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Ruthenium Pincer Complex Catalyzed Selective Synthesis of C-3 Alkylated Indoles and Bisindolylmethanes Directly from Indoles and Alcohols

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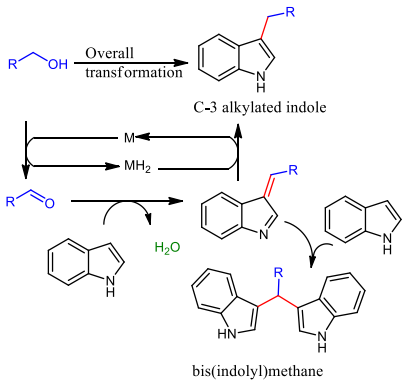
Abstract. Herein, we presented Ru-SNS complex that serves as a useful catalyst for C-3 alkylation of 1H-indoles with various aliphatic primary and secondary alcohols including cyclic alcohols as well as benzylic alcohols. The selective synthesis of bisindolylmethane derivatives is also achieved from the same set of indole and alcohol just by altering the reaction parameters. Furthermore, the sustainable synthesis of C-3 alkylated indoles directly from 2-(2-nitrophenyl)ethan-1-ol and alcohols catalysed by a Ru-complex *via* "borrowing hydrogen" strategy is reported. This protocol provides an atom-economical sustainable route to access structurally important compounds like arundine, vibrindole A and tryptamine based derivatives.

Keywords: Ruthenium, homogeneous catalysis, tridentate ligands, alkylation, borrowing hydrogen, indole.

Introduction

Indoles and their derivatives are considered to be among the most important heterocyclic scaffolds owing to their prevalence in many bioactive compounds,[1] natural products,[2] pharmaceuticals,[3] agro-chemicals[4] and functional materials.[5] Thus, the synthesis and functionalization of indole moiety have attracted significant attention. However, classical approach[6] for the synthesis of indole moiety or its selective functionalization [7] involves the use of toxic reagents, harsh reaction condition and/or pre-functionalization of substrates, which generates substantial amount of waste materials. Hence the development of green, atom-efficient and sustainable strategies for the synthesis of indole as well as C-3 functionalization of this scaffold is an area of intense research. In this perspective, acceptorless dehydrogenative (AD) synthesis of indole is considered as highly atom-economical and environmentally benign approach. Likewise C-3 alkylation[8] of 1H-indole using alcohols as alkylating agents *via* Borrowing Hydrogen Catalysis (BH)[9] is substantially more advantageous than conventional Friedel-Crafts type reaction,[7a] as the former does not necessitate the use Lewis and Brønsted acids[7b] or organocatalysts.[7d] The only byproduct formed in the process is water, which makes the overall system environmentally benign. The strategy comprises of three steps i) dehydrogenation of alcohol to form carbonyl compound ii) condensation reaction to form a α,β–unsaturated imine (vinylogous imine) derivative iii) hydrogenation of α,β–unsaturated imine derivative to C-3 alkylated indole (Scheme 1).



Scheme 1. Alkylation of 1H-indole *via* the borrowing hydrogen strategy.

In 2002, Yamaguchi and coworkers[10] reported an elegant method to synthesize indole *via* oxidative annulation of 2-aminophenethyl alcohol catalysed by iridium complex. In 2007, in a seminal work Grigg and coworkers[11] demonstrated $[Cp^*IrCl_2]_2$ catalysed synthesis of indole as well as C-3 alkylation of 1H-indole moiety. C-3 functionalization of indoles with wide range of aliphatic amines as alkylating agents was first illustrated by Beller and coworkers.[12] The use of alcohols as alkylating agent is highly advantageous as alcohols can be renewably obtained

from lignocellose biomass[13] and water is the only byproduct formed. The use of a diverse range of aliphatic alcohols as alkylating partners is challenging and hence has been largely unexplored.[8d,8h-8k,14,15] Shimizu and coworkers reported first heterogeneous Pt-catalysed C-3 alkylation of indoles with a diverse range of aliphatic alcohols.[14] However their protocol failed to achieve alkylation of indole with secondary alcohols. Very recently, synthesis of C-3 alkylated indoles was achieved directly from indoline and aliphatic primary alcohols in the presence of iridium catalyst.[15] Therefore, there is an increasing demand to develop new sustainable catalytic protocols to achieve C-3 functionalized indoles using both aliphatic primary and secondary alcohols as alkylating agents.

