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Ligand-Free $RuCl_3$-Catalyzed Alkylation of Methylazaarenes with Alcohols

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[§] Shanghai Institute of Organic Chemistry

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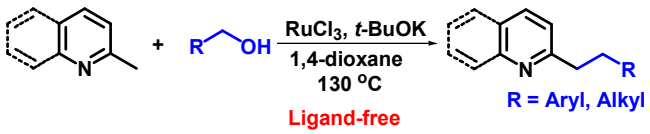


ABSTRACT: $RuCl_3$ efficiently catalyzes the alkylation of methylquinolines, methylpyridines, 2-methyl-benzooxazoles and 2-methyl-quinoxalines with alkyl- or aryl-alcohols as alkylating agents. This synthetically useful and atom economical transformation does not require additional ligand. The mechanistic study indicated the alkylation reaction underwent a step-wise transfer hydrogenation, aldol condensation and hydrogenation reaction pathway.

INTRODUCTION

Metal-catalyzed C(sp^3)-H bond functionalization is a useful transformation for the construction of C-C bonds.[1] The direct C(sp^3)-H bond activation of methylazaarenes provides valuable access to alkylazaarene derivatives with applications in medicinal chemistry,[2] organic catalysis,[3] and material sciences.[4] Oxidative functionalization of the benzylic C(sp^3)-H bonds of alkylazaarenes mediated by palladium,[5] copper,[6-8] rhodium,[9] Lewis acids,[10-13] Brønsted acids,[14] iodine,[15] microwave irradiation,[16] or metal-free catalysts[17-19] have been developed. Once activation is achieved, the reactive intermediate will add to the C=N bond of aldimines,[5a,5c,6c,11b,13a,17a] and imines,[17c] the C=C bond of olefins,[6a,7a] methylenemalononitriles,[10a] α,β-unsaturated carbonyls,[10c,12a,15c] but-2-ene-1,4-diones,[12a] and maleimide,[18c] the C=O bond of aldehydes,[10b,13b,14b,15b,16a,16b,16c,17c,19a,19c] isatins,[15a,16c] 1-methylindoline-2,3-dione,[3b,14a] α-trifluoromethyl carbonyls,[11c] aldehyde esters,[7b,11a] aryl glyoxals,[19b] and ketene,[9] the N=N double

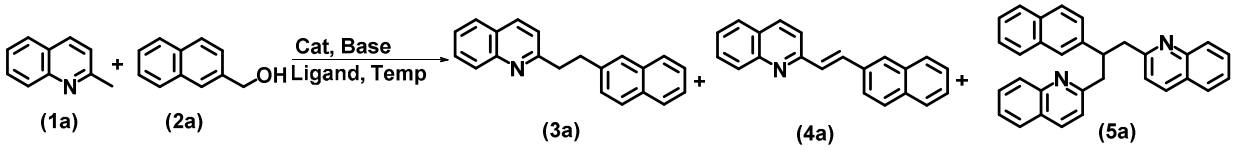
bonds of azodicarboxylates,[5b] and substitute for the C-N bond of amines,[6b,8b,17b] and the C-X bond of aryl halides,[5d] and bromoacrylate.[3d] Many coupling partners are known, but alcohols are underutilized in this respect, despite being easier to handle, generally less toxic and more readily available.[20] In recent years the α-alkylation of methyl aryl ketones,[21,22] secondary alcohols,[23,24] amides[25] and esters[26] with primary alcohols as alkylating agents has provided an economical and efficient method for C-C bond formation.[27,28] For example, Yus et al. demonstrated that $[Ru(DMSO)_4]Cl_2$ catalyzes α-alkylation reactions of ketones and secondary alcohols with primary alcohols as alkylating agents, respectively.[29] To date three papers reported the introduction of alkyl-chain moieties onto pyridines or quinolines using alcohols as the alkylating sources.[30-32] In 2010, Kempe and co-workers investigated the α-alkylation of methyl-N-heteroaromatic compounds with alcohols catalyzed by $[IrCl(cod)]_2$ coupled with P,N-ligand $Py_2NP(iPr)_2$ (Py = pyridinyl, Pr = propyl).[30] Obora and co-workers prepared alkylquinolines from 2-methylquinoline and alcohols catalyzed by $[Ir(OH)(cod)]_2/PPh_3$.[31] Shimizu *et al*. demonstrated the alkylation of 2-methylquinoline with alcohols using Pt nanoclusters supported by γ-Al_2O_3 (Pt/Al_2O_3) at high temperature (170 ºC).[32] These reactions required expensive metals and hard to separate phosphine ligands or high temperatures which limits the substrate scope. We have a long-standing interested in the hydrogen-transfer reaction[33] and have found that alcohol substrates themselves can act as labile ligands to accelerate the $RuCl_3$-catalyzed reductive N-alkylation of nitroarenes with alcohols. Herein we report a simple and versatile method for the preparation of various 2-alkylazaarenes from methylazaarenes and alcohols catalyzed by $RuCl_3$, without the need for additional ligands.

RESULTS AND DISCUSSION

The reaction of 2-methylquinoline (**1a**) with naphthalen-2-yl-methanol (**2a**) was chosen as a model reaction (Table 1). Reaction of **1a** (2.0 mmol) with **2a** (1.0 mmol) in the presence of 2.0 mol% $RuCl_2(PPh_3)_3$ as the catalyst and *t*-BuOK (0.5 mmol) as base provided the desired compound 2-2-(2-(naphthalen-2-yl)ethyl)quinoline (**3a**) in 75% isolated yield (Table 1, entry 1). The same reaction produced **3a** in a lower yield (70%) using $Ru(PPh_3)_2(CO)_2Cl_2$ as the catalyst, but the product was contaminated with 2-(2-(naphthalen-2-yl)vinyl)quinolone (**4a**) in 6% yield (entry 2). The addition of PPh_3, bisdiphenylphosphinomethane (dppm) or 1,2-bis(diphenylphosphino)ethane (dppe) did not increase the activity of $[Ru(p\text{-cymene})Cl_2]_2$, $Ru_3(CO)_{12}$ or $RuCl_3{\cdot}3H_2O$ (entries 3-7). Interestingly, $RuCl_3{\cdot}3H_2O$ alone gave the best results, with the yield up to 78% (entry 8). The base *t*-BuOK proved most effective (entry 8), slightly better than KOH (entry 9) while weak bases K_2CO_3 and K_3PO_4 were almost inactive (entries 10 and 11). An increased proportion of *t*-BuOK (60 mol%) led to a slightly higher yield (84%, entry 12), but beyond this amount, the yield actually decreased from 84% to 72% to 54% for stoichiometries of 60 mol%, 70 mol% and 90 mol%, respectively (entries 12-14). Higher or lower **1a**/**2a** molar ratios resulted in a decrease in the yield of **3a** (entries 15 and 16). When the catalyst loading was decreased from 2 mol% to 1 mol%, a lower yield was observed (entry 17) and a higher catalyst loading (3 mol%) produced **3a** in 74% together with a byproduct 2,2'-(2-(naphthalen-2-yl)propane-1,3-diyl)diquinoline (**5a**, in 5% yield, entry 18). A strong solvent dependence of the coupling reaction was observed. Dioxane proved to be the most suitable solvent (entry 12). The same reaction gave a 52% yield in toluene, 50% yield in chlorobenzene and 46% yield in mesitylene (entries 19-21). At a lower temperature (120 ºC), the reaction proceeded in a commensurately yield (69%, entry 22), while a higher temperature (140 ºC) did

not increase the yield. Thus the optimized reaction conditions were found to be 2 mol % of $RuCl_3 \cdot 3H_2O$ and 60 mol % of *t*-BuOK (as the base) in 1,4-dioxane as solvent at 130 ºC for 24 h.

