an important alternative to construct C–C and C–N bonds for the synthesis of more complicated molecules in one-step in the presence of a transition metal (TM) catalyst.[1] The BH approach is a tandem process, where alcohols are dehydrogenated followed by base-mediated condensation of the resulting carbonyls with an amine or carbon nucleophile and subsequently the unsaturated intermediate product is reduced. As a result of increasing interests for environmentally friendly chemical processes, the direct substitution of alcohols through a BH strategy has recently received significant attention and is considered one of the key green chemistry research areas by the pharmaceutical manufacturers.[2] The use of easily handled, renewable and inexpensive alcohols as alkylating agents, offers increased step efficiency and atom economy over the conventional stoichiometric activation and displacement method, and avoids the use of mutagenic alkyl halides and sulfonate esters as alkylating agents, resulting in water as the sole by-product.[1]

β-Alkylation of alcohols, which can be realized by means of BH strategy is one of the most fundamental C–C bond formation reactions for the synthesis of long chain and branched alcohols. Notably, until now, application of ruthenium,[3] rhodium,[4] iridium,[5] palladium[6] and other first row TM catalysts[7] or under TM-free conditions[8] has been known for β-alkylation of alcohols through a BH strategy. Despite significant advancements, these catalytic systems still have many drawbacks, such as in most cases they require expensive or high amount of bases and high catalyst loading so the final turnover numbers (TONs) for these reactions are still low and far from any practical application. There are only a few reports by Kundu *et. al.* on cross-coupling of alcohols to give β-alkylated alcohols in the presence of low catalyst loadings.[3b-e]

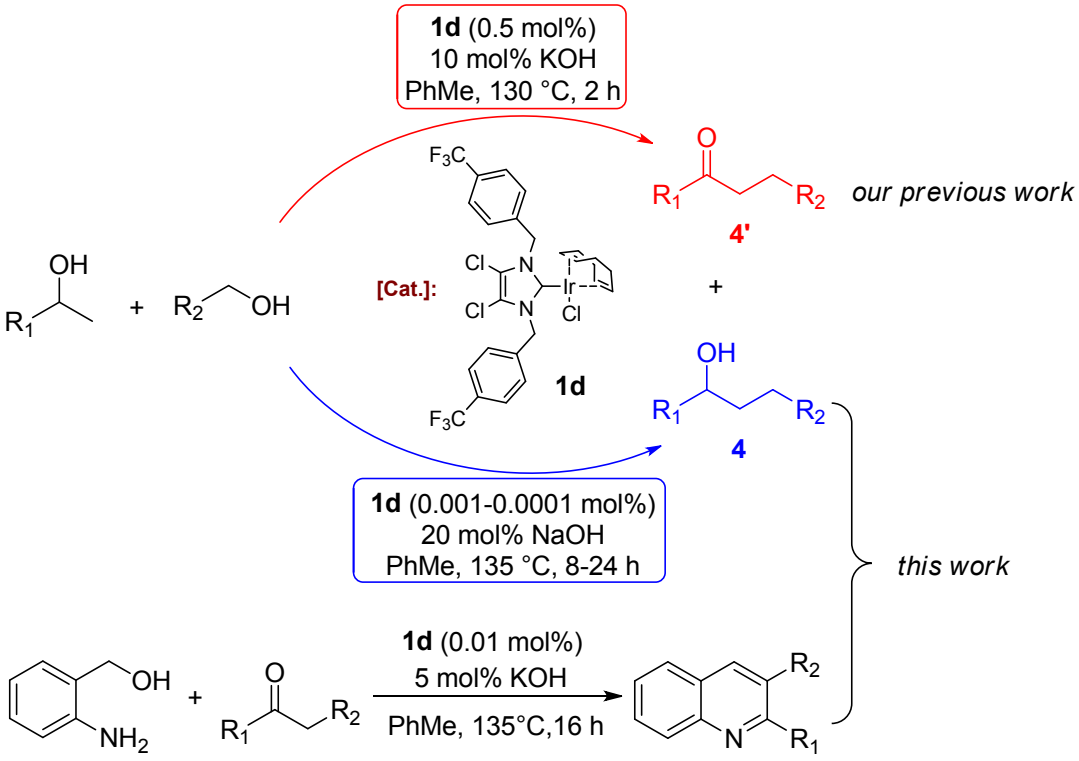
Very recently, they disclosed TONs of 288000 for the coupling of primary and secondary alcohols to give β-alkylated alcohols by using an (NHC)–Ru^{II}–NN complex. [3c] The main limitation of this system is that it requires 40 mol% of expensive $NaO^{i}Pr$ as a base and inert reaction conditions for these high activities. Therefore, the development of more efficient catalytic systems would be highly desirable to construct a new C–C bond by employing alcohols as alkylating agents by using a minute amount of catalyst and a low amount of common base under operationally simple conditions.

Another reaction based on the BH methodology is acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohols with secondary alcohols or ketones to give substituted quinolines.[1c,d,f,i,9] Heterocyclic aromatic organic compounds bearing quinoline scaffolds are very important class in organic synthesis, because quinoline moiety is found in a broad range of pharmacologically active compounds and natural products.[10] Although quinolines can be prepared from 2-aminobenzaldehyde and various ketones by following the classical Friendländer reaction, there are several limitations for its applicability, including the low stability of 2-aminobenzaldehyde, the requirement of harsh reaction conditions, numerous steps, lower stereoselectivity and low total yields.[11] Recently, remarkable effort has been dedicated for the development of the modified Friendländer quinoline synthesis catalyzed by various TM complexes including ruthenium,[12] rhodium,[13] iridium,[14] palladium,[15] manganese,[16] iron,[17] cobalt,[18] nickel,[19] and copper,[20] or TM-free conditions[21]. However, most of these methods require a stoichiometric amount of strong bases, high catalyst loadings, excess of ketones as a coupling partner, or a sacrificial hydrogen acceptor, which might cause environmental problems.

Our group is mainly focused on the application of NHC−Ir^{I} and NHC−Ir^{III} complexes as catalysts for transfer hydrogenation[22] and dehydrogenation[23] reactions. Recently, we have

synthesized a series of [IrCl(COD)(NHC)] (COD = 1,5-cyclooctadiene) complexes (**1**) and reported a remarkably active catalytic system with the highest turnover frequencies (TOFs) reported for the reaction of primary alcohols with secondary alcohols and also with ketones to give *α*–alkylated ketones (**4'**) by using 5-10 mol% KOH under air (Scheme 1).[24] Our mechanistic studies revealed that in the presence of 0.5 mol% **1d** as catalyst the reaction of primary and secondary alcohols results with a mixture of β-alkylated alcohol **4** and *α*–alkylated ketone **4′** then, **4** gradually dehydrogenates to give α-alkylated ketones (**4′**) selectively.[24] The alkylation of secondary alcohols with primary alcohols often results with a mixture of the β-alkylated alcohols (**4**) along with the corresponding α-alkylated ketones (**4′**) and this selectivity issue is crucial for the reaction. Encouraged by our previous findings, we envisioned that we could improve the selectivity of the reaction to the β-alkylated alcohols (**4**) if the final dehydrogenation of **4** to **4′** might be prevented. Herein, we disclose the selective formation of β-alkylated alcohols (**4**) by cross-coupling of secondary alcohols with primary alcohols in the presence of 1-10 ppm NHC–Ir^{I} complex (**1d**) as catalyst and 20 mol% of NaOH under air (Scheme 1) along withup to 940000 TON. Notably, when combined with our previous results, a single catalyst has allowed the selective synthesis of both β-alkylated alcohols (**4**) and α-alkylated ketones (**4′**) with slightly modified reaction conditions (Scheme 1). In addition, this catalytic system has also showed promising catalytic activity (up to 9200 TON) for the reaction of 2-aminobenzyl alcohol with ketones to give substituted quinolines (Scheme 1).

Scheme 1. NHC–Ir^{I} Catalyzed C–C and C–N Coupling Reactions.

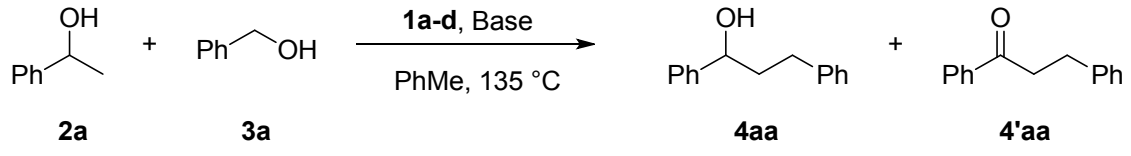


RESULTS and DISCUSSION

Catalytic Studies on NHC–Ir^{I} Catalyzed β-Alkylation of Alcohols. Initially, the reaction of 1-phenylethanol (**2a**) with benzyl alcohol (**3a**) was selected as the benchmark experiment to probe the potential of previously prepared [IrCl(COD)(NHC)] complexes (**1a-d**)[24] as catalyst in β-alkylation of equimolar amount of secondary alcohols with primary alcohols. The progress of the reaction was monitored by ^{1}H NMR spectroscopy and the yields are based on 1,3,5-trimethoxybenzene as internal standard (Table 1). The reaction was performed in the presence of NHC–Ir^{I} catalysts (**1a-d**) (0.01 mol%) and KOH (10 mol%) in toluene (0.5 mL) at 135 ºC oil bath temperature under air for 12 h (entries 1–4). Among all catalysts tested, the best conversion was obtained with catalyst **1d** (entry 4). It was observed that the catalytic activity of iridium

complexes was enhanced by introducing electron withdrawing groups on the NHC ligand and in all cases the reaction was mainly selective to alcohol product **4aa**. These results encouraged us to further decrease the amount of catalyst to 0.001 mol% (10 ppm: prepared from a stock solution of catalysts in toluene via serial dilution and stable for at least six months) and after 12 h, reaction resulted with a mixture of **4aa** and **4'aa** in 32% yield in the presence of 10 mol% KOH (entry 5). Replacing the KOH with NaOH increased the yield of the reaction to 76% with 99:1 **4aa**:**4'aa** ratio (entry 6), and KO^{t}Bu was inactive under same conditions (entry 7). Using the closed systems or inert reaction conditions did not improve the yield of the reaction significantly and the rest of the reactions were performed open to air (entries 8 and 9). The reaction proceeded faster when the amount of NaOH increased to 20 mol%. The desired product **4aa** was obtained in 99% yield within 8 h (entry 10). Almost full conversion was observed upon adding a drop of mercury to the reaction mixture, indicating the homogeneous nature of the catalyst system (entry 11).[25] We could reduce the catalyst loading down to 0.0001 mol% (1 ppm) and still obtained the desired product **4aa** in 65% (in the presence of 10 mol% NaOH) and 81% (in the presence of 20 mol% NaOH) yield within 16 h (entries 12 and 13). Without any iridium(I) complex the reaction - resulted with only 12% yield, and no conversion to products was observed in the absence of a base as expected (entries 14 and 15).