Engrossed by the striking benefit of AD[16] and BH[9] reaction and motivated by our continuous interests in heterocyclic synthesis,[17] herein, we described SNS-acridine derived Ru-pincer complex[17a] catalysed C-3 alkylation of indoles to get 3-substituted indoles. The one pot synthesis of C-3 alkylated indoles was also achieved directly from 2-(2-nitrophenyl)ethan-1-ol and primary alcohols *via* sequential multistep reaction. Furthermore, the selective synthesis of bis(indolyl)methane derivatives was also demonstrated.

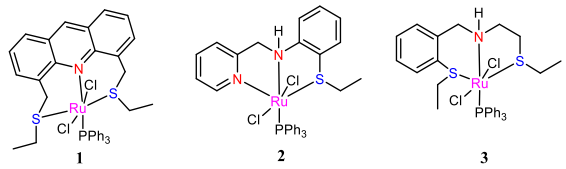
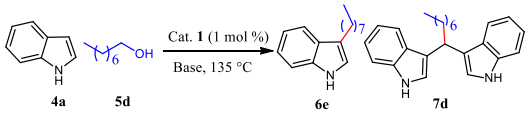


Figure 1. Ruthenium pincer complexes.

Results and Discussion

At the outset, the catalytic applicability of complex **1-3** toward the C-3 alkylation of indoles with various primary alcohols was examined. To find out the optimum reaction conditions, various reaction parameters were screened employing indole and 1-octanol as model substrates. When, a mixture of indole (1 mmol), 1-octanol (1 mmol) and KOH (1 mmol) was heated at 135 °C [18] under neat condition for 18 h in Ace pressure tube in the presence of 1 mol % catalyst **1**, 10% 3-octyl-1H-indole (**6e**) was obtained along with 65% 3,3'-(octane-1,1-diyl)bis(1H-indole) (**7d**) (Table 1, Entry 1). In an attempt to improve the yield of the 3-octyl-1H-indole (**6e**), the ratio of indole: 1-octanol was increased to 1:5 which resulted in 40% isolation of **6e** (Table 1, Entry 4). Gratifyingly, the yield of **6e** was further improved from 40% to 86% simply by lowering the amount of KOH to 0.5 mmol (Table 1, Entry 5). However, further lowering of the amount of base resulted in decrease of yield of the desired 3-octyl-1H-indole (Table 1, Entry 7). Bases like Cs_2CO_3, ^{t}BuOK and NaOH gave moderate yield (Table 1, Entries 11-13) under the similar reaction condition whereas $CsOH.H_2O$ and Na_2CO_3 gave poor yield (Table 1, Entries 14 and 15).[19] Thus, the observed selectivity is highly dependent on the nature and stoichiometry of the applied base and amount of the alkylating agent. We also tried solvent such as toluene (Table 1, entry 9) where the yield of the desired C-3 alkylated indole was found to be very poor.[20] Under the optimized reaction conditions, complex **2** or **3** gave inferior yield of the desired product **6e** (Table 1, Entries 16 and 17). Without the presence of any base, catalyst **1** failed to activate the alcohol. Similarly, in absence of catalyst **1**, 0.5 mmol KOH did not yield any desired 3-octyl-1H-indole (Table 1, Entries 19, 20). Thus the above results clearly underpin the importance of both catalyst and the base for the progress of the reaction.

Table 1. Optimization of the reaction condition for the C3-alkylation of indole.[a]



Entry	Cat.	Base (mmol)	Indole:alcohol	Time (h)	Yield (%) 6e	Yield (%) 7d
1	**1**	KOH (1)	1:1	18	10	65
2	**1**	KOH (1)	1:3	18	20	60
3	**1**	KOH (1)	1:4	18	30	45
4	**1**	KOH (1)	1:5	18	40	43
5	**1**	KOH (0.5)	1:5	18	86	-
6	**1**	KOH (0.5)	1:3	18	60	10
7	**1**	KOH (0.25)	1:5	18	48	25
8	**1**	KOH (0.05)	1:5	18	-	-
9[b]	**1**	KOH (0.5)	1:1	18	10	60
10	**1**	KOH (0.5)	1:5	10	60	-
11	**1**	Cs_2CO_3 (0.5)	1:5	18	65	-
12	**1**	^{t}BuOK (0.5)	1:5	18	70	-
13	**1**	NaOH (0.5)	1:5	18	70	-
14	**1**	$CsOH.H_2O$ (0.5)	1:5	18	30	-
15	**1**	Na_2CO_3 (0.5)	1:5	18	5	-
16	**2**	KOH (0.5)	1:5	18	30	-
17	**3**	KOH (0.5)	1:5	18	25	-
18[c]	**1**	KOH (0.5)	1:5	24	60	-
19	-	KOH (0.5)	1:5	24	-	-
20	**1**	-	1:5	24	-	-

[a] Reaction conditions: Indole (1 mmol), 1-octanol (5 mmol), Cat **1** (0.01 mmol, 1 mol %), 30 mL Ace pressure tube, 135 °C, 18 h. [b] In toluene (1 mL) [c] 0.5 mol % catalyst **1** loading.