Table 1. Optimizing reaction conditions for the alkylation reaction of 1a with 2a[a].



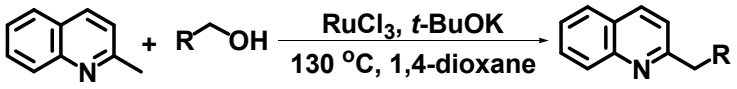
Entry	Cat.	Ligand (mol%)	Base (mol%)	Solvent	Yield[b]		
					3a	**4a**	**5a**
1	$RuCl_2(PPh_3)_3$		*t*-BuOK (50)	1,4-dioxane	75%	trace	
2	$Ru(PPh_3)_2(CO)_2Cl_2$		*t*-BuOK (50)	1,4-dioxane	70%	6%	
3	$Ru_3(CO)_{12}$	PPh_3 (5)	*t*-BuOK (50)	1,4-dioxane	55%	5%	
4	[Ru(*p*-cymene)Cl_2]$_2$	PPh_3 (5)	*t*-BuOK (50)	1,4-dioxane	68%	trace	
5	$RuCl_3 \cdot 3H_2O$	PPh_3 (5)	*t*-BuOK (50)	1,4-dioxane	77%		
6	$RuCl_3 \cdot 3H_2O$	dppm (2.5)	*t*-BuOK (50)	1,4-dioxane	73%		
7	$RuCl_3 \cdot 3H_2O$	dppe (2.5)	*t*-BuOK (50)	1,4-dioxane	75%		
8	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (50)	1,4-dioxane	78%		
9	$RuCl_3 \cdot 3H_2O$		KOH (50)	1,4-dioxane	70%	trace	
10	$RuCl_3 \cdot 3H_2O$		K_2CO_3 (50)	1,4-dioxane	trace		
11	$RuCl_3 \cdot 3H_2O$		K_3PO_4 (50)	1,4-dioxane	trace		
12	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	84%		
13	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (70)	1,4-dioxane	72%		
14	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (90)	1,4-dioxane	54%		
15[c]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	74%		

16[d]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	73%		
17[e]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	75%		
18[f]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	74%		5%
19	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	toluene	52%		
20	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	chlorobenzene	50%		
21	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	mesitylene	46%	trace	
22[g]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	69%		
23[h]	$RuCl_3 \cdot 3H_2O$		*t*-BuOK (60)	1,4-dioxane	84%		

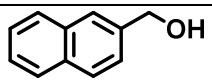
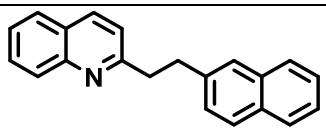
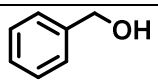
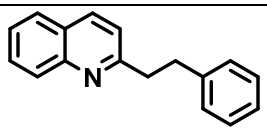
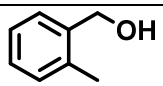
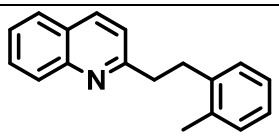
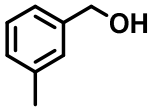
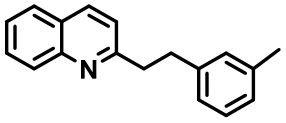
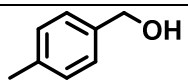
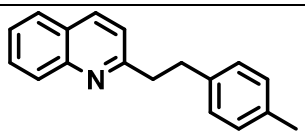
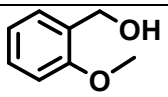
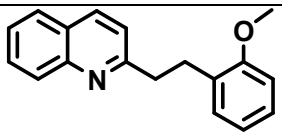
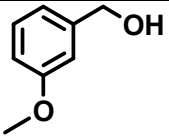
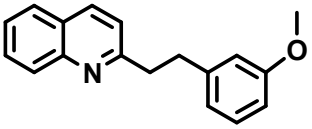
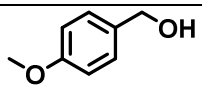
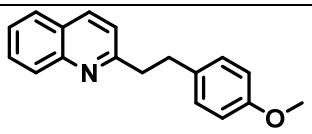
[a]**1a** (2.0 mmol, 286 mg), **2a** (1.0 mmol, 158 mg), Cat. (2 mol%) and base in solvent (1 mL) at 130 ºC for 24 h. [b]Isolated yield. [c]**1a** (1.8 mmol) and **2a** (1.0 mmol). [d]**1a** (2.2 mmol) and **2a** (1.0 mmol). [e]1 mol% $RuCl_3 \cdot 3H_2O$. [f]3 mol% $RuCl_3 \cdot 3H_2O$. [g]at 120 ºC [h]at 140 ºC.

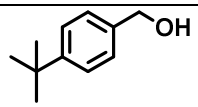
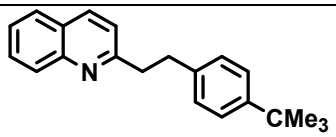
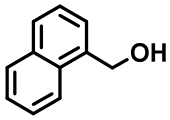
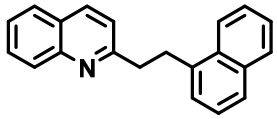
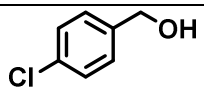
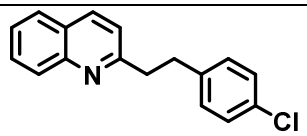
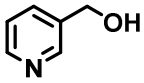
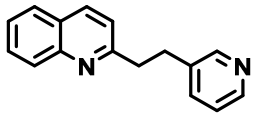
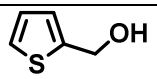
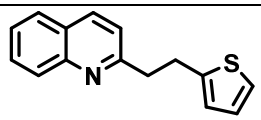
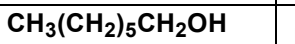
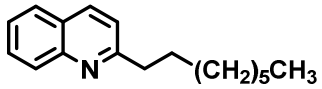
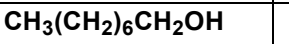
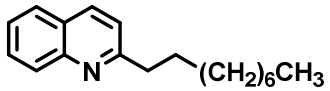
With the optimized reaction conditions in hand, a variety of benzyl alcohol derivatives bearing electron-rich, -neutral and -withdrawing substituents were investigated as substrates for this cross-coupling reaction (Table 2). The electronic nature of the substituents on the phenyl rings of the alcohols had some effect on the catalytic activity. Benzyl alcohols with electron-rich and electron-neutral groups reacted smoothly to produce the desired products in 78-90% yield (**3a-3j**). By contrast, (4-chlorophenyl)methanol with an electron-withdrawing group on phenyl provided product **3k** in 45% isolated yield. *Ortho*- or *meta*-positioned substituents did not hamper the alkylation reaction (entries 3, 4, 6 and 7). It is noteworthy that heteroatom-containing alcohols like pyridin-3-yl-methanol and thiophen-2-ylmethanol reacted smoothly to afford the corresponding products 2-(2-pyridin-3-yl-ethyl)-quinoline (**3l**, 65%) and 2-(2-thiophen-2-yl-ethyl)-quinoline (**3m**, 57%), respectively (entries 12 and 13). Non-activated primary aliphatic alcohols (heptan-1-ol and octan-1-ol) required higher alcohol/**1a** molar ratios to complete the alkylation reactions in 55% and 56% isolated yields (**3n** and **3o**), respectively.