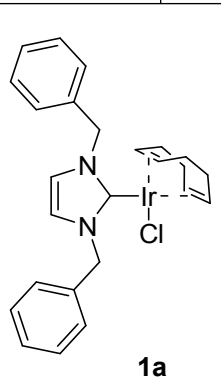
Table 1. Optimization of the conditions for the β-alkylation reaction of alcohols.[a]



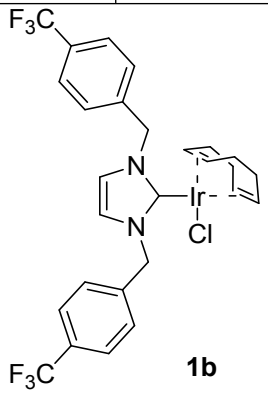
2a **3a** **4aa** **4'aa**

Entry	Cat. (mol%)	Base (mol%)	Time (h)	Yield (%) (**4aa** + **4'aa**)	Ratio (%) (**4aa** : **4'aa**)

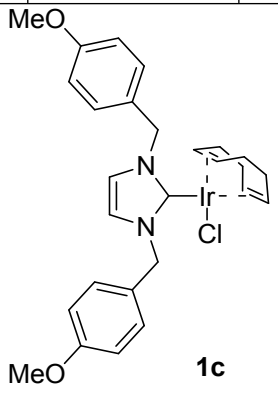
1	**1a** (0.01)	KOH (10)	12	63	99:1
2	**1b** (0.01)	KOH (10)	12	90	89:11
3	**1c** (0.01)	KOH (10)	12	35	84:16
4	**1d** (0.01)	KOH (10)	12	>99	85:15
5	**1d** (0.001)	KOH (10)	12	32	93:7
6	**1d** (0.001)	NaOH (10)	12	76	99:1
7	**1d** (0.001)	KO^{t}Bu (10)	12	18	90:10
8[b]	**1d** (0.001)	NaOH (10)	12	79	99:1
9[c]	**1d** (0.001)	NaOH (10)	12	78	99:1
10	**1d** (0.001)	NaOH (20)	8	>99	99:1
11[d]	**1d** (0.001)	NaOH (20)	8	97	99:1
12	**1d** (0.0001)	NaOH (10)	16	65	99:1
13	**1d** (0.0001)	NaOH (20)	16	81	99:1
14	–	NaOH (20)	16	12	ND
15	**1d** (0.001)	–	16	0	ND



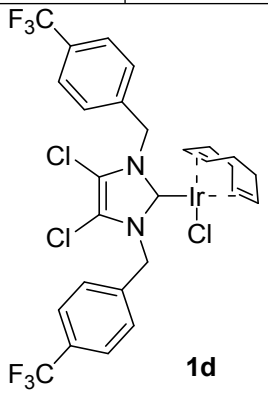
1a



1b



1c

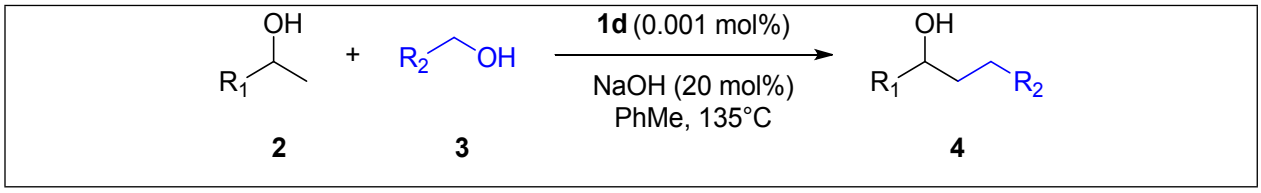


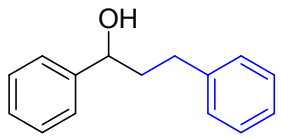
1d

[a] Reaction conditions: 1-Phenylethanol (1.0 mmol), benzyl alcohol (1.0 mmol), **1a-d** (0.01-0.0001 mol%), base (10-20 mol%), toluene (0.5 mL), 135 °C, under air. Yields and ratios were determined by ^{1}H NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. ND = Not determined. [b] Reaction was performed in a 20 mL closed tube. [c] Reaction was performed under an argon atmosphere. [d] A drop of mercury was added.

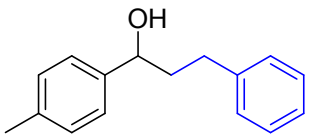
To evaluate the substrate scope of the β-alkylation of various secondary alcohols (**2**) with a variety of primary alcohols (**3**) was conducted under the optimized reaction conditions (0.001 mol % **1d**, 20 mol% NaOH, 0.5 mL toluene, 135 °C, 8h, under air) (Table 2). The reaction of *para*-substituted 1-phenylethanols bearing electron donating –Me and –OMe substituents and electron-withdrawing –Br, –Cl and $–CF_3$ substituents with benzyl alcohols gave the desired products **4aa-4fa** 85-97% isolated yields. Additionally, 1-(2-naphthyl)ethanol (**2g**) and α–tetralol (**2h**) gave the corresponding alcohols **4ga** and **4ha** in 91% and 94% yields under similar conditions. Next, we examined the scope of β–alkylation reaction with respect to primary alcohols (**3**). In this case, 1-phenylethanol (**2a**) reacted smoothly with a variety of primary alcohols (**3b**–**l**) to give well to excellent isolated yields (78–97%) of desired alkylated alcohols (**4ab**–**4al**).

Table 2. Scope of the β-alkylation of secondary alcohols with primary alcohols.[a]

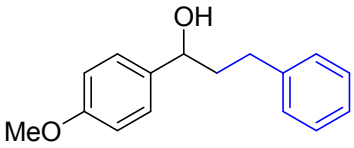




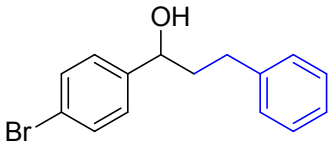
8h, **4aa**: 97% yield



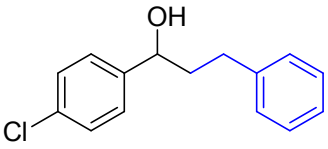
8h, **4ba**: 88% yield



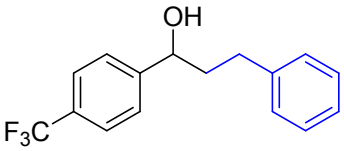
8h, **4ca**: 95% yield



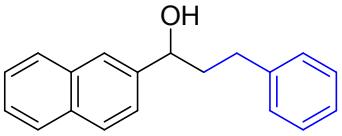
8h, **4da**: 85% yield



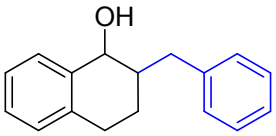
8h, **4ea**: 89% yield



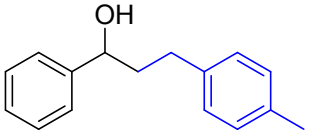
8h, **4fa**: 96% yield



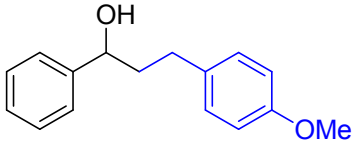
8h, **4ga**: 91% yield



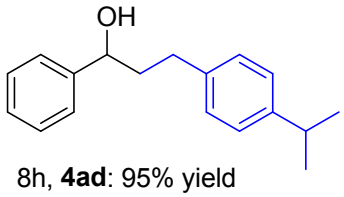
8h, **4ha**[b]: 94% yield



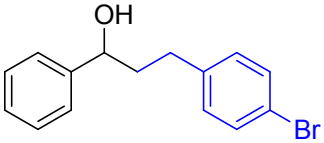
8h, **4ab**: 93% yield



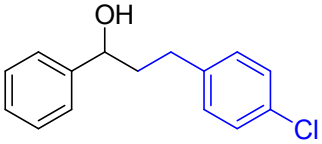
8h, **4ac**: 91% yield



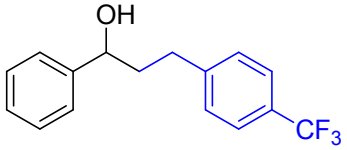
8h, **4ad**: 95% yield



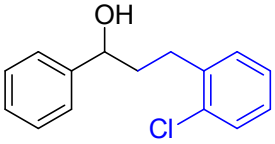
8h, **4ae**: 91% yield



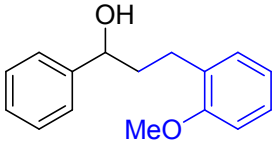
8h, **4af**: 90% yield



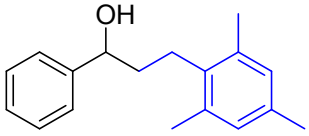
24h, **4ag**: 97% yield



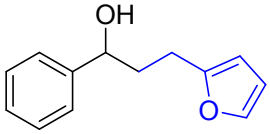
8h, **4ah**: 78% yield



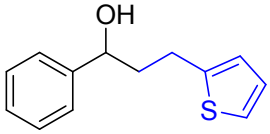
8h, **4ai**: 92% yield



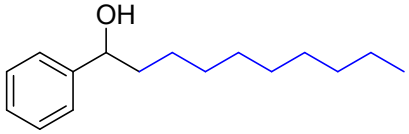
24h, **4aj**: 90% yield



24h, **4ak**[c]: 87% yield



24h, **4al**: 96% yield



24h, **4am**[c]: 54% yield

[a] Reaction conditions: Secondary alcohol (**2**) (1.0 mmol), primary alcohol (**3**) (1.0 mmol), **1d** (0.001 mol% = 10 ppm), NaOH (20 mol%), toluene (0.5 mL), 135 °C, under air. Isolated yield. [b]Mixture of diastereoisomers (68:32). [c]**1d** (0.01 mol%)

The reaction of 1-phenylethanol with *para*- and *ortho*-substituted benzyl alcohols bearing electron donating 4–Me, 4–OMe, 4–^{i}Pr and 2–OMe, substituents and electron-withdrawing 4–Br, 4–Cl and 2–Cl all resulted with high yields under optimized reaction conditions however, 4–trifluoromethylbenzyl alcohol (**3g**), 2,4,6–trimethylbenzyl alcohol (**3j**) and 2–thiophenemethanol (**3l**) as primary alcohols longer reaction time (24 h) was required for high yields. In the case of 2-furanmethanol (**3k**) and 1-octanol (**3m**) the amount of catalyst increased to 0.01 mol% and the corresponding alcohols **4ak** and **4am** were isolated in 87% and 54% yield respectively within 24 h.

Next, encouraged by these promising results, the substrate scope was extended to a cyclic secondary alcohol 5α-cholestan-3β-ol (**2i**), a saturated derivative of cholesterol. For this purpose **2i** was reacted with one equivalent benzyl alcohol (**3a**) under standard conditions and reaction resulted with complete conversion of **2i** along with β-alkylated cholesterol derivatives **4ia**[7a] and its diastereoisomer **4''ia** with a ratio of 73:27 (calculated by NMR analysis) after 20 h (Scheme 2). Pleasingly, we have isolated both diastereoisomers **4ia**[7a] (66% isolated yield) and **4''ia** (19% isolated yield). The structure of the minor diastereoisomer was assigned to be **4''ia** by 2D NMR studies (Supporting Information). The cholesterol derivative **2i** was also reacted similarly with 4-methoxybenzyl alcohol (**3c**) and corresponding diastereoisomers **4ic** and **4''ic** were isolated in 71% and 18% yield respectively (Scheme 2). Configrations of all diastereoisomers are specified by using NOESY experiments and discussed in supporting information.