After achieving the optimized reaction condition, we sought to explore the generality and the limitations of the developed protocol. To manifest the practical applicability of the system, various alcohols and representative substituted indoles were investigated. The reactions of indoles with a variety of primary aliphatic alcohols afforded C-3 alkylated

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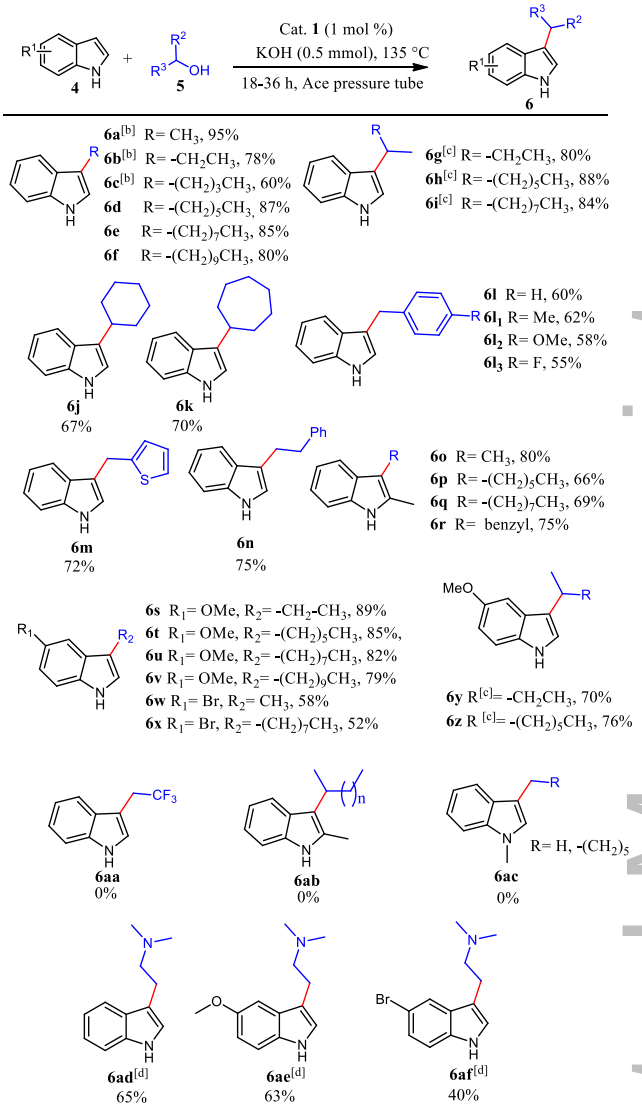
product from good to excellent yields (**6a-6f** 60-95%). Thermodynamic data suggested that activating methanol to its corresponding formaldehyde required large enthalpy (approx. 31.0 Kcal)[16a] which in many cases can limit the scope of the reaction. In contrast, to our delight, reaction of indole with methanol resulted in excellent conversion to the desired product **6a** with yield of 95%. Similarly, ethanol and butanol also gave rise to good yield of the desired products **6b** and **6c** (78% and 60% respectively). Excellent yields of the desired C-3 alkylated indoles were obtained by employing longer chain alcohols as alkylating agents. (Table 2, Entries **6d-6f**). Intrigued by this result, we moved our attention to probe the reactivity of secondary aliphatic alcohols like 2-butanol, 2-octanol, 2-decanol toward the alkylation of indole. We were pleased to observe that the reaction afforded excellent yield of the desired products (Table 2, Entries **6g-6i**); however, it requires higher loading of catalyst **1** (2 mol %) as well as longer reaction time (36 h). This is a significant improvement compared to the work of Shimizu and coworkers who achieved a low yield of 4% using 2-octanol.[14] Interestingly, cyclic alcohols too could be easily applied as alkylating agents in the present protocol (Table 2, Entries **6j** & **6k**). For aromatic alcohols the yields were moderate to good **6l-6l$_3$** 55%-62%, with useful bis(3-indolyl)phenylmethane[21] derivatives as minor products. Heteroaromatic alcohol like 2-thiophenemethanol worked well in our present catalytic system with 72% of **6m** being isolated. Next, we investigated the reaction of substituted indoles with primary as well as secondary aliphatic alcohols. 2-methyl-indole reacted smoothly with primary alcohols to give the corresponding products in high yield **6o-6r** (66-80%). However in case of secondary aliphatic alcohols, no product formation was observed. This might be due to the steric effect from the methyl group towards the incoming alkylating agents.[12] Indoles having both activating and deactivating groups were compatible with both primary and secondary aliphatic alcohols for C-3 alkylation and afforded good to excellent isolated yields of **6s-6z** (52-89%). 5-Bromoindole gave moderate yield of the corresponding product **6w-6x** with some dehalogenated by-product. Our catalyst failed to activate 2,2,2-trifluoroethanol as desired **6aa** was not formed. Also N-methylindole did not undergo C-3 alkylation (Table 2, Entry **6ac**), which suggested that the anion generated on the nitrogen atom in the presence of base plays an important role in this reaction.