Table 2. $RuCl_3$-Catalyzed Reactions of 1a with Primary Alcohol (2).



(1a) (2) (3)

Entry[a]	Alcohol	Product		Yield[b]
1			**3a**	84%
2			**3b**	88%
3			**3c**	78%
4			**3d**	79%
5			**3e**	80%
6[c]			**3f**	78%
7[c]			**3g**	79%
8[c]			**3h**	85%

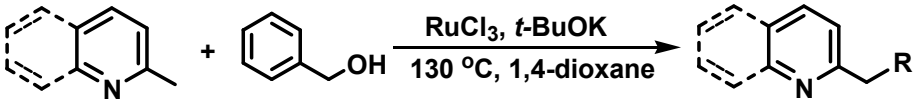
9			**3i**	82%
10			**3j**	90%
11			**3k**	45%
12[c]			**3l**	65%
13[d]			**3m**	57%
14[d,e]			**3n**	55%
15[d,e]			**3o**	56%

[a]**1a** (2.0 mmol), **2** (1.0 mmol), $RuCl_3 \cdot 3H_2O$ (2 mol%) and *t*-BuOK (60 mol%) in 1,4-dioxane (1 mL) at 130 ºC for 24 h. [b]Isolated yield. [c]*t*-BuOK (70 mol%). [d]*t*-BuOK (90 mol%). [e]**1a** (1.0 mmol) and **2** (2.0 mmol).

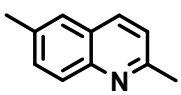
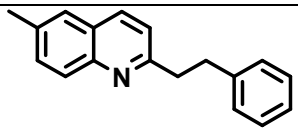
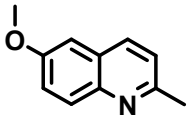
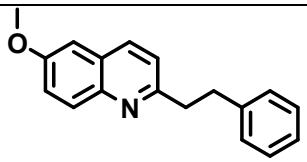
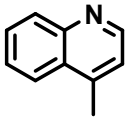
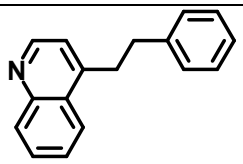
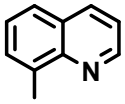
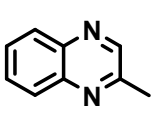
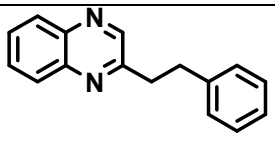
Encouraged by the high efficiency for the reaction of 2-methylquinoline with alcohols described above, we investigated other methyl azaarenes as potential substrates (Table 3). This alkylation reaction was compatible with a variety of 2- and 4-methyl analogues including 4-methylquinoline, 2-methylquinoxaline, 2-methylpyridine, 4-methylpyridine, and 2-methyl-benzooxazole under the standard or similar reaction conditions. 2,6-Dimethyl-quinoline and 6-methoxy-2-methyl-quinoline gave the expected products in high yields (87% (**3p**), 89% (**3q**)). 4-Methyl-quinoline reacted to give **3r** in 60% yield under standard conditions while 8-

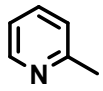
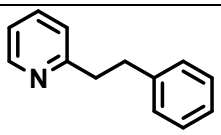
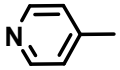
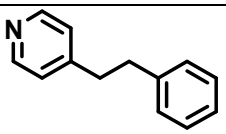
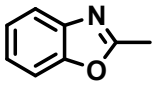
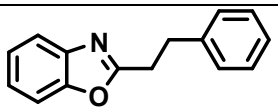
methylquinoline was inert. 2-Methylquinoxaline gave the desired methyl-alkylated product (**3s**) in 84% isolated yield (entry 5). The alkylation of 2- or 4-methylpyridine in the presence of 100 mol% *t*-BuOK afforded the corresponding products (**3t** and **3u**) albeit in moderate yields (entries 6 and 7). The use of 2-methyl-benzooxazole gave the corresponding methyl-alkylated product (**3v**) in a good yield (entry 8).

Table 3. $RuCl_3$-Catalyzed Reactions of Methylazaarene (1) with Benzyl Alcohol (2b).



(1) (2b) (3)

Entry[a]	Alcohol	Product		Yield[b]
1			**3p**	87%
2			**3q**	89%
3			**3r**	60%
4		-	-	-
5			**3s**	84%

6[c,d]			**3t**	34%
7[c,d]			**3u**	29%
8			**3v**	56%

[a]**1** (2.0 mmol), **2b** (1.0 mmol), $RuCl_3 \cdot 3H_2O$ (2 mol%) and *t*-BuOK (60 mol%) in 1,4-dioxane (1 mL) at 130 ºC for 24 h. [b]Isolated yield. [c]**1** (3.0 mmol) and **2b** (1.0 mmol). [d]*t*-BuOK (90 mol%).

The coupling of **1a** and **2a** was monitored over time using HPLC to help elucidating the reaction mechanism (Figure 1). Intermediates 2-(2-(naphthalen-2-yl)vinyl)quinoline (**4a**) and 2-naphthaldehyde (**6a**) were formed initially, concomitant with a sharp decrease in the concentration of **1a** and **2a**, and then replaced by product **3a**. In a separate experiment, the reaction of **6a** and 2-methylquinoline for half an hour in the presence of *t*-BuOK resulted in the formation of **4a** in 27% yield coupled with product **3a** in 1.5% yield (Eq. 1), supporting the hypothesis that **4a** is an intermediate in the reaction. Moreover, in another check experiment, the transfer hydrogenation of **4a** by benzyl alcohol with $RuCl_3$/*t*-BuOK (Eq. 2, Scheme 1) gave the hydrogenated product **3a** in 81% yield. Unsaturated intermediate **4a** could also be reacted with **1a** under the optimized reaction conditions and likewise gave the transfer hydrogenation product **3a** (32% yield) together with addition product **5a** (28% yield, Eq. 3). However, the transfer hydrogenation reaction of **4a** with **2a** is significantly faster than the reaction of **4a** with **1a** under the same conditions.