In addition, to make this process practically viable, gram scale reactions were also carried out by using ppm amount of NHC–Ir^{I} catalyst. Cross-coupling of 1-arylethanols (5 mmol) with different benzyl alcohols (5 mmol) were resulted in 81-94% isolated yields for five examples in

the presence of only 1 ppm (0.0001 mol%) of **1d** as catalyst and 20 mol% NaOH after 24 h and this system disclosed up to 940000 TON(Table 3).

Scheme 2. NHC–Ir^{I} Catalyzed β-Alkylation of Cholestanol ([a]isolated yield).

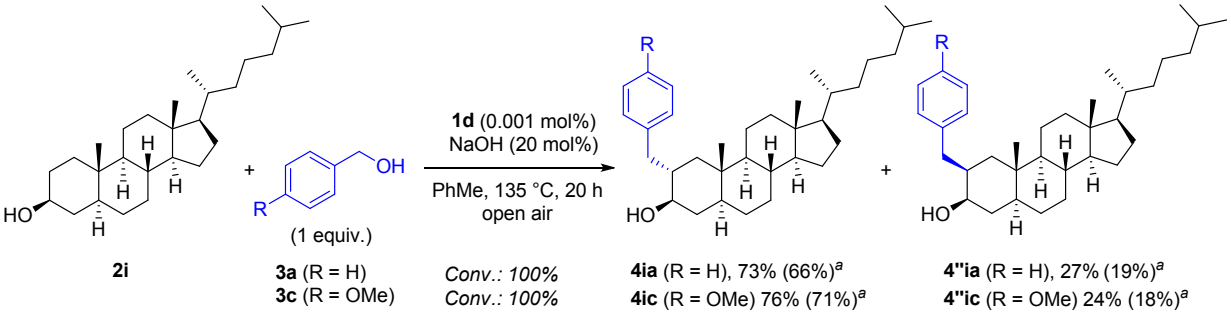
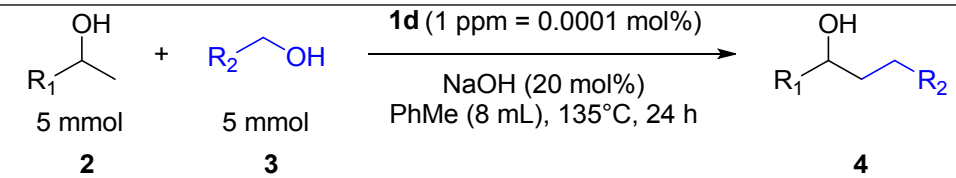
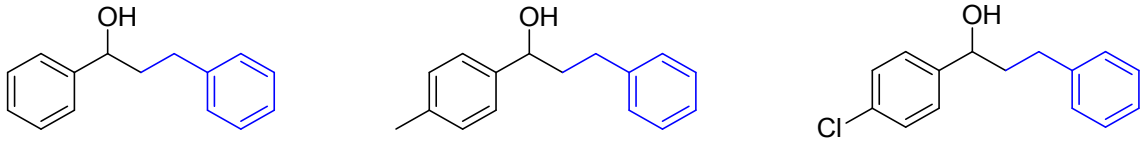


Table 3. Gram scale β-alkylation reaction of secondary alcohols with primary alcohols.[a]

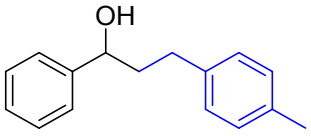




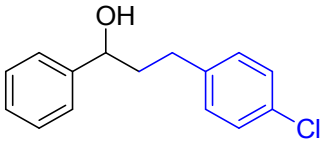
4aa: 91% (0.95 g)

4ba: 90% (1.02 g)

4ea: 94% (1.16 g)



4ab: 93% (1.05 g)

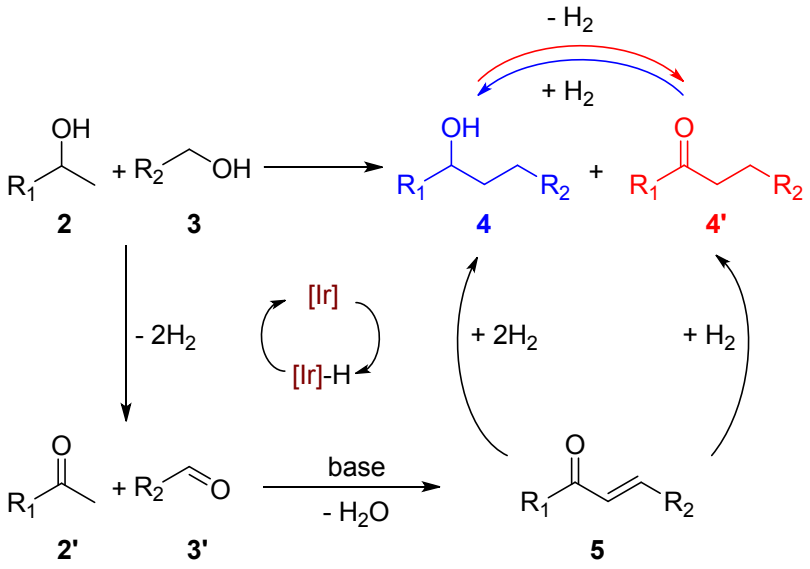


4af: 81% (0.99 g)

[a] Reaction conditions: Secondary alcohol (**2**) (5.0 mmol), primary alcohol (**3**) (5.0 mmol), **1d** (0.0001 mol% = 1 ppm), NaOH (20 mol%), toluene (8 mL), 135 °C, under air. Isolated yield. Brand-new glassware and stirring bar were used.

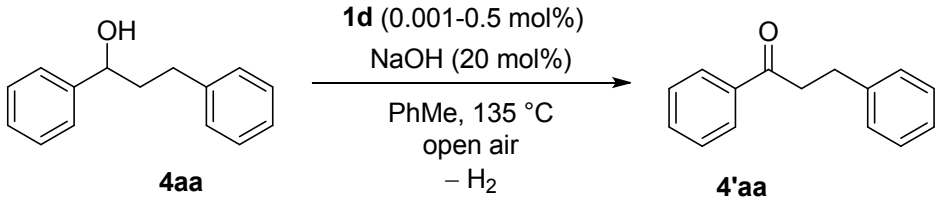
Mechanistic Studies on NHC–Ir^{I} Catalyzed β-Alkylation of Alcohols. A plausible mechanism for this cross-coupling of secondary alcohols with primary alcohols, in view of literature reports by us [24] and other groups [3b-f,5a,j,7b] and also the experimental data, can be shown in Scheme 3. The mechanism involves the dehydrogenation of alcohols (**2** and **3**) to give corresponding carbonyls (**2'** and **3'**) along with *in situ* generated transient iridium–hydride.[5a,24] These resulting carbonyl compounds may give the *α,β*–unsaturated ketone (**5**) in the presence of a base. This *α,β*–unsaturated ketone can be reduced to give the **4′** and **4** by iridium–hydride. In a very recent study we observed that, in the presence of 0.5 mol% **1d** the reaction of **2** and **3** was very fast and complete within 12.5 minutes along with a mixture of **4** and **4′** in a 51:49 ratio, then, **4** gradually dehydrogenated to give α-alkylated ketones (**4′**) selectively. [24] In the present study, we aimed to exploit these observations to improve the selectivity of the reaction to favor the β-alkylated alcohols (**4**) instead of α-alkylated ketones (**4′**). In other words, the main idea of the present study was to prevent the final dehydrogenation of **4** to **4′** by decreasing the amount of catalyst used.

Scheme 3. Plausible Reaction Mechanism for NHC–Ir^{I} Catalyzed β-Alkylation of Alcohols



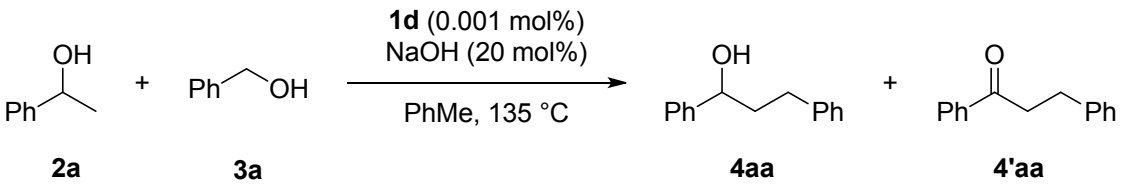
To obtain more information regarding final dehydrogenation of the β-alkylated alcohol (**4**) to α-alkylated ketone (**4′**) a series of control experiments were executed. For this purpose, dehydrogenation of 1,3-diphenylpropan-1-ol (**4aa**) was carried out in the presence of **1d** (0.5 to 0.001 mol%) and NaOH (20 mol%) (Scheme 4). In the presence of 0.5 mol% catalyst the reaction resulted in 92% conversion to 1,3-diphenylpropan-1-one (**4′aa**) within 2 h. Lowering the catalyst loading to 0.1 mol% and 0.01 mol% resulted with 45% and 6% conversion to **4′aa** within 2 h respectively. As expected, lower conversion to the **4′aa** was observed even after 24 h of the reaction in the presence of 0.001 mol% **1d**. It is clear that by decreasing the amount of catalyst used, final dehydrogenation step (dehydrogenation of **4** to **4′**) of the reaction can be prevented and this results with selective formation of β-alkylated alcohols (**4**).

Scheme 4. NHC–Ir[I] Catalyzed Dehydrogenation of 1,3-Diphenylpropan-1-ol (**4aa**) (^{1}H NMR conversions).