To examine the practical applicability of the present protocol, we extended our study to synthesize tryptamine based alkaloid derivatives, which are known for their biological importance.[22] Conventionally, multistep reactions[23] are involved in the synthesis of 2-(5-methoxy-1H-indol-3-yl)-N,N-dimethylethan-1-amine **6ae** which is an intermediate of biologically active Bufotinine.[24] Gratifyingly, we were able to synthesize **6ae** directly from indole and *N*,*N*-Dimethylethanolamine in one step (63% yield).

Table 2. Substrate scope for C-3 alkylation of indole with alcohols.[a]



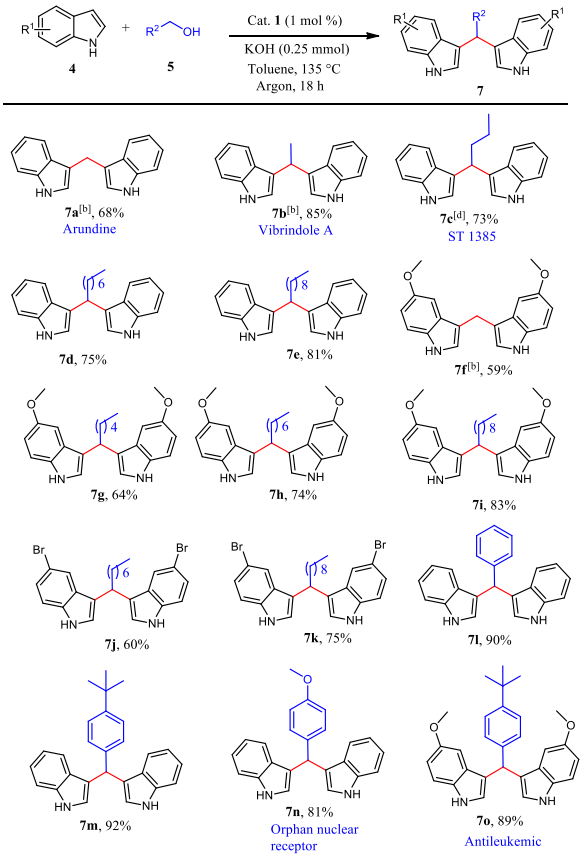
[a] Reaction condition: Indole (1 mmol), 1-octanol (5 mmol), Cat **1** (0.01 mmol, 1 mol %), KOH (0.5 mmol), 30 mL Ace pressure tube, 135 °C, 18-36 h. [b] 1 mL alcohol. [c] 2 mol % catalyst **1**, 36 h. [d] Catalyst **1** (2 mol %), Cs_2CO_3 (1.1 mmol), 24 h.

During the course of our optimization reaction condition for the synthesis of C-3 alkylated indoles, we found that the 3,3'-(octane-1,1-diyl)bis(1H-indole) was obtained as major product when the reaction was performed either in toluene solvent or with the lower amount of alcohol (Table 1, Entries 1 & 9). Thus, we were interested toward the synthesis of bisindolylmethane derivatives as they are found in many natural product and bioactive compounds.[25] They are also used as antibacterial, anti-inflammatory, anticancer and anti-fungal agent.[26] Although the concept of the synthesis of bisindolylmethane derivatives directly from indole with activated benzyl

alcohols has been largely explored,[27,8d] the construction of structurally important bisindolylalkanes using aliphatic alcohols as alkylating agent is very scanty.[28] Therefore, synthesis of diverse range of bisindolylalkanes using indole and aliphatic alcohols is highly desirable.