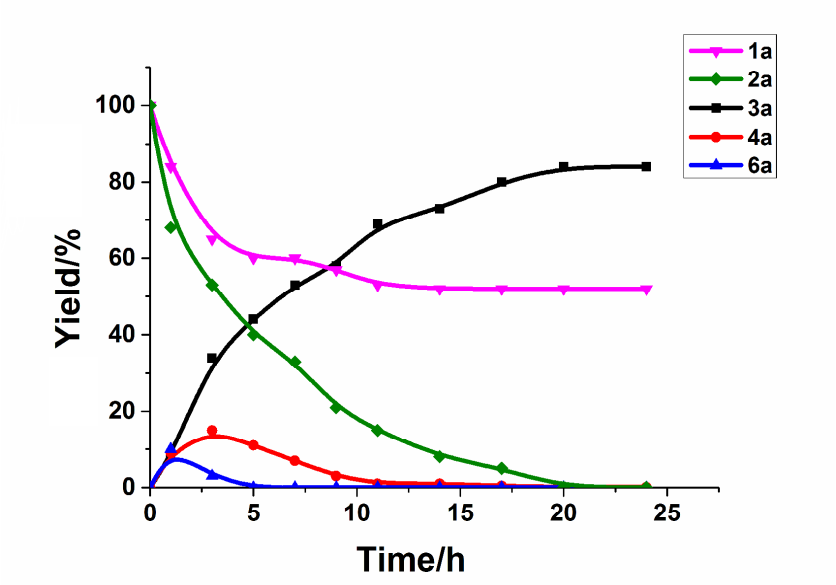
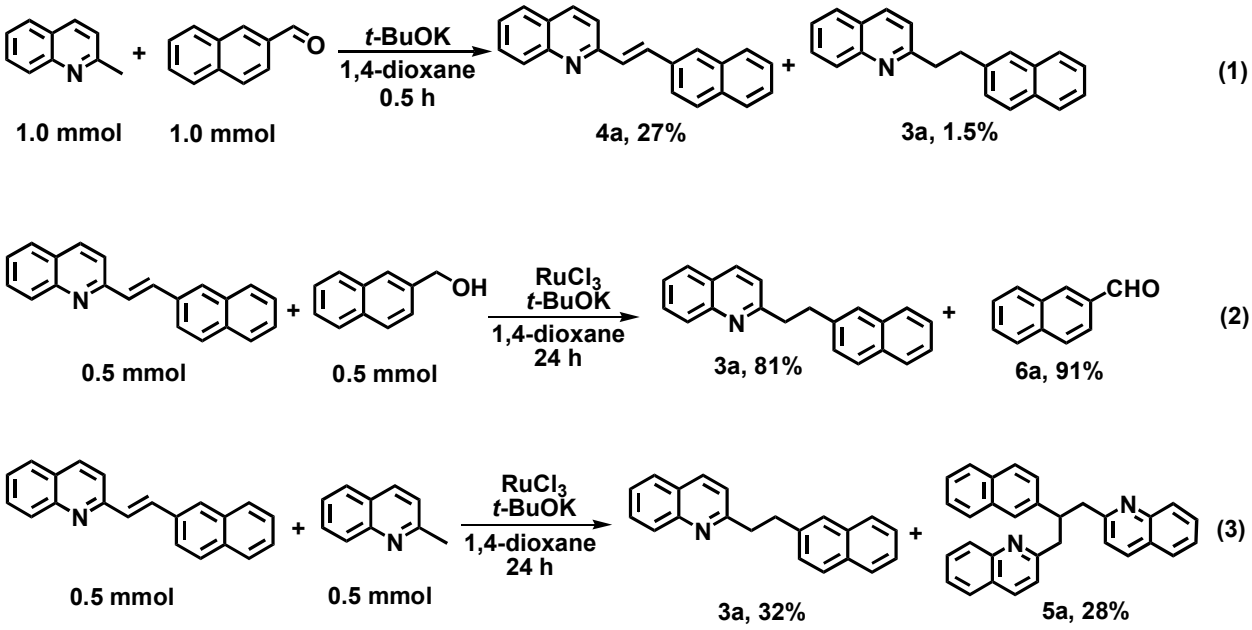


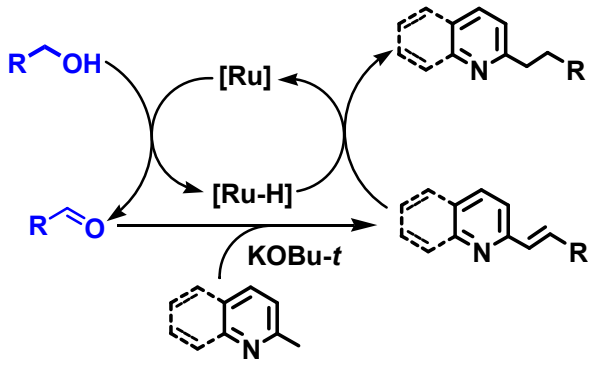
Figure 1. Time-course monitoring of the reaction of **1a** with **2a**.



These results, coupled with the experimental data from the previous reports[30-32] can be used to formulate a mechanism for the alkylation of methylazaarenes with alcohols (Scheme 1). Step 1 is the dehydrogenation of alcohol to aldehyde and formation of a ruthenium-hydride

intermediate. This aldehyde undergoes condensation with methylazaarene in Step 2 to produce an alkenylquinoline intermediate. Step 3 involves the hydrogenation of alkenylquinoline by a ruthenium hydride complex to generate the alkylated quinoline.

Scheme 1. Proposed Mechanism for the Alkylation of Methylazaarenes with Alcohols.



CONCLUSIONS

An efficient and convenient ligand-free $RuCl_3$-catalyzed alkylation of methylquinoline with alcohols has been developed. Various benzylic and aliphatic alcohols can be used as the alkylating agent and this simple catalytic system also promotes the α-alkylation of methylpyridines, 2-methyl-benzooxazole and 2-methyl-quinoxaline. The reaction proceeds through a one-pot sequence of transfer hydrogenation/aldol condensation/hydrogenation steps and is an easy-to-perform and atom-economical protocol for the synthesis of alkylazaarenes.

EXPERIMENTAL SECTION

General Procedure

General. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 151 MHz, respectively, in $CDCl_3$ or DMSO-d_6 using a BRUKER AVANCE III HD spectrometer. ^{1}H and ^{13}C chemical shifts are reported in parts per million relative to Me_4Si using the residual solvent signal as an internal reference. High resolution mass spectra (HRMS) were obtained with a GCT Premier (Micromass UK limited) chemical ionization time-of-flight mass spectrometer (CI-TOF). The uncorrected melting points were measured on a Mel-Temo II apparatus.

Typical Reaction (Table 2, entry 1). A mixture of $RuCl_3 \cdot 3H_2O$ (5 mg, 0.02 mmol), *t*-BuOK (68 mg, 0.6 mmol), **1a** (286 mg, 2 mmol), and **2a** (158 mg, 1 mmol) in 1,4-dioxane (1 mL) was stirred at 130 °C for 24 h under N_2. The product **3a** was isolated by column chromatography (300−400 mesh silica gel, petroleum ether/ethyl acetate = 20/1) in 84% yield (240 mg) as a white solid.

2-(2-(naphthalen-2-yl)ethyl)quinolone (3a).[31] Yield: 237 mg (84%), pale yellow solid, mp: 118.3-119.1 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.25 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.88–7.76 (m, 4H), 7.72 (t, J = 7.5 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.51–7.37 (m, 4H), 3.37–3.24 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.5, 147.3, 139.1, 136.1, 133.1, 131.6, 129.4, 128.4, 127.7, 127.7, 127.4, 127.4, 127.3, 126.5, 126.2, 125.9, 125.7, 125.2, 121.7, 39.7, 34.8. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{18}N$ 284.1439; Found 284.1442.

2-phenethylquinoline (3b).[31] Yield: 205 mg (88%), pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.25 (d, J = 8.4 Hz, 1H), 7.94 (dd, J = 17.6, 8.2 Hz, 2H), 7.72 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 3.3 Hz, 4H), 7.21–7.11 (m, 1H),

3.26–3.18 (m, 2H), 3.14–3.06 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.4, 147.3, 141.4, 136.0, 129.2, 128.4, 128.3, 128.2, 127.7, 126.4, 125.8, 125.6, 121.6, 39.9, 34.7. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{17}H_{16}N$ 234.1283; Found 234.1290.

2-(2-methylphenethyl)quinolone (3c).[31] Yield: 193 mg (78%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 17.6, 8.5 Hz, 2H), 7.78 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.50 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.23–7.18 (m, 2H), 7.17–7.07 (m, 3H), 3.29–3.22 (m, 2H), 3.17–3.11 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1, 148.1, 139.8, 136.4, 136.2, 130.3, 129.6, 129.0, 129.0, 127.7, 126.9, 126.3, 126.2, 125.9, 121.6, 39.8, 33.4, 19.5. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}N$ 248.1439; Found 248.1436.