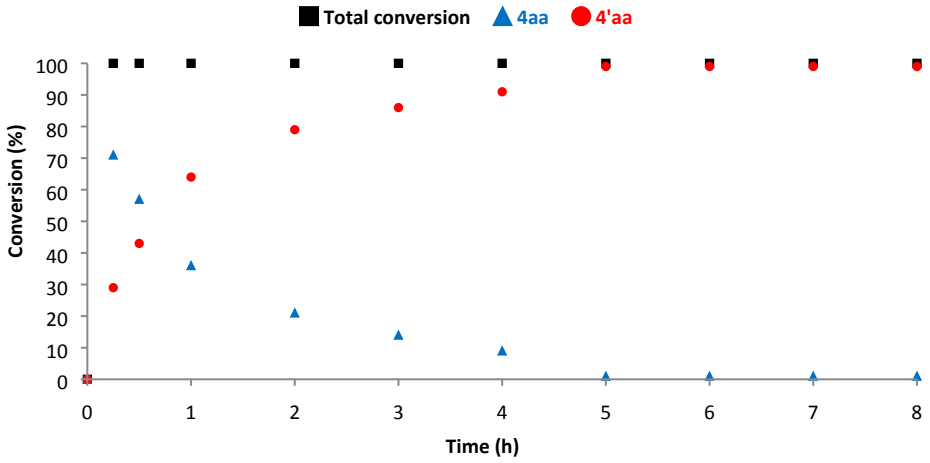


1d (0.5 mol%) / 2 h: 92 % conv. to **4'aa**
1d (0.1 mol%) / 2 h: 45 % conv. to **4'aa**
1d (0.01 mol%) / 2 h: 6 % conv. to **4'aa**
1d (0.001 mol%) / 2 h: <1 % conv. to **4'aa**
1d (0.001 mol%) / 24 h: 4 % conv. to **4'aa**

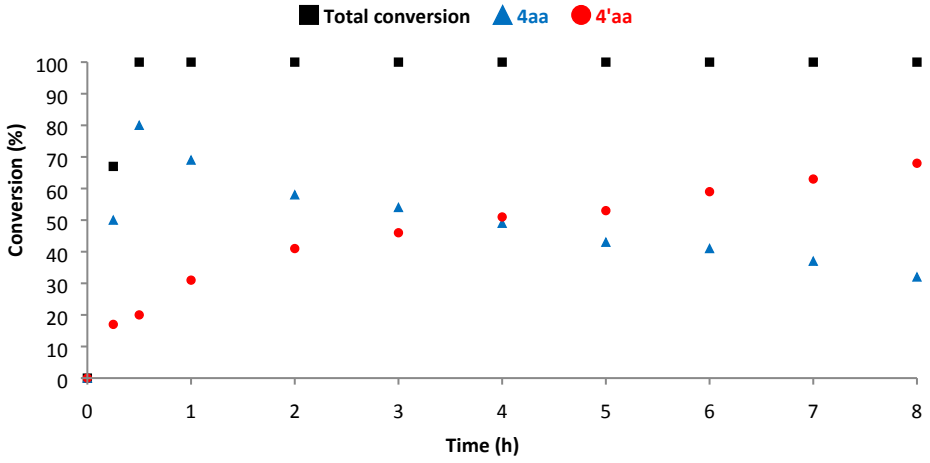
Then, we monitored the progress of the model reaction between 1-phenylethanol (**2a**) and benzyl alcohol (**3a**) as a function of time with catalyst loadings ranging between 0.5–0.001 mol% (Figure 1). The reaction of **2a** and **3a** is very fast and results in complete conversion to a mixture of **4aa** and **4′aa** within 15, 30 and 120 min. in the presence of 0.5, 0.1 and 0.01 mol% **1d** respectively. Then, initially formed **4aa** gradually undergoes dehydrogenation to form **4′aa** (Figure 1a-c). However, in the presence of 0.001 mol% **1d**, the concentration of **4′aa** was minimal (< 1%) and did not altered significantly during the progress of the reaction (Figure 1d). In addition, no accumulation of the α,β-unsaturated ketone (chalcone, **5aa**), resultant from the cross-condensation process, was observed during the whole course of the reaction, which suggests that the reduction of intermediate product **5aa** was very fast. From these observations, it can be suggested that the dehydrogenation of the alcohol substrates **2** and **3** is most likely the rate-limiting step.[7b]



a) 0.5 mol% **1d**



b) 0.1 mol% **1d**



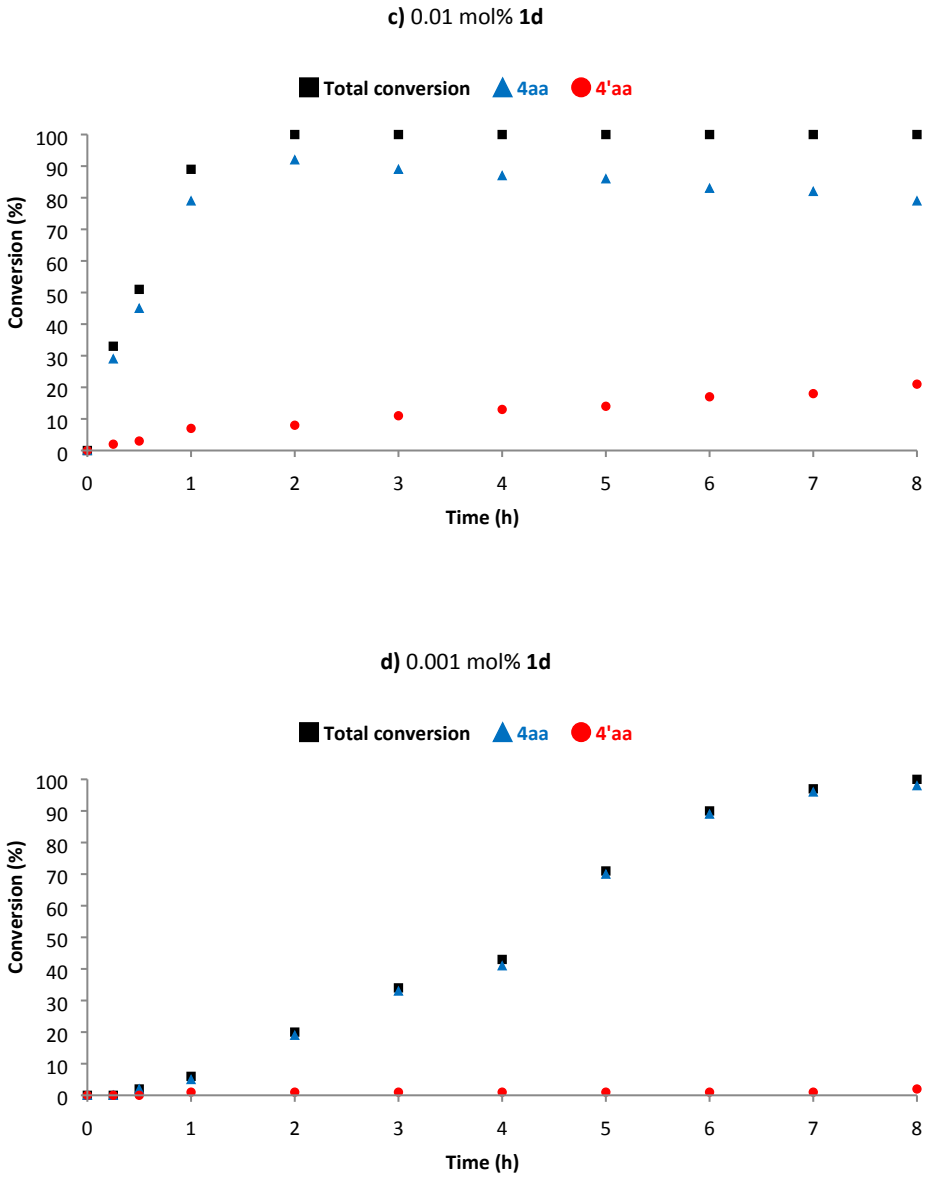
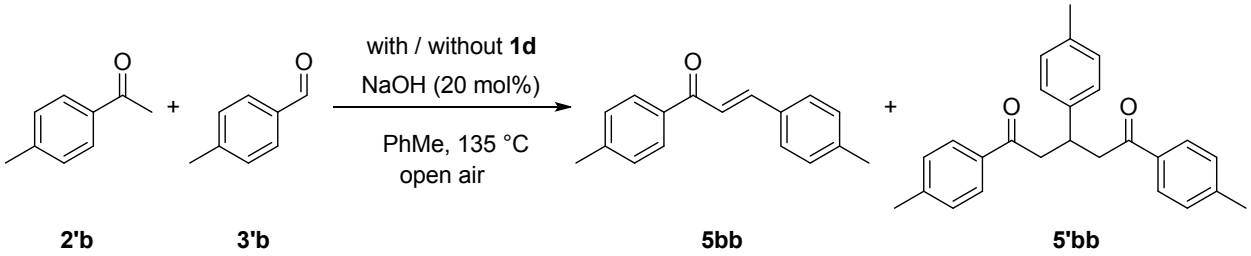


Figure 1. Time course of the reaction of benzyl alcohol with 1-phenylethanol. Reaction Conditions: **2a** (1.0 mmol), **3a** (1.0 mmol), **1d** (0.5-0.001 mol%), NaOH (20 mol%), toluene (0.5 mL), 135 ºC, under air. Yields and ratios were determined by ^{1}H NMR analysis of the independent reaction mixtures using 1,3,5-trimethoxybenzene as an internal standard: (a) 0.5 mol% **1d**; (b) 0.1 mol% **1d**; (c) 0.01 mol% **1d**; (d) 0.001 mol% **1d**.

There are some reports which supports the involvement of transition metal catalyst in cross-aldol condensation step.[3e,5b] In order to confirm the possible involvement of the used catalyst in this step, a reaction of 4-methylacetophenone (**2′b**) and *p*-tolualdehyde (**3′b**) was also performed in the presence and absence of **1d** using the standard catalytic conditions (Scheme 5). In the presence of **1d** (0.001 mol%) the reaction resulted with a mixture of products, containing 38% of 1,3-di-*p*-tolylprop-2-en-1-one (4,4'-dimethylchalcone, **5bb**) and 10% of 1,3,5-tri-*p*-tolylpentane-1,5-dione (**5′bb**), which was the product of the 1,4-addition of 4-methylacetophenone (**2′b**) on 4,4'-dimethylchalcone (**5bb**), after 4 h. The reaction also gave a similar mixture (36% of **5bb** and 9% of **5′bb**) in the absence of catalyst and these results may indicate that the catalyst was not involved in the cross-aldol condensation step of the present catalytic system. Interestingly, after the 16 h reaction of **2′b** and **3′b** in the presence of 0.001 mol% **1d** and 20 mol% NaOH unreacted **2′b** was not detected as it was converted to a mixture of **5bb (**33%) and 1,4-addition product **5′bb** (30%) and more importantly, increasing the molar ratio of **2′b**:**3′b** to 2:1 resulted with 91% and 82% formation of 1,4-addition product **5′bb** after 4 h in the presence of 0.001 mol% and absence of catalyst **1d** respectively. With Ni-based catalysts, similar results on the formation of this 1,4-addition products have also reported very recently.[26]

Scheme 5. Control Experiments on the Involvement of Catalyst in Cross-Aldol Condensation Step of the β-Alkylation of Alcohols (^{1}H NMR conversions).