Thus, when a mixture of indole (1 mmol), 1-octanol (0.5 mmol), KOH (0.25 mmol) and catalyst **1** (1 mol %) was refluxed in toluene (1 mL) in an argon atmosphere for 18 h, 75% 3,3'-(octane-1,1-diyl)bis(1H-indole) **7d** was isolated. Further increase of the chain length of alcohol resulted in slight increase of the yield to 81% (Table 3, Entry **7e**). Next, we were interested to synthesize arundine (**7a**)[29] which is known as preventive for breast cancers. To our delight, we were able to isolate arundine (**7a**) in 68% yield by reacting indole with MeOH.

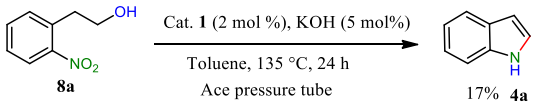
Table 3. Substrate Scope for the synthesis of bisindolylmethane. [a]



[a] Reaction conditions: Indole (1 mmol), alcohol (0.5 mmol), catalyst **1** (0.005 mmol, 1 mol %), KOH (0.25 mmol), toluene (1 mL), 135 °C, 18 h. [b] 0.5 mL MeOH, Indole (2 mmol), KOH (1.5 mmol) Toluene (1 mL), 100 mL Ace pressure tube [c] 0.5 mL EtOH, Indole (2 mmol), Toluene (1 mL), 100 mL Ace pressure tube. [d] 0.5 mL BuOH, Indole (2 mmol), Toluene (1 mL), 100 mL Ace pressure tube.

Our protocol also provides a route to synthesize vibrindole A (**7b**)[30] in excellent yield (85%). Vibrindole A is used to treat fibromyalgia and bowel syndrome. Afterwards differently substituted indoles were reacted with wide range of aliphatic alcohols to obtain moderate to good yield of the corresponding product (**7c, 7e-7l**). Benzyl alcohols reacted well with indoles and structurally important [31] **7n** and **7o** were isolated in excellent yield (81% and 89% respectively).

Presently, the major natural source of indole is coal tar,[32] from where it has been isolated. In the context of the rapid depletion of fossil fuels and growing environmental awareness, the synthesis of indole *via* atom economical, environmentally benign approach has attracted significant attention in the recent years. In this context, the dehydrogenative *N*-heterocyclization of 2-aminophenethyl alcohol in presence of various transition metal catalysts has been reported.[33] Recently, the strategy of reducing nitro group to the amine group *via* hydrogen auto-transfer and subsequent condensation with the formed carbonyl compounds showed their efficacy toward the synthesis of heterocyclic compounds.[34, 10,11] Thus, we envisioned the synthesis and functionalization of indole in one pot *via* sequential de(hydrogenation) reactions. Therefore, the scope of our catalyst to synthesize indole directly from 2-(2-nitrophenyl)ethan-1-ol (**8a**)[10] was first studied.



Scheme 2. Indole synthesis from 2-(2-nitrophenyl)ethan-1-ol.

In order to utilize the liberated hydrogen molecule from dehydrogenation of alcohols, we used 2-(2-nitrophenyl)ethan-1-ol as a starting reagent to form indole. When, 2-(2-nitrophenyl)ethan-1-ol (0.5 mmol), KOH (5 mol %), catalyst **1** (2 mol %) were refluxed at 135 °C for 24 h in 15 mL Ace pressure tube, 17% indole was isolated. Inspired by our initial effort, we were interested to study the scope and limitaion of our protocol toward the one-pot synthesis of C-3 alkylated indoles directly from 2-(2-nitrophenyl)ethan-1-ol and aliphatic alcohols. On initial trial, a mixture of 2-(2-nitrophenyl)ethan-1-ol (0.5 mmol) and 1-hexanol (1.5 mmol) was heated in an Ace pressure tube in the presence of catalyst **1** (2 mol %) and KOH (0.5 mmol) for 48 h. The desired 3-hexyl-1H-indole **6d** was obtained in 20% yield (Table 4, Entry 1). Interestingly, with increasing the amount of alcohol (2.5 mmol), the yield of **6d** was enhanced to 40% (Table 4, Entry 2). The yield of **6d** was further improved to 70% just by increasing the amount of the base (Table 4, Entry 3). Here the excess base is required possibly to assist the multiple oxidation and reduction steps. [11] Next, we focussed on the effect of different bases toward the progress of the reaction. It was observed that bases like ^{t}BuOK, K_3PO_4, Cs_2CO_3 and K_2CO_3 proved incompetent for the improvements of the yields (Table 4, Entries 5, 7, 8 & 9).