2-(3-methylphenethyl)quinolone (3d).[31] Yield: 195 mg (79%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.75 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.68 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.47 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.08 (s, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 3.27 (dd, *J* = 10.0, 6.2 Hz, 2H), 3.11 (dd, *J* = 9.9, 6.4 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.0, 148.0, 141.5, 138.0, 136.3, 129.5, 129.4, 128.9, 128.4, 127.6, 126.9, 126.8, 125.9, 125.6, 121.6, 41.1, 36.0, 21.5. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}N$ 248.1439; Found 248.1440.

2-(4-methylphenethyl)quinolone (3e).[31] Yield: 198 mg (80%), pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, *J* = 8.4 Hz, 1H), 7.94 (dd, *J* = 19.5, 8.2 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.14 (d, *J* = 7.7 Hz, 2H), 7.06 (d, *J* = 7.6 Hz, 2H), 3.23–3.15 (m, 2H), 3.09–3.01 (m, 2H), 2.24 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.5, 147.3, 138.3, 136.1, 134.7, 129.3, 128.8, 128.4, 128.2, 127.7, 126.4, 125.7,

121.7, 40.0, 34.3, 20.6. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}N$ 248.1439; Found 248.1427.

2-(2-methoxyphenethyl)quinolone (3f).[3a] Yield: 205 mg (78%), pale yellow liquid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 8.4 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 7.76–7.58 (m, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.27–7.07 (m, 3H), 6.83 (dd, J = 14.5, 7.6 Hz, 2H), 3.76 (s, 3H), 3.33–3.21 (m, 2H), 3.19–3.09 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 162.4, 157.5, 147.9, 136.0, 129.9, 129.8, 129.2, 128.8, 127.4, 127.3, 126.7, 125.6, 121.6, 120.4, 110.1, 55.1, 39.2, 30.6. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}NO$ 264.1388; Found 264.1377.

2-[2-(3-Methoxy-phenyl)-ethyl]-quinoline (3g). Yield: 208 mg (79%), pale yellow liquid. Yield: 79% (208 mg), yellow liquid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.4 Hz, 1H), 7.20 (dt, J = 10.0, 8.1 Hz, 2H), 6.87–6.78 (m, 2H), 6.74 (d, J = 8.1 Hz, 1H), 3.73 (s, 3H), 3.32–3.24 (m, 2H), 3.16–3.08 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.7, 159.7, 148.0, 143.2, 136.3, 129.4, 129.4, 128.8, 127.6, 126.8, 125.8, 121.6, 120.9, 114.1, 111.5, 55.1, 40.9, 36.0. IR (KBr disc): 2955(w), 2930(w), 2833(w), 1637(s), 1617(s), 1600(s), 1584(m), 1491(m), 1426(w), 1384(w), 827(m), 783(w), 745(w) cm^{-1}. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}NO$ 264.1388; Found 264.1397.

2-(4-methoxyphenethyl)quinolone (3h).[31] Yield: 223 mg (85%), pale yellow solid, mp: 55.1-56.3 ºC. ^1H NMR (400 MHz, DMSO-d_6): δ 8.24 (d, J = 8.4 Hz, 1H), 7.94 (dd, J = 19.3, 8.2 Hz, 2H), 7.71 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.17 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 3.69 (s, 3H), 3.18 (t, J = 7.8 Hz, 2H), 3.03 (t, J = 7.8 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.6, 157.5, 147.3, 136.1, 133.3, 129.3, 129.3, 128.4,

127.7, 126.5, 125.7, 121.7, 113.7, 54.9, 40.2, 33.9. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{18}H_{18}NO$ 264.1388; Found 264.1394.

2-(4-(tert-butyl)phenethyl)quinolone (3i).[31] Yield: 237 mg (82%), pale yellow solid, mp: 68.6-69.4 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.25 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.27 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.1 Hz, 2H), 3.20 (dd, J = 9.4, 6.5 Hz, 2H), 3.11–3.02 (m, 2H), 1.23 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.6, 148.0, 147.3, 138.4, 136.1, 129.3, 128.4, 128.0, 127.7, 126.5, 125.7, 125.0, 121.6, 40.0, 34.2, 34.0, 31.2. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{24}N$ 290.1909; Found 290.1913.

2-(2-(naphthalen-1-yl)ethyl)quinolone (3j).[3a] Yield: 255 mg (90%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (dd, J = 14.8, 8.4 Hz, 2H), 7.92 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.68 (dd, J = 16.1, 8.8 Hz, 3H), 7.52–7.40 (m, 3H), 7.36–7.27 (m, 2H), 7.11 (d, J = 8.4 Hz, 1H), 3.64–3.55 (m, 2H), 3.44–3.35 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.9, 148.1, 137.6, 136.2, 133.9, 131.9, 129.4, 129.0, 128.8, 127.6, 126.9, 126.8, 126.1, 125.9, 125.8, 125.6, 125.5, 123.82, 121.6, 40.1, 32.9. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{18}N$ 284.1439; Found 284.1443.

2-(4-chlorophenethyl)quinolone (3k).[31] Yield: 120 mg (45%), pale yellow solid, mp: 57.2-58.1 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, J = 23.4, 8.4 Hz, 2H), 7.80–7.66 (m, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.19 (dt, J = 13.4, 8.0 Hz, 5H), 3.31–3.21 (m, 2H), 3.18–3.09 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.3, 148.0, 140.0, 136.3, 131.7, 129.9, 129.5, 128.9, 128.5, 127.6, 126.8, 125.9, 121.5, 40.7, 35.1. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{17}H_{15}ClN$ 268.0893; Found 268.0882.

2-(2-Pyridin-3-yl-ethyl)-quinoline (3l). Yield: 152 mg (65%), white solid, mp: 70.5-71.9 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.48 (s, 1H), 8.38 (d, J = 4.2 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.94 (dd, J = 13.2, 8.3 Hz, 2H), 7.77–7.66 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46 (d, J = 8.4 Hz, 1H), 7.29 (dd, J = 7.5, 4.9 Hz, 1H), 3.29–3.22 (m, 2H), 3.14 (t, J = 7.7 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 161.0, 149.6, 147.2, 147.1, 136.2, 135.9, 129.4, 128.4, 127.8, 126.5, 125.8, 121.7, 39.2, 31.5. IR (KBr disc): 3049(w), 2922(w), 2859(w), 1617(m), 1598(m), 1562(w), 1574(w), 1425(m), 1400(m), 1384(m), 867(w), 847(w), 827(m), 774(w) cm^{-1}. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2$ 235.1235; Found 235.1232.

2-(2-(thiophen-2-yl)ethyl)quinolone (3m).[3a] Yield: 136 mg (57%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (dd, J = 24.3, 8.4 Hz, 2H), 7.79–7.64 (m, 2H), 7.47 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.09 (d, J = 4.8 Hz, 1H), 6.86 (dd, J = 18.6, 14.2 Hz, 2H), 3.36 (dd, J = 14.4, 5.9 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.0, 147.9, 144.2, 136.3, 129.5, 128.8, 127.6, 126.9, 126.7, 125.9, 124.6, 123.2, 121.5, 41.0, 29.7. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{15}H_{14}NS$ 240.0847; Found 240.0835.

2-octylquinoline (3n).[3a] Yield: 133 mg (55%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 3.03–2.92 (m, 2H), 1.87–1.72 (m, 2H), 1.43–1.23 (m, 10H), 0.87 (t, J = 6.2 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.2, 147.8, 136.5, 129.5, 128.8, 127.6, 126.8, 125.8, 121.5, 39.4, 32.0, 30.2, 29.7, 29.6, 29.4, 22.8, 14.2. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{17}H_{24}N$ 242.1909; Found 242.1913.