2'b **3'b** **5bb** **5'bb**

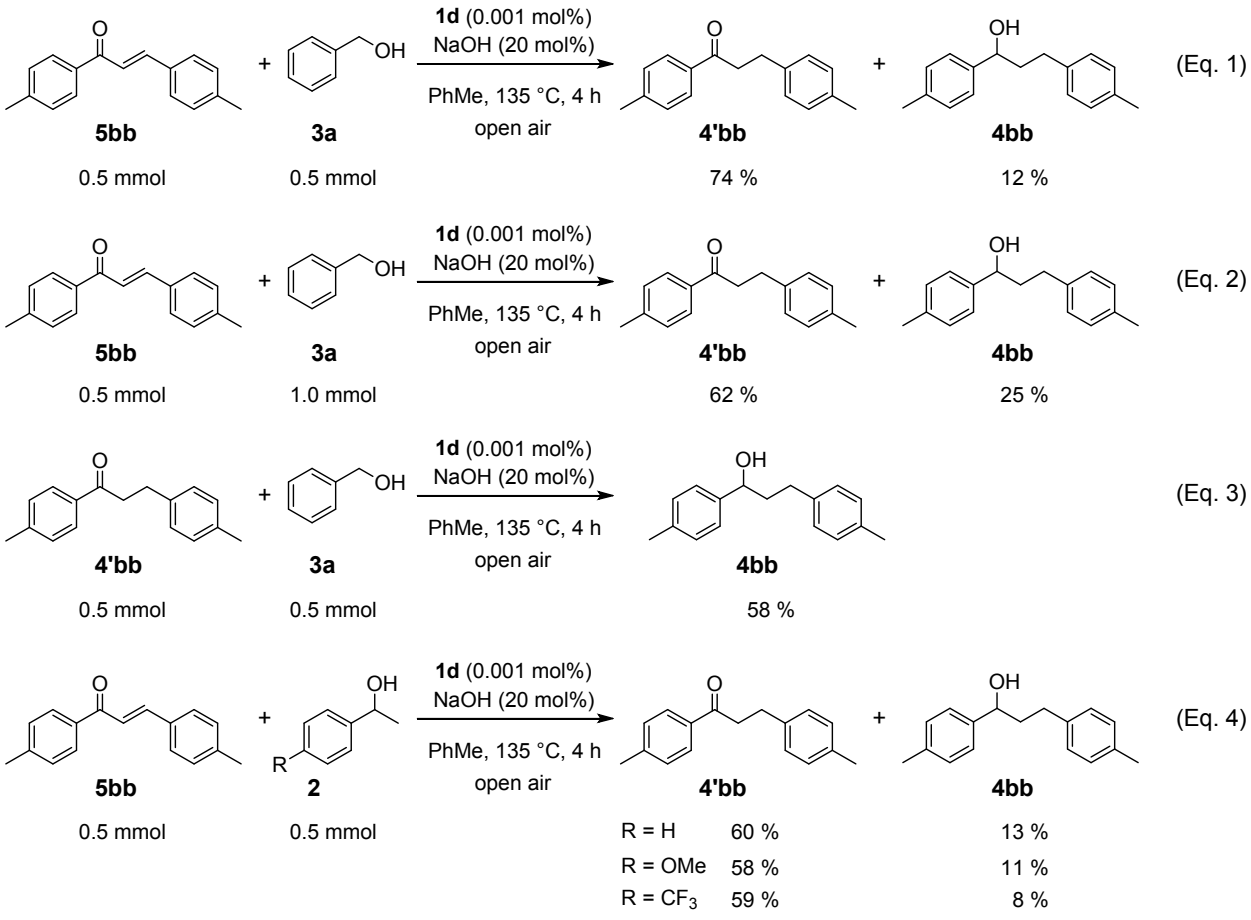
2'b (mmol)	**3'b** (mmol)	**1d** (mol%)	Time (h)	Yield (%**5bb** / %**5'bb**)[a]
1	1	0.001	4	38 / 10
1	1	–	4	36 / 9
1	1	0.001	16	33 / 30
2	1	0.001	4	4 / 91
2	1	–	4	9 / 82

[a] ^{1}H NMR yield, 1,3,5-trimethoxybenzene used as an internal standard.

Next, we investigated the reduction of α,β-unsaturated ketones (**5**) and α-alkylated ketones (**4′**) by using primary or secondary alcohols as hydrogen source. For this purpose, 4,4'-dimethylchalcone (**5bb**) and 1,3-di-*p*-tolylpropan-1-one (**4′bb**) were used as the model substrate (Scheme 6). Reduction of **5bb** in the presence of benzyl alcohol (1 equiv.) by using optimized reaction conditions afforded 74% of 1,3-di-*p*-tolylpropan-1-one (**4′bb**) and 12% of 1,3-di-*p*-tolylpropan-1-ol (**4bb**) after 4 h (Eq. 1). Increasing the amount of benzyl alcohol (2 equiv.) under similar conditions resulted with 62% **4′bb** and 25% **4bb** after 4 h (Eq. 2). Transfer hydrogenation of **4′bb** in the presence of benzyl alcohol (1 equiv.) under similar reaction conditions were also carried out and 58% conversion to **4bb** was observed after 4 h (Eq. 3). In addition, **5bb** can also be reduced by using 1 equiv. secondary alcohols (**2**). Irrespective from their electronic nature, in the presence of all the tested secondary alcohols (**2**) 4,4'-

dimethylchalcone (**5bb**) was reduced to give a mixture of **4′bb** (58-60%) and **4bb** (8-13%) within 4 h. All these results further suggest that NHC–Ir^{I} complex (**1d**) can efficiently catalyze the transfer of hydrogen from the substrate alcohols (**2** and **3**) to the C=C and C=O bonds.

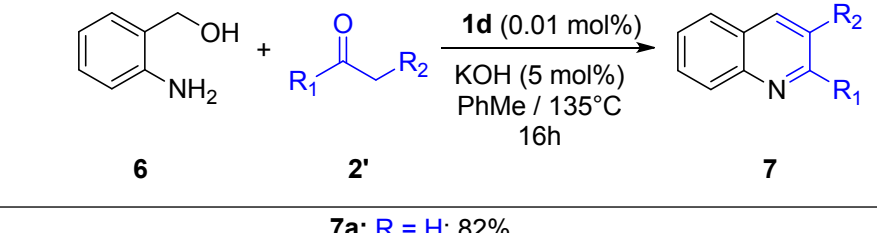
Scheme 6. Control Experiments on Reduction of Intermediate Products with Primary and Secondary Alcohols.

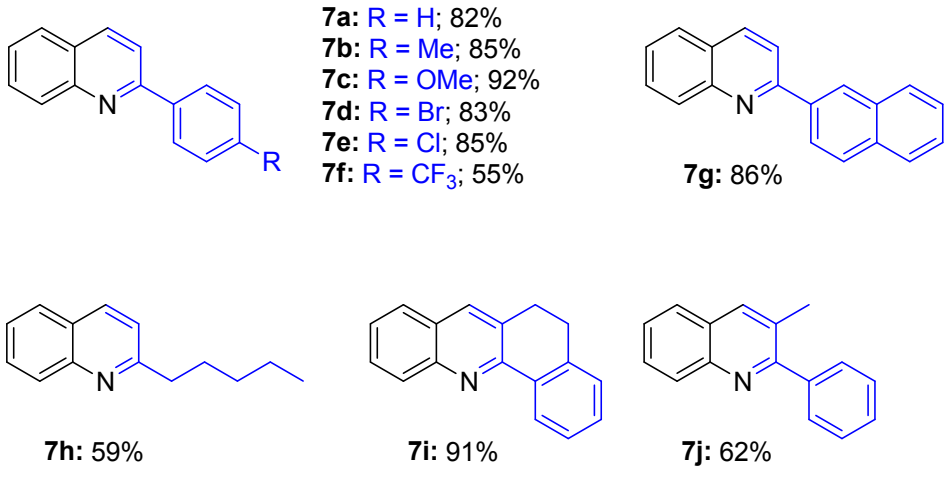


Catalytic Studies on NHC–Ir^{I} Catalyzed Acceptorless Cyclization of 2-Aminobenzyl Alcohol with Ketones. Following the advantages of BH technique and high activity of NHC–Ir^{I} complexes (**1**) in related reactions, we assumed that these complexes can catalyze acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohol (**6**) with ketones (**2′**) to give substituted

quinoline derivatives (**7**) in the presence of low amount of catalyst and strong base. Initially, several experiments were carried out to optimize the reaction conditions for this transformation (Supporting Information, Table S1). Reaction of equimolar amount of 2-aminobenzyl alcohol (**6**) with a variety of ketone (**2′**) in presence of complex **1d** (0.01 mol%) and KOH (5 mol%) at 135 ºC in toluene for 16 h resulted with moderate to high isolated yields (55-92%) to desired substituted quinoline derivatives (**7a-j**, (Table 4). To the best of our knowledge, one of the highest TON (up to 9200) - reported for the reaction or 2-aminobenzyl alcohol with ketones to give substituted quinolines.

Table 4. Scope for the reaction of 2-aminobenzyl alcohol with ketones to give quinolines.[a]





[a] Reaction conditions: 2-Aminobenzyl alcohol (**6**) (1.0 mmol), ketone (**2′**) (1.0 mmol), **1d** (0.01 mol%), KOH (5 mol%), toluene (1 mL), 135 °C,16 h, under air. Isolated yield.

CONCLUSIONS

In summary, we reported here a highly active catalytic system for the cross-coupling of alcohols to give β-alkylated alcohols (up to 940000 TONs) and acceptorless dehydrogenative cyclization of 2-aminobenzyl alcohol with ketones to synthesize substituted quinoline derivatives (up to 9200 TON) following borrowing hydrogen strategy by using catalytic amount of NaOH or KOH without using any inert reaction conditions. Varieties of β-alkylated alcohols, including cholesterol derivatives, and substituted quinolines were obtained in good isolated yields by using this efficient and operationally simple catalytic system. Furthermore, when combined with our previous results, selectivity can be controlled by a single catalyst: both β-alkylated alcohols (**4**) and α-alkylated ketones (**4′**) can be obtained by the reaction of secondary and primary alcohols with slightly modified reaction conditions.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated all reactions and work-up procedures were carried out in open air, all reagents and solvents were obtained commercially and used without further purification. [IrCl(COD)(NHC)] complexes **1a**[27] and **1b-d**[24] were synthesized according to published procedure. The physical properties and spectroscopic features of known complexes and isolated alcohols and quinolines are in good agreement with those reported in the literatures. Due to small quantities of catalyst that were used in the reactions, different catalyst solutions were prepared via serial dilution of prepared stock solutions and these solutions are stable for at least six months. NMR spectra were recorded on Varian AS 400 Mercury NMR spectrometer at 400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR and 376 MHz for ^{19}F in $CDCl_3$ and reported in units of parts per million (ppm) relative to tetramethyl silane (δ = 0 ppm) or $CDCl_3$ (δ = 7.26

ppm for ^{1}H and δ = 77.0 ppm for ^{13}C NMR). Coupling constants (J) are reported in Hertz (Hz). Melting points were determined on Gallenkamp electrothermal melting point apparatus without correction. HRMS analyses were performed on an Agilent 6530 Accurate-Mass Q-TOF mass spectrometer at Atatürk University East Anatolia High Technology Application and Research Center.

General Procedure for β-Alkylation of Secondary Alcohols with Primary Alcohols. Base (0.1-0.2 mmol, 10-20 mol%), secondary alcohol (1.0 mmol), primary alcohol (1.0 mmol) and a solution of complex **1** (0.0001-0.000001 mmol, 0.01-0.0001 mol%) in toluene (0.5 mL) were added under air atmosphere to a 20 mL reaction tube (1 cm × 20 cm) with a reflux condenser. The reaction mixture was vigorously stirred (1200 rpm) under reflux in a preheated oil bath at 135 ºC for required time. Then the reaction mixture was cooled to ambient temperature and in the case of optimization studies, 1,3,5-trimethoxybenzene (0.25 mmol) were added into the reaction mixture as an internal standard and the conversions and selectivity were calculated through ^{1}H NMR analysis. For the substrate scope experiments, all the crude products were purified by silica gel column chromatography using hexane and ethyl acetate (9:1 v/v) mixture as eluent to afford the desired alcohol.