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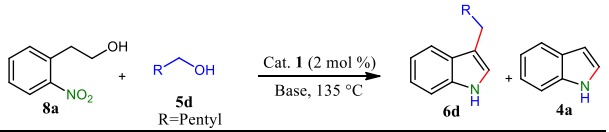
Table 4. Optimization of the reaction condition for the synthesis of C-3 alkylated indoles from 2-(2-nitrophenyl)ethan-1-ol and alcohols. [a]

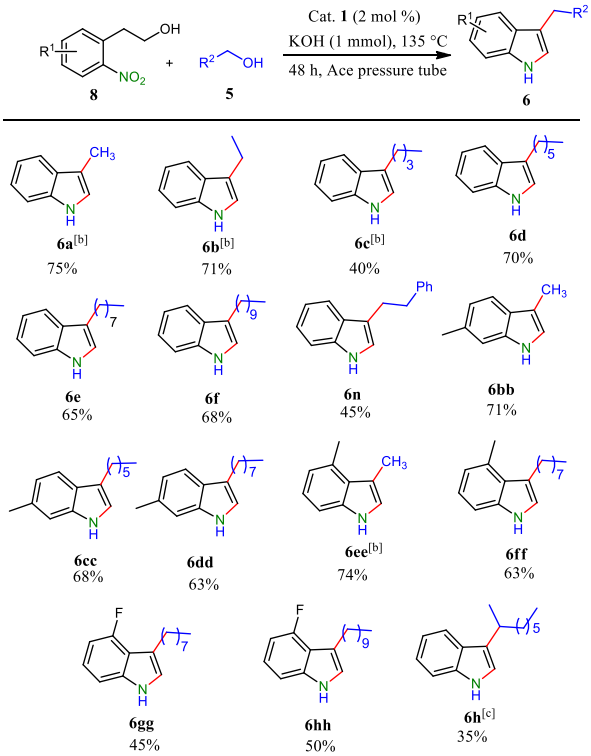


Entry	**10a** (mmol)	**5d** (mmol)	Base (mmol)	Time (h)	**6d**	**4a**
1	0.5	1.5	KOH (0.5 mmol)	48	20	30
2	0.5	2.5	KOH (0.5 mmol)	48	40	10
3	0.5	2.5	KOH (1 mmol)	48	70	-
4	0.5	5	KOH (1 mmol)	48	50	-
5	0.5	2.5	^{t}BuOK (1 mmol)	48	30	-
6	0.5	2.5	KOH (1 mmol)	24	10	30
7	0.5	2.5	K_3PO_4 (1 mmol)	48	35	-
8	0.5	2.5	Cs_2CO_3 (1 mmol)	48	-	-
9	0.5	2.5	K_2CO_3 (1 mmol)	48	-	-

[a] Reaction conditions: 2-(2-nitrophenyl)ethan-1-ol (0.5 mmol), 1-hexanol (2.5 mmol), Cat **1** (0.01 mmol, 2 mol %) 15 mL Ace pressure tube, 135 °C, 48 h.

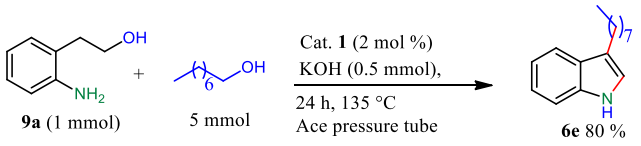
Next, we turned our attention to investigate the scope and limitation of the present protocol with respect to various aliphatic alcohols. Various primary aliphatic alcohols responded well with 2-(2-nitrophenyl)ethan-1-ol providing moderate to good yield (40%-75%) (Table **5**, Entries **6a-6n**).

Table 5. Substrate scope for the synthesis of C-3 alkylated indoles from 2-(2-nitrophenyl)ethan-1-ol and alcohols.[a]