2-nonylquinoline (3o).[31] Yield: 143 mg (56%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 2H), 7.78 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.48 (t, J =

7.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 3.03–2.93 (m, 2H), 1.87–1.75 (m, 2H), 1.41–1.22 (m, 12H), 0.87 (t, J = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 163.2, 147.7, 136.6, 129.6, 128.7, 127.6, 126.9, 125.9, 121.5, 39.4, 32.0, 30.2, 29.7, 29.7, 29.7, 29.4, 22.8, 14.2. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}N$ 256.2065; Found 256.2061.

6-methyl-2-phenethylquinoline (3p).[34a] Yield: 215 mg (87%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, J = 16.9, 8.6 Hz, 2H), 7.51 (s, 2H), 7.22 (dt, J = 18.7, 7.6 Hz, 6H), 3.31–3.21 (m, 2H), 3.18–3.08 (m, 2H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.9, 146.6, 141.7, 135.7, 135.7, 131.8, 128.6, 128.6, 128.5, 126.9, 126.5, 126.1, 121.6, 40.9, 36.1, 21.6. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}N$ 248.1439; Found 248.1432.

6-methoxy-2-phenethylquinoline (3q).[34b] Yield: 234 mg (89%), pale yellow solid, mp: 70.1-70.9 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (dd, J = 14.7, 8.8 Hz, 2H), 7.35 (dd, J = 9.0, 1.7 Hz, 1H), 7.30–7.15 (m, 6H), 7.04 (s, 1H), 3.91 (s, 3H), 3.30–3.20 (m, 2H), 3.18–3.09 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 159.3, 157.4, 144.0, 141.7, 135.2, 130.3, 128.6, 128.5, 127.8, 126.1, 122.1, 121.9, 105.3, 55.63, 40.8, 36.2. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{18}NO$ 264.1388; Found 264.1375.

4-phenethylquinoline (3r).[31] Yield: 140 mg (60%), pale yellow solid, mp: 101.2-102.1 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.77 (d, J = 4.3 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.36 (d, J = 4.2 Hz, 1H), 7.29 (d, J = 4.2 Hz, 4H), 7.20 (dd, J = 8.3, 4.1 Hz, 1H), 3.39–3.33 (m, 2H), 3.05–2.97 (m, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 150.1, 147.89, 147.2, 141.0, 129.7, 129.1, 128.4, 128.3, 126.9, 126.5, 126.0, 123.9, 121.0, 35.5, 33.0. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{16}N$ 234.1283; Found 234.1287.

2-phenethylquinoxaline (3s).[31] Yield: 197 mg (84%), pale yellow liquid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.85 (s, 1H), 8.05 (d, J = 7.6 Hz, 2H), 7.86–7.75 (m, 2H), 7.27 (d, J = 4.2 Hz, 4H), 7.18 (dd, J = 8.2, 4.2 Hz, 1H), 3.34–3.28 (m, 2H), 3.13 (t, J = 7.8 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 156.7, 146.4, 141.4, 140.9, 140.6, 130.1, 129.2, 128.8, 128.5, 128.4, 128.3, 126.0, 37.0, 34.1. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2$ 235.1235; Found 235.1224.

2-phenethylpyridine (3t).[31] Yield: 62 mg (34%), pale yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.56 (t, J = 7.4 Hz, 1H), 7.23 (dd, J = 25.3, 6.6 Hz, 5H), 7.14–7.00 (m, 2H), 3.08 (d, J = 4.1 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 161.3, 149.3, 141.6, 136.5, 128.6, 128.5, 126.1, 123.1, 121.3, 40.3, 36.1. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}N$ 184.1126; Found 184.1129.

4-phenethylpyridine (3u).[34c] Yield: 53 mg (29%), pale yellow solid, mp: 68.4-69.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (d, J = 3.1 Hz, 2H), 7.27 (t, J = 7.0 Hz, 2H), 7.23–7.17 (m, 1H), 7.14 (d, J = 7.1 Hz, 2H), 7.07 (d, J = 3.8 Hz, 2H), 2.92 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 150.6, 149.7, 140.7, 128.5, 128.5, 126.3, 124.0, 37.1, 36.6. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{14}N$ 184.1126; Found 184.1125.

2-phenethylbenzo[d]oxazole (3v).[31] Yield: 48 mg (56%), pale yellow solid, mp: 55.2-56.1 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.55 (m, 1H), 7.43–7.34 (m, 1H), 7.26–7.09 (m, 7H), 3.14 (s, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 166.3, 150.9, 141.4, 140.2, 128.7, 128.4, 126.6, 124.7, 124.2, 119.7, 110.4, 32.9, 30.6, 1.1. HRMS (CI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}NO$ 224.1075; Found 224.1081.

2-(2-(naphthalen-2-yl)vinyl)quinolone (4a).[31] Yield: 125 mg (56%), pale yellow solid, mp: 165.2-166.1 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (d, J = 8.4 Hz, 1H), 8.19 (s, 1H), 7.98 (ddd, J = 25.4, 14.2, 5.6 Hz, 8H), 7.77 (t, J = 7.4 Hz, 1H), 7.68–7.50 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 155.6, 147.7, 136.5, 134.1, 133.9, 133.2, 133.0, 129.8, 129.2, 128.7, 128.4, 128.1, 127.8, 127.8, 127.6, 127.0, 126.6, 126.5, 126.2, 123.8, 120.0. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{21}H_{16}N$ 282.1283; Found 282.1289.

2,2'-(2-(naphthalen-2-yl)propane-1,3-diyl)diquinoline (5a). A mixture of $RuCl_3 \cdot 3H_2O$ (7.5 mg, 0.03 mmol), *t*-BuOK (68 mg, 0.6 mmol), **1a** (286 mg, 2 mmol), and **2a** (158 mg, 1 mmol) in 1,4-dioxane (1 mL) were stirred at 130 °C for 24 h under N_2. The product **5a** was isolated by column chromatography (300−400 mesh silica gel, petroleum ether/ethyl acetate = 5/1) in 5% yield (21 mg) as a white solid, mp: 117.6-118.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.4 Hz, 2H), 7.76–7.58 (m, 8H), 7.41 (ddd, J = 16.7, 12.7, 6.9 Hz, 5H), 7.09 (d, J = 8.4 Hz, 2H), 4.25 (p, J = 7.5 Hz, 1H), 3.62–3.48 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 160.7, 147.9, 141.4, 135.8, 133.5, 132.3, 129.2, 128.9, 128.0, 127.7, 127.6, 127.5, 126.7, 126.6, 126.4, 125.8, 125.7, 125.3, 122.1, 46.2, 45.8. IR (KBr disc): 3056(w), 2922(w), 2850(w), 1636(s), 1618(s), 1599(s), 1561(m), 1425(m), 1400(m), 1384(m), 855(m), 820(m), 748(m) cm^{-1}. HRMS (CI-TOF) *m*/*z*: $[M + H]^+$ Calcd for $C_{31}H_{25}N_2$ 425.2018; Found 425.2015.

ASSOCIATED CONTENTS

Supporting Information.