*1,3-diphenylpropan-1-ol (**4aa**)*[8b]. Pale yellow oil; 97% yield (206 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.38-7.20 (m, 10H), 4.72- 4.68 (m, 1H), 2.82-2.66 (m, 2H), 2.21-2.01 (m, 2H, bs, 1H, OH); $^{13}C\{^{1}H\}$ NMR (CDCl3, 100 MHz) δ (ppm): 144.6, 141.8, 128.5, 128.5, 128.4, 127.6, 126.0, 125.9, 73.9, 40.5, 32.1.

*3-phenyl-1-(p-tolyl)propan-1-ol (**4ba**)*[28]. Colorless oil; 88% yield (199 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7,37-721 (m, 9H), 4,67 (dd, J_1 = 7.4 Hz, J_2 = 5.6 Hz, 1H), 2.83-2.67 (m, 2H),

2.42 (s, 3H), 2.29 (bs, 1H, OH), 2.21-2.02 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 142.0, 141.7, 137.3, 129.2, 128.5, 128.4, 126.0, 125.9, 73.7, 40.4, 32.2, 21.2.

*1-(4-methoxyphenyl)-3-phenylpropan-1-ol (**4ca**)*[3g]. White solid; 95% yield (230 mg); m.p.: 52 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.31-7.26 (m, 4H), 7.21-7.17 (m, 3H), 6.89 (d, J = 8.8 Hz, 2H), 4.64 (t, J = 6.2 Hz, 1H), 3.81 (s, 3H), 2.77-2.61 (m, 2H), 2.19-1.97 (m, 2H), 1.88 (bs, 1H, OH); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 159.1, 141.8, 136.7, 128.4, 128.3, 127.2, 125.8, 113.9, 73.5, 55.3, 40.3, 32.1.

*1-(4-bromophenyl)-3-phenylpropan-1-ol (**4da**)*[5e]. Colorless oil; 85% yield (248 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.48 (d, J = 8.4 Hz, 2H), 7.33-7.29 (m, 2H), 7.24-7.19 (m, 5H), 4.63 (dd, J_1 = 7.6 Hz, J_2 = 5.6 Hz, 1H), 2.77- 2.63 (m, 2H), 2.24 (bs, 1H, OH), 2.14-1.95 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 143.6, 141.5, 131.6, 128.5, 128.4, 127.7, 126.0, 121.3, 73.2, 40.4, 31.9.

*1-(4-chlorophenyl)-3-phenylpropan-1-ol (**4ea**)*[7d,8b]. Colorless oil; 89% yield (220 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.35-7.19 (m, 9H), 4.65 (t, J = 6.4 Hz, 1H), 2.77-2.63 (m, 2H), 2.15-1.96 (m, 2H), 2.12 (bs, 1H, OH); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 143.1, 141.5, 133.2, 128.6, 128.5, 128.4, 127.3, 125.9, 73.1, 40.5, 31.9.

*3-phenyl-1-(4-(trifluoromethyl)phenyl)propan-1-ol (**4fa**)*[7a,8b]. Colorless oil; 96% yield (269 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.63 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.32 (t, J = 7.2 Hz, 2H), 7.25-7.20 (m, 3H), 4.74 (dd, J_1 = 7.6 Hz, J_2 = 5.2 Hz, 1H), 2.81-2.67 (m, 2H), 2.31 (bs, 1H, OH), 2.17-1.99 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 149.0, 148.5, 141.4, 129.8 (q, J(C,F) = 32.0 Hz), 128.5, 128.4, 128.2, 126.2, 126.1, 125.5 (q, J(C,F) = 3.8 Hz), 124.2 (q, J(C,F) = 271.6 Hz), 73.2, 40.5, 31.8.

*1-(naphthalen-2-yl)-3-phenylpropan-1-ol (**4ga**)*[3g,7a,8b]. White solid; 91% yield (239 mg); m.p.: 65 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.86-7.82 (m, 3H), 7.79 (s, 1H), 7.53-7.47 (m, 3H), 7.33-7.28 (m, 2H), 7.22 (d, J = 7.6 Hz, 3H), 4.86 (dd, J_1 = 6.8 Hz, J_2 = 6.0 Hz, 1H), 2.83-2.68 (m, 2H), 2.29-2.09 (m, 2H), 2.07 (bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 141.9, 141.8, 133.3, 133.1, 128.5, 128.4, 128.3, 128.0, 127.7, 126.2, 126.0, 125.8, 124.7, 124.1, 74.0, 40.3, 32.1.

*Trans-2-benzyl-1,2,3,4-tetrahydronaphthalen-1-ol (**trans-4ha**)*[3c,29]. White solid; 64% yield (153 mg); m.p.: 116 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.51 (d, J = 6.8 Hz, 1H) 7.33-7.18 (m, 7H), 7.09 (d, J = 6.8 Hz, 1H), 4.51 (t, J = 7.2 Hz, 1H), 3.08 (dd, J_1 = 13.6 Hz, J_2 = 5.2 Hz, 1H), 2.81-2.73 (m, 2H), 2.52 (dd, J_1 = 13.6 Hz, J_2 = 8.8 Hz, 1H), 2.11-1.95 (m, 2H), 1.69 (d, J = 7.2 Hz, 1H), 1.54-1.46 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 140.4, 138.6, 136.8, 129.3, 128.7, 128.4, 128.3, 127.4, 126.3, 126.0, 73.0, 43.9, 38.4, 27.6, 24.5.

*Cis-2-benzyl-1,2,3,4-tetrahydronaphthalen-1-ol (**cis-4ha**)*[3c,29]. White solid; 30% yield (71); m.p.: 78 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.38-7.15 (m, 9H), 4.55 (s, 1H), 3.00 (dd, J_1 = 13.6 Hz, J_2 = 7.6 Hz, 1H), 2.95-2.89 (m, 1H), 2.82-2.74 (m, 2H), 2.11-2.03 (m, 1H), 1.93-1.82 (m, 1H), 1.78-1.71 (m, 1H), 1.66 (bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 140.8, 138.6, 136.9, 130.1, 129.3, 129.1, 128.4, 128.0, 126.2, 125.9, 69.4, 41.8, 38.2, 29.2, 22.6.

*1-phenyl-3-(p-tolyl)propan-1-ol (**4ab**)*[3c,6,8b]. White solid; 93% yield (211 mg); m.p.: 55 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.40-7.37 (m, 4H), 7.33-7.28 (m, 1H), 7.14-7.08 (m, 4H), 4.69 (t, J = 5.8 Hz, 1H), 2.77-2.62 (m, 2H), 2.36 (s, 3H), 2.19-1.99 (m, 2H), 1.96 (bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.7, 138.7, 135.3, 129.1, 128.5, 128.3, 127.6, 125.9, 73.9, 40.6, 31.6, 20.9.

*3-(4-methoxyphenyl)-1-phenylpropan-1-ol (**4ac**)*[6,8a,b]. White solid; 91% yield (221 mg); m.p.: 64 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.39-7.34 (m, 4H), 7.32-7.27 (m, 1H), 7.12 (d, J = 8.8 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 4.68 (dd, J_1 = 7.6 Hz, J_2 = 5.6 Hz, 1H), 3.79 (s, 3H), 2.74-2.59 (m, 2H), 2.16-1.96 (m, 2H, bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.8, 144.7, 133.8, 129.3, 128.5, 127.6, 125.9, 113.9, 73.8, 55.3, 40.7, 31.1.

*3-(4-isopropylphenyl)-1-phenylpropan-1-ol (**4ad**)*[17]. Colorless oil; 95% yield (242 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.39 (d, J = 4.4 Hz, 4H), 7.37-7.30 (m, 1H), 7.22-7.16 (m, 4H),), 4.71 (dd, J_1 = 7.6 Hz, J_2 = 5.6 Hz, 1H), 2.99-2.89 (m, 1H), 2.81- 2.64 (m, 2H), 2.22- 2.03 (m, 2H), 2.16 (bs, 1H, OH), 1.31 (d, J = 6.8 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 146.4, 144.7, 139.1, 128.5, 128.4, 127.6, 126.5, 126.0, 74.0, 40.5, 33.7, 31.7, 24.1.

*3-(4-bromophenyl)-1-phenylpropan-1-ol (**4ae**)*[3c,7a,8b]. Colorless oil; 91% yield (265 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.42-7.28 (m, 7H), 7.06 (d, J = 8.4 Hz, 2H), 4.65 (dd, J_1 = 7.6 Hz, J_2 = 5.6 Hz, 1H), 2.74-2.59 (m, 2H), 2.15-1.94 (m, 2H, bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.4, 140.8, 131.4, 130.2, 128.6, 127.7, 125.9, 119.6, 73.7, 40.2, 31.4.

*3-(4-chlorophenyl)-1-phenylpropan-1-ol (**4af**)*[3c,5j,8b]. White solid; 90% yield (222 mg); m.p.: 73 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.39-7.28 (m, 5H), 7.26 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 4.65 (t, J = 5.2 Hz, 1H), 2.76-2.60 (m, 2H), 2.17 (bs, 1H, OH), 2.15-1.95 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.4, 140.3, 131.6, 129.8, 128.6, 128.5, 127.7, 125.9, 73.7, 40.3, 31.4.

*1-phenyl-3-(4-(trifluoromethyl)phenyl)propan-1-ol (**4ag**)*[5j]. Colorless oil; 97% yield (272 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.93 (d, J = 8.4 Hz, 2H), 7.39-7.28 (m, 7H), 4.71-4.66 (m, 1H), 2.86-2.70 (m, 2H), 2.19-1.98 (m, 2H), 1.92 (bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100

MHz) δ (ppm): 146.0, 144.3, 128.7, 128.5, 128.1 (q, J(C,F) = 32.0 Hz), 127.8, 125.9, (t, J(C,F) = 272.6 Hz), 125.3 (q, J(C,F) = 3.8 Hz), 73.7, 40.1, 31.9.

*3-(2-chlorophenyl)-1-phenylpropan-1-ol (**4ah**)*[3c,7a,8a]. Colorless oil; 78% yield (192 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.39-7.35 (m, 5H), 7.33-7.28 (m, 1H), 7.25-7.13 (m, 3H), 4.72 (dd, J_1 = 7.6 Hz, J_2 = 5.6 Hz, 1H), 2.95-2.76 (m, 2H), 2.21 (bs, 1H, OH), 2.16-2.02 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.4, 139.5, 134.0, 130.4, 129.5, 128.5, 127.7, 127.4, 126.8, 125.9, 74.0, 38.7, 30.1.