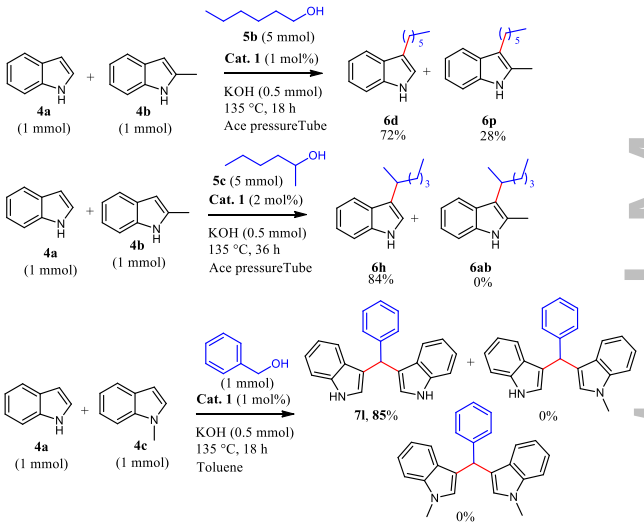
[a] Reaction conditions: 2-(2-nitrophenyl)ethan-1-ol (0.5 mmol), 1-hexanol (2.5 mmol), catalyst **1** (0.01 mmol, 2 mol %), KOH (1 mmol), 15 mL Ace pressure tube, 135 °C, 48 h. [b] 1 mL alcohol. [c] 72 h.

The reactions between substituted 2-(2-nitrophenyl)ethan-1-ol and other primary alcohols has also been studied. The representative substrates reacted well with methanol, 1-hexanol and 1-octanol, 1-decanol (Table-**5**, Entries **6bb-6hh**) under same condition. Secondary alcohol like 2-octanol furnish desired product with 35% yield (**6h**).



Scheme 3. C-3 alkylated indoles from 2-(2-Aminophenyl)ethan-1-ol.

To prove that the reaction proceeds through the formation of 2-(2-Aminophenyl)ethan-1-ol (**9a**), we reacted octanol with it under the standard reaction conditions. To our delight, the desired C-3 alkylated indole was isolated in good yield which indicated the involvement of 2-(2-Aminophenyl)ethan-1-ol as an intermediate in the reaction.

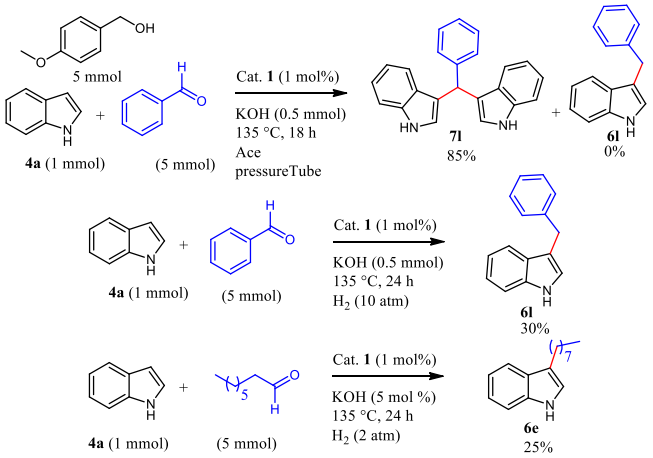


Scheme 4. Competitive Reactions.

It was of interest to us to explore the reactivity and selectivity difference between indole and 2-substituted indole and primary and secondary alcohol (Scheme 4). Thus, when an equimolar mixture of indole and 2-methylindole (1 mmol) was reacted with 1-hexanol (5 mmol) in presence of 1 mol% cat **1** and 0.5 mmol base, **6d** and **6p** were formed in a ratio of 72:28 after 18 h. Under the similar reaction condition when the equimolar mixture of indole and 2-methyl indole was reacted with secondary alcohol such as 2-hexanol, **6h** was obtained in 84% yield whereas no **6ab** was isolated. Thus, in the competitive C-3 alkylation, 2-methylindole reacts slower. Next, we

thought to examine the scope of our protocol to synthesize unsymmetrical bis(indolyl)methanes [35] by reacting 1:1 mixture of indole and 1-methylindole with benzyl alcohol. However, exclusively symmetrical bis(indolyl)methanes **7l** was isolated in 85% yield.

To shed light on the proposed mechanistic pathway, we performed some control experiments (Scheme 5). During the synthesis of C-3 alkylated indole, the corresponding aldehyde is detected which indicates the dehydrogenation of the alcohol under the reaction conditions. Then, we wanted to investigate the hydrogenation step of *α,β*–unsaturated imine (vinylogous imine). Thus, indole was reacted with a mixture of benzaldehyde and 4-methoxybenzyl alcohol under the optimized reaction condition. 3,3'-(Phenylmethylene)bis(1H-indole) **7l** was obtained exclusively (85%) and no 3-benzylated indole was observed. This suggested that the rate of formation of 3,3'-(phenylmethylene)bis(1H-indole) from indole and aldehyde is much faster than the dehydrogenation. Hence, vinylogous imine converted completely to the bisindolylmethane before the generation of a sufficient amount of H_2. Then, we reacted indole with octanal/benzaldehyde under H_2 pressure. We observed the formation of C-3 alkylated indole together with bisindolylmethane. Interestingly, the hydrogenation of aldehyde to the corresponding alcohol was also observed. These results suggested that the developed catalyst is capable of dehydrogenating alcohol and also can hydrogenate aldehyde under H_2 pressure. In the C-3 alkylation reaction, the formed aldehyde is immediately captured by the indole to form vinylogous imine, which is only available for hydrogenation to give the desired C-3 alkylated indole. These results strongly allowed us to hypothesize that the slow generation of aldehyde and its coordination to the complex might be the key factor to get the good yield of the desired product in the C-3 alkylation reaction of indole.