Copies of ^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Shaw, M. H.; Shurtleff, V. W.; Terrett, J. A.; Cuthbertson, J. D.; MacMillan D. W. C. *Science* **2016**, *352*, 1304-1308. (b) Wu, Y. W.; Chen, Y. Q.; Liu, T.; Eastgate, M. D.; Yu, J. Q. *J. Am. Chem. Soc.* **2016**, *138*, 14554-14557. (c) Liao, K. B.; Negretti, S.; Musaev, D. G.; Bacsa, J.; Davies, H. M. L. *Nature* **2016***, 533*, 230-234. (d) Gunanathan, C.; Milstein, D. *Chem. Rev.* **2014**, *114*, 12024-12087.

(2) (a) Dai, J.; Liu, Z. Q.; Wang, X. Q.; Lin, J.; Yao, P. F.; Huang, S. L.; Ou, T. M.; Tan, J. H.; Li, D.; Gu, L. Q.; Huang, Z. S. *J. Med. Chem.* **2015**, *58*, 3875-3891. (b) Zouhiri, F.; Danet, M.; Bénard, C.; Normand-Bayle, M.; Mouscadet, J. F.; Leh, H.; Thomas, C. M.; Mbemba, G.; d'Angelo, J.; Desmaële, D. *Tetrahedron Lett.* **2005**, *46*, 2201-2205. (c) Basak, A.; Abouelhassan, Y.; Norwood IV, V. M.; Bai, F.; Nguyen, M. T.; Jin, S.; Huigens III, R. W. *Chem. Eur. J.* **2016**, *22*, 9181-9189.

(3) (a) Tan, Z. D.; Jiang, H. F.; Zhang, M. *Chem. Commun.* **2016**, *52*, 9359-9362. (b) Kumari, K.; Allam, B. K.; Singh, K. N. *RSC Adv.* **2014**, *4*, 19789-19793. (c) Lee, H. S.; Lee, S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2011**, *52*, 5039-5042. (d) Zhao, L. Q.; Derridj, F.; Djebbar, S.; Bruneau, C.; Doucet, H. *Tetrahedron Lett.* **2015**, *56*, 4354-4358.

(4) (a) Chiu, Y. H.; dos Santos, O.; Canary, J. W. *Tetrahedron* **1999**, *55*, 12069-12078. (b) Pickaert, G.; Cesario, M.; Ziessel, R. *J. Org. Chem.* **2004**, *69*, 5335-5341. (c) Ziessel, R.; Pickaert, G.; Camerel, F.; Donnio, B.; Guillon, D.; Cesario, M.; Prangé, T. *J. Am. Chem. Soc.* **2004**, *126*, 12403-12413. (d) Zhu, Y.; Pavlos, C. M.; Toscano, J. P.; Dore, T. M. *J. Am. Chem. Soc.* **2006**, *128*, 4267-4276.

(5) (a) Qian, B.; Guo, S. M.; Shao, J. P.; Zhu, Q. M.; Yang, L.; Xia, C. G.; Huang, H. M. *J. Am. Chem. Soc.* **2010**, *132*, 3650-3651. (b) Liu, J. Y.; Niu, H. Y.; Wu, S.; Qu, G. R.; Guo, H. M. *Chem. Commun.* **2012**, *48*, 9723-9725. (c) Best, D.; Kujawa, S.; Lam, H. W. *J. Am. Chem. Soc.* **2012**, *134*, 18193-18196. (d) Niwa, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 2643-2645.

(6) (a) Wang, G. W.; Cheng, M. X.; Ma, R. S.; Yang, S. D. *Chem. Commun.* **2015**, *51*, 6308-6311. (b) Xie, H.; Liao, Y. F.; Chen, S. Q.; Chen, Y.; Deng, G. J. *Org. Biomol. Chem.* **2015**, *13*, 6944-6948. (c) Rueping, M.; Tolstoluzhsky, N. *Org. Lett.* **2011**, *13*, 1095-1097.

(7) (a) Wang, G. W.; Li, S. X.; Wu, Q. X.; Yang, S. D. *Org. Chem. Front.* **2015**, *2*, 569-573. (b) Jin, J. J.; Niu, H. Y.; Qu, G. R.; Guo, H. M.; Fossey, J. S. *RSC Adv.* **2012**, *2*, 5968-5971.

(8) (a) Tan, Z. D.; Zhao, H.; Zhou, C. J.; Jiang, H. F.; Zhang, M. *J. Org. Chem.*, **2016**, *81*, 9939-9946. (b) Li, Z.; Wu, S. S.; Luo, Z. G.; Liu, W. K.; Feng, C. T.; Ma, S. T. *J. Org. Chem.* **2016**, *81*, 4386-4392.

(9) Yu, S. J.; Li, Y. Z.; Kong, L. H.; Zhou, X. K.; Tang, G. D.; Lan, Y.; Li, X. W. *ACS Catal.* **2016**, *6*, 7744-7748.

(10) (a) Qian, B.; Shi, D. J.; Yang, L.; Huang, H. M. *Adv. Synth. Catal.* **2012**, *354*, 2146-2150. (b) Mao, D.; Hong, G.; Wu, S. Y.; Liu, X.; Yu, J. J.; Wang, L. M. *Eur. J. Org. Chem.* **2014**, 3009-3019. (c) Komai, H.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Org. Lett.* **2011**, *13*, 1706-1709.

(11) (a) Pi, D. W.; Jiang, K.; Zhou, H. F.; Sui, Y. B.; Uozumi, Y.; Zou, K. *RSC Adv.* **2014**, *4*, 57875-57884. (b) Komai, H.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Synthesis* **2012**, *44*, 2185-2194. (c) Graves, V. B.; Shaikh, A. *Tetrahedron Lett.* **2013**, *54*, 695-698.

(12) (a) Chatterjee, S.; Bhattacharjee, P.; Temburu, J.; Nandi, D.; Jaisankar, P. *Tetrahedron Lett.* **2014**, *55*, 6680-6683. (b) Yavari, I.; Naeimabadi, M.; Halvagar, M. R. *Tetrahedron Lett.* **2016**, *57*, 3718-3721. (c) Li, Y. F.; Guo, F. F.; Zha, Z. G.; Wang, Z. Y. *Chem. Asian J.* **2013**, *8*, 534-537.

(13) (a) Qian, B.; Xie, P.; Xie, Y. J.; Huang, H. M. *Org. Lett.* **2011**, *13*, 2580-2583. (b) Jamal, Z.; Teo, Y. C. *Synlett* **2014**, *25*, 2049-2053.

(14) (a) Niu, R.; Xiao, J.; Liang, T.; Li, X. W. *Org. Lett.* **2012**, *14*, 676-679. (b) Jin, J. J.; Wang, D. C.; Niu, H. Y.; Wu, S.; Qu, G. R.; Zhang, Z. B.; Guo, H. M. *Tetrahedron* **2013**, *69*, 6579-6584.

(15) (a) Vuppalapati, S. V. N.; Lee, Y. R. *Tetrahedron* **2012**, *68*, 8286-8292. (b) Kumar, A.; Gupta, G.; Srivastava, S. *Org. Lett.* **2011**, *13*, 6366-6369. (c) Kumar, A.; Gupta, L. P.; Kumar, M. *RSC Adv.* **2013**, *3*, 18771-18774.

(16) (a) Rao, N. N.; Meshram, H. M. *Tetrahedron Lett.* **2013**, *54*, 5087-5090. (b) Li, V. M.; Gavrishova, T. N.; Budyka, M. F. *Russ. J. Org. Chem.* **2012**, *48*, 823-828. (c) Staderino, M.; Cabezas, N.; Bolognesi, M. L.; Menéndez, J. C. *Synlett* **2011**, *17*, 2577-2579. (d) Meshram, H. M.; Rao, N. N.; Rao, C. L.; Kumar, S. N. *Tetrahedron Lett*. **2012**, *53*, 3963-3966.