*3-(2-methoxyphenyl)-1-phenylpropan-1-ol (**4ai**)*[3c]. Colorless oil; 92% yield (223 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.41-7.19 (m, 7H), 6.93 (td, J_1 = 7.4 Hz, J_2 = 1.2 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 4.66 (t, J = 5.8 Hz, 1H), 3.85 (s, 3H), 2.79 (t, J = 7.6 Hz, 2H), 2.49 (bs, 1H, OH), 2.15-1.99 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.5, 144.9, 130.3, 130.2, 128.4, 127.4, 127.3, 126.1, 120.7, 110.5, 73.7, 55.4, 39.4, 26.6.

*3-mesityl-1-phenylpropan-1-ol (**4aj**)*. White solid; 90%yield (229 mg); m.p.: 76 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.43-7.30 (m, 5H), 6.85 (s, 2H), 4.81-4.77 (m, 1H), 2.81-2.74 (m, 1H), 2.60-2.53 (m, 1H), 2.27 (s, 3H), 2.25 (s, 6H), 2.02-1.84 (m, 2H, bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.5, 135.9, 135.6, 135.0, 129.0, 128.5, 127.7, 125.9, 74.8, 38.2, 25.5, 20.8, 19.6. HRMS (APCI) m/z [M] calcd for $C_{18}H_{22}O$ 254.1671; found 254.1672.

*3-(furan-3-yl)-1-phenylpropan-1-ol (**4ak**)*[3c,8b]. Pale yellow oil; 87% yield (176 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.34-7.27 (m, 6H), 6.29 (dd, J_1 = 3.2 Hz, J_2 = 2.0 Hz, 1H), 6.01 (dd, J_1 = 3.2 Hz, J_2 = 0.8 Hz, 1H), 4.70 (dd, J_1 = 7.8 Hz, J_2 = 5.2 Hz, 1H), 2.79-2.67 (m, 2H), 2.18-2.02 (m, 2H, bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 155.6, 144.3, 140.9, 128.5, 127.7, 125.9, 110.1, 105.0, 73.7, 37.2, 24.4.

*1-phenyl-3-(thiophen-3-yl)propan-1-ol (**4al**)*[3c]. Colorless oil; 96% yield (210 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.41-7.29 (m, 5H), 7.15 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 6.96 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 1H), 6.86-6.82 (m, 1H), 4.72 (t, J = 6.4 Hz, 1H), 3.02-2.89 (m, 2H), 2.27 (bs, 1H, OH), 2.25-2.06 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.7, 144.4, 128.6, 127.7, 126.8, 125.9, 124.3,123.1, 73.5, 40.7, 26.2.

*1-phenyldecan-1-ol (**4am**)*[6]. Colorless oil; 54% yield (127 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.35-7.25 (m, 5H), 4.66 (dd, J_1 = 7.2 Hz, J_2 = 6.0 Hz, 1H), 1.89 (bs, 1H, OH), 1.85-1.63 (m, 2H), 1.45-1.25 (m, 14H), 0.88 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 144.9, 128.4, 127.4, 125.9, 74.7, 39.1, 31.9, 29.6, 29.5, 29.3, 25.8, 22.7, 14.1.

*(2R,3R,5S,8R,9S,10S,13R,14S,17R)-2-benzyl-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (**4ia**)*[7a]. White solid; 66% yield (316 mg); m.p.: 116 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.29-7.16 (m, 5H), 3.29 (td, J_1 = 10.4 Hz, J_2 = 4.8 Hz, 1H), 3.08 (dd, J_1 = 13.6 Hz, J_2 = 4.0 Hz, 1H), 2.37 (dd, J_1 = 13.4 Hz, J_2 = 8.8 Hz, 1H), 1.91 (dt, J_1 = 12.0 Hz, J_2 = 2.8 Hz, 1H), 1.82-1.69 (m, 2H), 1.64-0.93 (m, 27H), 0.88 (s, 3H), 0.86 (d, J = 0,8 Hz, 3H), 0.85 (d, J = 1.6 Hz, 3H), 0.73 (s, 3H), 0.60 (s, 3H), 0.59 (m, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 140.7, 129.3, 128.2, 125.7, 74.9, 56.5, 56.3, 54.4, 44.9, 42.8, 42.6, 42.3, 40.0, 39.5, 39.4, 38.3, 36.2, 36.1, 35.8, 35.3, 32.0, 28.4, 28.3, 28.0, 24.2, 23.9, 22.8, 22.6, 21.2, 18.7, 12.9, 12.1.

*(2S,3R,5S,8R,9S,10S,13R,14S,17R)-2-benzyl-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (**4''ia**)*. White solid;19% yield (91 mg); m.p.: 122 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.30-7.17 (m, 5H), 3.70 (s, 1H), 2.68 (dd, J_1 = 13.6 Hz, J_2 = 8.8 Hz, 1H), 2.52 (dd, J_1 = 13.2 Hz, J_2 = 6.4 Hz, 1H), 1.96 (dt, J_1 = 12.0 Hz, J_2 =

3.2 Hz, 1H), 1.86-1.76 (m, 2H), 1.69-1.62 (m, 1H), 1.60-0.94 (m, 26H), 0.90 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 2.0 Hz, 3H), 0.86 (d, J = 1.6 Hz, 3H), 0.76 (s, 3H), 0.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 140.9, 129.0, 128.2, 125.7, 67.7, 56.5, 56.2, 54.4, 42.6, 40.0, 39.5, 39.3, 39.2, 39.2, 39.1, 36.7, 36.4, 36.1, 35.8, 35.4, 32.0, 28.2, 28.0, 24.2, 23.8, 22.8, 22.6, 20.8, 18.7, 12.2, 12.1. HRMS (APCI) m/z [M] calcd for $C_{34}H_{54}O$ 478.4175; found 478.4217.

*(2R,3R,5S,8R,9S,10S,13R,14S,17R)-2-(4-methoxybenzyl)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (**4ic**)*. White solid; 71% yield (361); m.p.: 104 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.08 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H) 3.79 (s, 3H), 3.28 (td, J_1 = 10.4 Hz, J_2 = 5.2 Hz, 1H), 2.99 (dd, J_1 = 13.6 Hz, J_2 = 4.0 Hz, 1H), 2.33 (dd, J_1 = 13.4 Hz, J_2 = 8.0 Hz, 1H), 1.92 (d, J = 12.0 Hz, 1H), 1.84-1.73 (m, 1H), 1.72-0.92 (m, 28H), 0.89 (s, 3H), 0.87 (d, J = 2.0 Hz, 3H), 0.85 (d, J = 2.0 Hz, 3H), 0.72 (s, 3H), 0.61 (s, 3H), 0.57 (m, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.7, 132.6, 130.2, 113.6, 74.9, 56.5, 56.3, 55.2, 54.4, 44.9, 42.8, 42.6, 42.4, 40.0, 39.5, 38.5, 38.2, 36.2, 36.1, 35.8, 35.3, 32.0, 28.3, 28.2, 28.0, 24.2, 23.8, 22.8, 22.6, 21.3, 18.6, 12.9, 12.0. HRMS (APCI) m/z [M] calcd for $C_{35}H_{56}O_2$ 508.4280; found 508.4304.

*(2S,3R,5S,8R,9S,10S,13R,14S,17R)-2-(4-methoxybenzyl)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (**4''ic**)*. White solid; 18% yield (92 mg); m.p.: 114 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.11 (d, J = 8.8 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.70 (s, 1H), 2.62 (dd, J_1 = 13.4 Hz, J_2 = 8.8 Hz, 1H), 2.45 (dd, J_1 = 13.4 Hz, J_2 = 6.8 Hz, 1H), 1.94 (dt, J_1 = 12.4 Hz, J_2 = 3.2 Hz, 1H), 1.84-1.72 (m, 2H), 1.65 (dd, J_1 = 12.8 Hz, J_2 = 3.2 Hz, 1H) 1.55-0.95 (m, 26H), 0.89 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 2.0 Hz, 3H), 0.86 (d, J = 1.6 Hz, 3H), 0.75 (s, 3H), 0.73 (m, 1H), 0.64 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.7, 132.9, 129.9, 113.6, 67.7, 56.5, 56.2, 55.2, 54.4, 42.6, 40.0,

39.5, 39.3, 39.2, 39.1, 38.4, 36.7, 36.3, 36.2, 35.8, 35.4, 32.0, 28.2, 27.9, 24.2, 23.8, 22.8, 22.6, 20.8, 18.6, 12.2, 12.1. HRMS (APCI) m/z [M] calcd for $C_{35}H_{56}O_2$ 508.4280; found 508.4328.

Gram Scale β-Alkylation of Secondary Alcohols with Primary Alcohols. Base (1.0 mmol, 20 mol%), secondary alcohol (5.0 mmol), primary alcohol (5.0 mmol) and a solution of complex **1** (0.000001 mmol, 0.0001 mol%) in toluene (8 mL) were added under air atmosphere to a 50 mL reaction tube with a reflux condenser. The reaction mixture was vigorously stirred (1200 rpm) under reflux in a preheated oil bath at 135 ºC for 24 h. Then the reaction mixture was cooled to ambient temperature. The crude products were purified by silica gel column chromatography using hexane and ethyl acetate (9:1 v/v) mixture as eluent to afford the desired alcohols; **4aa**: 91% yield (0.95 g); **4ba**: 90% yield (1.02 g); **4ea**: 94% yield (1.16 g); **4ab**: 93% yield (1.05 g); **4af**: 81% yield (0.99 g).

*(E)-1,3-di-p-tolylprop-2-en-1-one (**5bb**)*[30]. Pale green solid; m.p.: 132 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.32-7.17 (m, 6H), 7.11 (s, 2H), 4.66 (dd, J_1 = 7.4 Hz, J_2 = 5.6 Hz, 1H), 2.80-2.59 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H).

*1,3,5-triphenylpentane-1,5-dione. (**5'bb**)*[31]. White solid; m.p.: 101 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.48 (d, J = 8.0 Hz, 4H), 7.33 (d, J = 8.0 Hz, 4H), 7.16 (d, J = 8.0 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 4.04-3.97 (m, 1H), 3.43 (dd, J_1 = 16.4 Hz, J_2 = 6.8 Hz, 2H), 3.28 (dd, J_1 = 16.4 Hz, J_2 = 6.8 Hz, 2H), 2.39 (s, 6H), 2.28 (s, 3H).

*1,3-di-p-tolylpropan-1-ol (**4bb**)*[7d]. White solid; m.p.: 70 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.32-7.17 (m, 6H), 7.11 (s, 2H), 4.66 (dd, J_1 = 7.4 Hz, J_2 = 5.6 Hz, 1H), 2.80-2.59 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 2.21-1.97 (m, 2H), 1.91 (bs, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$,

100 MHz) δ (ppm): 141.6, 138.7, 137.3, 135.2, 129.2, 129.1, 128.3, 125.9, 73.7, 40.5, 32.1, 31.6, 21.1.

*1,3-di-p-tolylpropan-1-one (**4'bb**)*[32]. Pale yellow solid; m.p.: 64 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.88 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.15 (dd, J_1 = 16.4 Hz, J_2 = 8 Hz, 4H), 3.27 (t, J = 7.8 Hz, 2H), 3,04 (t, J = 7.8 Hz, 2H), 2.42 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 198.9, 143.8, 138.3, 135.6, 134.4, 129.3, 129.2, 128.3, 128.2, 40.5, 29.8, 21.6, 21.0.