Scheme 5. Control experiments

Conclusion

In summary, we have developed an acridine-derived air-stable ruthenium pincer complex catalysed C-3 alkylation of indoles with alcohols. A highly atom economical and environmentally benign "borrowing hydrogen" strategy was applied to activate a wide range of primary and secondary aliphatic alcohols for the synthesis of several C-3 alkylated indoles. Interestingly, we are also able to construct selectively bis(indolyl)methane scaffold from the same set of alcohols and indoles just by tuning the reaction conditions. The present protocol is successfully applied to synthesize different structurally important compounds such as arundine, vibrindole A and tryptamine based alkaloid derivatives. Furthermore, we demonstrated the first ruthenium catalysed one-pot synthesis of C-3 alkylated indole directly from 2-(2-nitrophenyl)ethan-1-ol and primary alcohol *via* sequential multistep reaction.

Experimental Section

General procedure for C-3 alkylation of indoles:

Indole (1 mmol), alcohol (5 mmol), complex **1** (7.6 mg, 0.01 mmol), and KOH (28 mg, 0.5 mmol) were placed in a 30 mL Ace pressure tube under argon atmosphere. The tube was sealed with screw cap and then it was immersed in an oil bath at 135 °C and stirred at this temperature for 18 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane, and filtered over a plug of celite. The solvent was evaporated under reduced pressure and the residue obtained was purified by column chromatography (Hexane:Ethylacetate 50:1) on silica gel to afford the desired product.

General procedure for synthesis of bisindolylmethane from indoles and alcohols:

Indole (1 mmol), alcohol (0.5 mmol), complex **1** (3.8 mg, 0.005 mmol), and KOH (14 mg, 0.25 mmol) were placed in a 2-neckd round bottom flask fitted with a coil condenser in argon atmosphere and added 1 mL toluene. Then, the reaction was refluxed for 18 h at 135 °C. After that, the reaction mixture was filtered through celite and the purification of the crude product was done by column chromatography using 10% ethylacetate in hexane.

General procedure for one-pot synthesis of substituted indoles from 2-(2-nitrophenyl)ethan-1-ol and alcohols:

2-(2-nitrophenyl)ethan-1-ol (0.5 mmol), alcohol (2.5 mmol), complex **1** (7.6 mg, 0.01), and KOH (28 mg, 0.5 mmol) were placed in a 15 mL Ace pressure tube under argon atmosphere. The tube was sealed with screw cap and then it was immersed in an oil bath at 135 °C and stirred at this temperature for 48 h. After that, the reaction mixture was cooled to room temperature, diluted with dichloromethane and filtered over a plug of celite. The solvent was evaporated under reduced pressure and the residue obtained was purified by flash chromatography (Hexane:Ethylacetate 50:1).

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[18] We observed that the acceptorless dehydrogenation step become less favourable below 135 °C.[17a] Thus, in the C-3 alkylation reaction of indole, the first step, which is the acceptorless dehydrogenation become less facile leading to very poor yield of the desired product.

[19] We are not able to find out any interaction of cation with our complex. The optimum basicity and solubility might be an essential factor in this type of reaction. In the case of $CsOH.H_2O$, the water of crystallization might be responsible for the reduced reactivity.

[20] In toluene, the liberation of H_2, might be more favourable under this vigorous refluxing condition. Thus, the hydrogenation of α,β–unsaturated imine

(vinylogous imine) becomes less favourable which increases the chance of formation bisindolylmethanes *via* nucleophilic attack to vinylogous imine by another indole molecule. Thus, toluene was used for the synthesis of bisindolylmethane.

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FULL PAPER

Ruthenium Pincer Catalyzed Selective Synthesis of C-3 Alkylated Indoles and Bisindolylmethanes Directly from Indoles and Alcohols

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