(17) (a) Yan, Y. Z.; Xu, K.; Fang, Y.; Wang, Z. Y. *J. Org. Chem.* **2011**, *76*, 6849-6855. (b) Gong, L.; Xing, L. J.; Xu, T.; Zhu, X. P.; Zhou, W.; Kang, N.; Wang, B. *Org. Biomol. Chem.* **2014**, *12*, 6557-6560. (c) Zhang, Y. G.; Xu, J. K.; Li, X. M.; Tian, S. K. *Eur. J. Org. Chem.* **2013**, 3648-3652.

(18) (a) Jiang, L.; Huang, Y. Y.; Yan, Y. Y.; Xie, Y. Y. *Tetrahedron Lett.* **2016**, *57*, 4149-4151. (b) Gulakova, E. N.; Sitin, A. G.; Kuz'mina, L. G.; Fedorova, O. A. *Russ. J. Org. Chem.* **2011**, *47*, 245-252. (c) Li, H. Y.; Xing, L. J.; Xu, T.; Wang, P.; Liu, R. H.; Wang, B. *Tetrahedron Lett.* **2013**, *54*, 858-860.

(19) (a) Xu, L. B.; Shao, Z. Z.; Wang, L.; Zhao, H. L.; Xiao, J. *Tetrahedron Lett.* **2014**, *55*, 6856-6860. (b) Li, B. B.; Wei, H. P.; Li, H. Y.; Pereshivko, O. P.; Peshkov, V. A. *Tetrahedron Lett.* **2015**, *56*, 5231-5234. (c) Fu, S. H.; Wang, L.; Dong, H. X.; Yu, J. Q.; Xu, L. B.; Xiao, J. *Tetrahedron Lett.* **2016**, *57*, 4533-4536.

(20) (a) Huang, F.; Liu, Z. Q.; Yu, Z. K. *Angew. Chem. Int. Ed.* **2016**, *55*, 862-875. (b) Li, H. F.; Zheng, B.; Huang, K. W. *Coord. Chem. Rev.* **2015**, *293-294*, 116-138.

(21) (a) Schlepphorst, C.; Maji, B.; Glorius, F. *ACS Catal.* **2016**, *6*, 4184-4188. (b) Frost, J. R.; Cheong, C. B.; Akhtar, W. M.; Caputo, D. F. J.; Stevenson, N. G.; Donohoe, T. J. *J. Am.*

Chem. Soc. **2015**, *137*, 15664−15667. (c) Elangovan, S.; Sortais, J. B.; Beller, M.; Darcel, C. *Angew. Chem. Int. Ed.* **2015**, *54*, 14483-14486.

(22) (a) Quan, X.; Kerdphon, S.; Andersson, P. G.; *Chem. Eur. J.* **2015**, *21*, 3576-3579. (b) Onodera, G.; Nishibayashi, Y.; Uemura, S. *Angew. Chem. Int. Ed.* **2006**, *45*, 3819-3822. (c) Wang, R. Z.; Ma, J.; Li, F. *J. Org. Chem.* **2015**, *80*, 10769-10776.

(23) (a) Wang, Q. F.; Wu, K. K.; Yu, Z. K. *Organometallics* **2016**, *35*, 1251-1256. (b) Chakrabarti, K.; Paul, B.; Maji, M.; Roy, B. C.; Shee, S.; Kundu, S. *Org. Biomol. Chem.* **2016**, *14*, 10988-10997. (c) Cheung, H. W.; Lee, T. Y.; Lui, H. Y.; Yeung, C. H.; Lau, C. P. *Adv. Synth. Catal.* **2008**, *350*, 2975-2983.

(24) (a) Makarov, I. S.; Madsen, R. *J. Org. Chem.* **2013**, *78*, 6593-6598. (b) Zhang, S. Y.; Tu, Y. Q.; Fan, C. A.; Jiang, Y. J.; Shi, L.; Cao, K.; Zhang, E. *Chem. Eur. J.* **2008**, *14*, 10201-10205. (c) Musa, S.; Ackermann, L.; Gelman, D. *Adv. Synth. Catal.* **2013**, *355*, 3077-3080.

(25) (a) Yao, W. B.; Ma, X. C.; Guo, L.; Jia, X. Q.; Hu, A. G.; Huang, Z. *Tetrahedron Lett.* **2016**, *57*, 2919-2921. (b) Chaudhari, M. B.; Bisht, G. S.; Kumari, P.; Gnanaprakasam, B. *Org. Biomol. Chem.* **2016**, *14*, 9215-9220. (c) Kuwahara, T.; Fukuyama, T.; Ryu, I. *RSC Adv.* **2013**, *3*, 13702-13704. (d) Guo, L.; Liu, Y.; Yao, W.; Leng, X.; Huang, Z. *Org. Lett.* **2013**, *15*, 1144-1147.

(26) (a) Deibl, N.; Kempe, R. *J. Am. Chem. Soc.* **2016**, *138*, 10786-10789. (b) Dang, T. T.; Seayad, A. M. *Adv. Syn. Catal.* **2016**, *358*, 3373-3380. (c) Guo, L.; Ma, X. C.; Fang, H. Q.; Jia, X. Q.; Huang, Z. *Angew. Chem., Int. Ed.* **2015**, *54*, 4023-4027. (d) Iuchi, Y.; Obora, Y.; Ishii, Y. *J. Am. Chem. Soc.* **2010**, *132*, 2536-2537.

(27) (a) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704-712. (b) Obora, Y. *ACS Catal.* **2014**, *4*, 3972-3981. (c) Shimizu, K.-i. *Catal. Sci. Technol.* **2015**, *5*, 1412-1427.

(28) (a) Guillena, G.; Ramón, D. J.; Yus, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2358-2364. (b) Nixon, T. D.; Whittlesey, M. K.; Williams, J. M. J. *Dalton Trans.* **2009**, 753-762.

(29) (a) Martínez, R.; Gabriel, J. B.; Ramón, D. J.; Yus, M. *Tetrahedron Lett.* **2005**, *46*, 3683-3686. (b) Martínez, R.; Ramón, D. J.; Yus, M. *Tetrahedron* **2006**, *62*, 8982-8987.

(30) Blank, B.; Kempe, R. *J. Am. Chem. Soc.* **2010**, *132*, 924-925.

(31) Obora, Y.; Ogawa, S.; Yamamoto, N. *J. Org. Chem.* **2012**, *77*, 9429-9433.

(32) Chaudhari, C.; Siddiki, S. M. A. H.; Shimizu, K. *Tetrahedron Lett.* **2013**, *54*, 6490-6493.

(33) (a) Tan, D. W.; Li, H. X.; Young, D. J.; Lang, J. P. *Tetrahedron* **2016**, *72*, 4169-4176. (b) Tan, D. W.; Li, H. X.; Zhang, M. J.; Yao, J. L.; Lang, J. P. *ChemCatChem* **2017**, ASAP, **DOI:** 10.1002/cctc.201601459.

(34) (a) Shan, G.; Sun, X. Y.; Xia, Q.; Rao. Y. *Org. Lett.* **2011**, *13*, 5770-5773. (b) Bergstrom, F. W.; Norton, T. R.; Seibert, R. A. *J. Org. Chem.* **1945**, *10*, 452-457. (c) Lautens, M.; Roy, A.; Fukuoka, K.; Fagnou, K.; Martin-Matute, B. *J. Am. Chem. Soc.* **2001**, *123*, 5358-5359.