General Procedure for the Synthesis of Substituted Quinolines. Base (0.05 mmol, 5 mol%), 2-aminobenzyl alcohol (1.0 mmol), ketone (1.0 mmol) and a solution of complex **1** (0.0005-0.0001 mmol, 0.05-0.01 mol%) in toluene (0.5 mL) were added under air atmosphere to a 20 mL reaction tube (1 cm × 20 cm) with a reflux condenser. The reaction mixture was vigorously stirred (1200 rpm) under reflux in a preheated oil bath at 135 ºC for required time. Then the reaction mixture was cooled to ambient temperature and in the case of optimization studies, 1,3,5-trimethoxybenzene (0.25 mmol) were added into the reaction mixture as an internal standard and the conversions were calculated through ^{1}H NMR analysis. For the substrate scope experiments, all the crude products were purified by silica gel column chromatography using hexane and ethyl acetate (9:1 to 8:2 v/v) mixture as eluent to afford the desired quinolines.

*2-phenylquinoline (**7a**)*[14a,17,33]. White solid; 82% yield (168 mg); m.p.: 85 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.24-8.17 (m, 4H), 7.88 (d, J= 8.8 Hz, 1H), 7.83 (d, J= 8.0 Hz, 1H), 7.74 (t, J=7.8 Hz, 1H), 7.56-7.49 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.4, 148.3, 139.7, 136.7, 129.8, 129.6, 129.3, 128.8, 127.6, 127.5, 127.2, 126.3, 119.0.

*2-(p-tolyl)quinoline (**7b**)*[14a,33]. Yellow solid; 85% yield (187 mg); m.p.: 83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.18 (dd, J_1= 8.4 Hz, J_2= 5.6 Hz, 2H), 8.09 (d, J= 8.0 Hz, 2H), 7.86 (d, J= 8.4 Hz, 1H), 7.81 (d, J= 8.4 Hz, 1H), 7.72 (t, J= 7.4 Hz, 1H), 7.51 (t, J= 7.2 Hz, 1H), 7.34 (d, J= 8.0 Hz, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.3, 148.4, 139.4, 136.9, 136.6, 129.7, 129.6, 129.6, 127.5, 127.4, 127.1, 126.1, 118.8, 21.3.

*2-(4-methoxyphenyl)quinoline (**7c**)* [14a,17,33]. White solid; 92% yield (217 mg); m.p.: 123 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.19-8.13 (m, 4H), 7.84 (d, J= 8.8 Hz, 1H), 7.81 (d, J= 8.0 Hz, 1H), 7.71 (t, J= 7.6 Hz, 1H), 7.50 (t, J= 7.6 Hz, 1H), 7.05 (d, J= 8.4 Hz, 2H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 160.9, 156.9, 148.3, 136.6, 132.3, 129.6, 129.6, 128.9, 127.4, 126.9, 125.9, 118.5, 114.2, 55.4.

*2-(4-bromophenyl)quinoline (**7d**)* [14a,33]. Yellow solid; 83% yield (236 mg); m.p.: 119 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.22 (d, J= 8.4 Hz, 1H), 8.16 (d, J= 8.4 Hz, 1H), 8.06 (d, J= 8.4 Hz, 2H), 7.83 (dd, J_1= 8.4 Hz, J_2= 3.6 Hz, 2H), 7.74 (t, J= 7.6 Hz, 1H), 7.65 (d, J= 8.4 Hz, 2H), 7.54 (t, J= 7.4 Hz, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 156.0, 148.3, 138.5, 136.9, 132.0, 129.9, 129.7, 129.1, 127.5, 127.2, 126.6, 123.9, 118.4.

*2-(4-chlorophenyl)quinoline (**7e**)* [14a,17,33]. Yellow solid; 85% yield (204 mg); m.p.: 112 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.22 (d, J= 8.8 Hz, 2H), 8.16 (d, J= 8.8 Hz, 1H), 8.13 (d, J= 8.8 Hz, 1H), 7.83 (dd, J_1=8.4 Hz, J_2= 3.2 Hz, 1H), 7.74 (t, J= 7.8 Hz, 1H), 7.56-7.49 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz) δ (ppm): 155.9, 148.3, 138.1, 136.9, 135.5, 129.8, 129.7, 129.0, 128.8, 127.5, 127.2, 126.5, 118.5.

*2-(4-(trifluoromethyl)phenyl)quinoline (**7f**)*[14a]. Pale yellow solid; 55% yield (150 mg); m.p.: 124 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.27 (t, J= 9.2 Hz, 3H), 8.19 (d, J= 8.4 Hz, 1H),

7.89 (d, *J*= 8.8 Hz, 1H), 7.85 (d, *J*= 8.4 Hz, 1H), 7.79-7.74 (m, 3H), 7.57 (t, *J*= 7.4 Hz, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 155.6, 148.3, 142.9, 137.1, 131.2, 130.9, 130.0, 129.9, 127.8, 127.5, 127.4, 126.8, 125.8, 125.7, 125.7, 125.7, 125.6, 122.9, 118.7.

*2-(naphthalen-2-yl)quinoline (**7g**)*[33]. Yellow solid; 86% yield (220 mg); m.p.: 163 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.63 (s, 1H), 8.38 (d, *J*= 8.8 Hz, 1H), 8.27 (d, *J*= 8.8 Hz, 1H), 8.23 (d, *J*= 8.4 Hz, 1H), 8.06-7.99 (m, 3H), 7.92-7.85 (m, 2H), 7.76 (t, *J*= 7.2 Hz, 1H), 7.57-7.53 (m, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 157.1, 148.4, 137.0, 136.8, 133.9, 133.6, 129.8, 129.7, 128.9, 128.6, 127.8, 127.5, 127.3, 127.2, 126.7, 126.3, 125.1, 119.1.

*2-pentylquinoline (**7h**)*[18a]. Yellow oil; 59% yield (118 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.05 (d, *J*= 8.8 Hz, 1H), 8.01 (d, *J*= 8.4 Hz, 1H), 7.73 (d, *J*= 8.0 Hz, 1H), 7.65 (td, J_1= 7.8 Hz, J_2= 1.2 Hz, 1H), 7.44 (td, J_1= 7.4 Hz, J_2= 1.2 Hz, 1H), 7.25 (d, *J*= 8.8 Hz, 1H), 2.95 (t, *J*= 8.0 Hz, 2H), 1.85-1.77 (m, 2H), 1.41-1.34 (m, 4H), 0.89 (t, *J*= 2.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 163.0, 147.9, 136.0, 129.2, 128.8, 127.4, 126.7, 125.5, 121.3, 39.3, 31.7, 29.7, 22.5, 14.0.

*5,6-dihydrobenzo[c]acridine (**7i**)*[14a,17]. Pale yellow solid; 91% yield (210 mg); m.p.: 65 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.59 (d, *J*= 7.6 Hz, 1H), 8.14 (d, *J*= 8.4 Hz, 1H), 7.92 (s, 1H), 7.75 (d, *J*= 8.0 Hz, 1H), 7.66 (td, J_1= 7.6 Hz, J_2= 3.6 Hz, 1H), 7.50-7.36 (m, 3H), 7.27 (t, *J*= 6.4 Hz, 1H), 3.15-3.12 (m, 2H), 3.03-3.00 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 153.4, 147.7, 139.4, 134.8, 133.7, 130.6, 129.7, 129.5, 128.6, 127.9, 127.9, 127.3, 126.9, 126.1, 126.1, 28.9, 28.4.

*3-methyl-2-phenylquinoline (**7j**)* [14a,17,33]. Pale yellow oil; 62% yield (136 mg). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 8.18 (d, *J*= 8.0 Hz, 1H), 7.98 (s, 1H), 7.76 (d, *J*= 8.4 Hz, 1H), 7.67

(td, J_1= 7.7 Hz, J_2= 0.8 Hz, 1H), 7.63-7.60 (m, 2H), 7.52-7.43 (m, 4H), 2.45 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz) δ (ppm): 160.5, 146.7, 140.9, 136.7, 129.4, 129.2, 128.9, 128.7, 128.3, 128.2, 127.6, 126.8, 126.4, 20.6.

ASSOCIATED CONTENT

The following files are available free of charge.

Traces of ^1H, ^{13}C NMR and HRMS spectra (PDF)

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Notes

The authors declare no competing financial interest.

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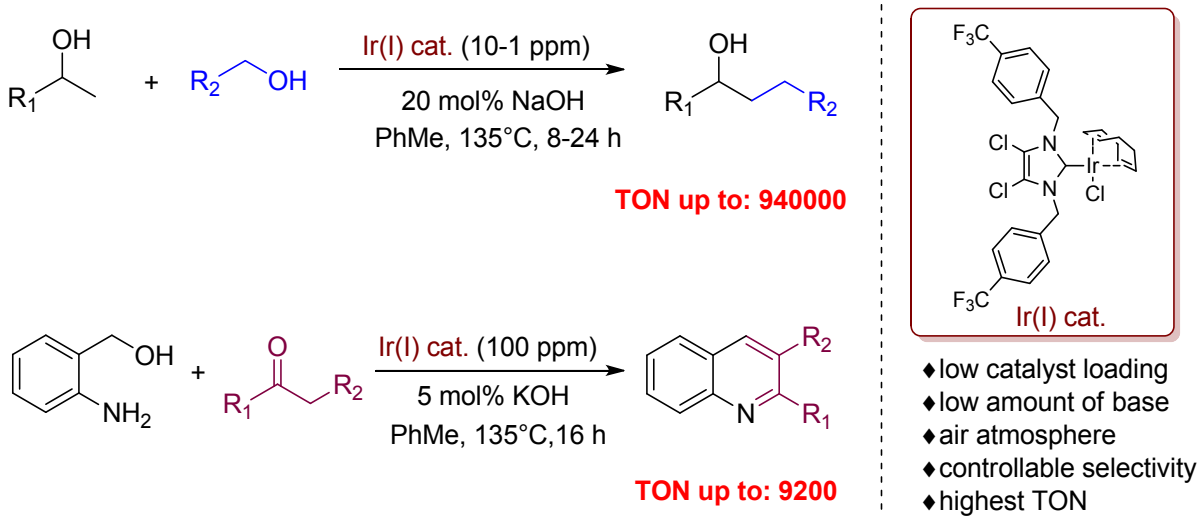
TOC Graphic:


OH
R1
+
R2
OH
Ir(I) cat. (10-1 ppm)
20 mol% NaOH
PhMe, 135°C, 8-24 h
OH
R1
R2
TON up to: 940000
OH
NH2
+
O
R1
R2
Ir(I) cat. (100 ppm)
5 mol% KOH
PhMe, 135°C,16 h
R2
N
R1
TON up to: 9200
F3C
Cl
N
Ir
Cl
Cl
N
Cl
F3C
Ir(I) cat.
♦low catalyst loading
♦low amount of base
♦air atmosphere
♦controllable selectivity
♦highest TON