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N-Heterocyclization of Naphthylamines with 1,2- and 1,3-Diols Catalyzed by an Iridium Chloride/BINAP System

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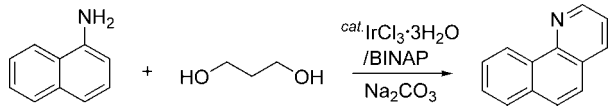

Benzoquinoline derivatives were successfully synthesized by iridium-catalyzed *N*-heterocyclization of naphthylamines with diols. For instance, the reaction of 1-naphthylamine with 1,3-propanediol catalyzed by $IrCl_3$ combined with BINAP as a ligand produced 7,8-benzoquinoline in quantitative yield. The *N*-heterocyclization reaction was found to be markedly influenced by the ligands employed. Benzoindoles were also synthesized by the same strategy from napthylamines with 1,2-diols. A reaction mechanism for the *N*-heterocyclization of naphthylamines with 1,3-diols by $IrCl_3$ was proposed.

Introduction

Indole and quinoline derivatives are a very important class of compounds for the production of pharmaceuticals, herbicides, dyes, etc.[1] There have been several classical methods for the synthesis of these compounds from various starting materials,[2] but it is desired to improve the efficiency of the reaction and to start the reaction from easily available starting materials. The Ru-catalyzed *N*-heterocylization of anilines with diols leading to indoles and quinolines is developed by Tsuji and Watanabe et al.[3a,b] Thereafter, the $RuCl_3/SnCl_2$ system is used in the indole synthesis from aniline and ethylene glycols[3c] or trialkanolamines.[3d] Recently, we reported the Ir-catalyzed quinoline synthesis from 2-aminobenzyl alcohols and ketones without any solvent under relatively mild conditions (at 100 °C for 3 h).[4] Similar Ir-catalyzed quinoline synthesis from anilines and two different aldehydes is also reported.[5] On the other hand, much effort has been spent on the development of a synthetic method for benzoindole and benzoquinoline derivatives,[6] but to our the best knowledge, the synthesis of these compounds by the direct catalytic cyclization of naphthylamines and diols is restricted to 7,8-benzoquinoline synthesis from naphthylamine and 1,3-propanediol by $RuCl_3$ catalyst.[3b]

We have now found that benzoquinoline and benzoindole derivatives can be efficiently synthesized in high yields by the direct catalytic cyclization of naphthylamines with 1,3- and 1,2-diols, respectively, by $IrCl_3$ under the influence of a suitable phosphine ligand.

In this paper, we would like to report a facile Ir-catalyzed synthesis of a wide variety of benzoquinoline and benzoindole derivatives from naphthylamines and diols.

Results and Discussion

To confirm an optimum reaction condition, the reaction of 1-naphtylamine (**1a**) with 1,3-propanediol (**2a**) was chosen as a model reaction and carried out under various conditions. A typical reaction is performed as follows: a mixture of **1a** (5 mmol) and **2a** (2 mmol) in the presence of $IrCl_3 \cdot 3H_2O$ (0.10 mmol), ligand (0.15 mmol), and Na_2CO_3 (0.16 mmol) was allowed to react under air at refluxing temperature (169 °C) of mesitylene for 15 h (standard conditions) (Table 1).

The effect of ligand on the cyclization of **1a** with **2a** by $IrCl_3 \cdot 3H_2O$ was first examined. The reaction was found to be markedly influenced by the ligands employed. No reaction was induced in the absence of any ligand (entry 1). When a

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(2) (a) Robinson, B. *Chem. Rev.* **1963**, *63*, 373. (b) Augustine, R. L.; Gustavesen, A. J.; Wanat, S. F.; Pattison, I. C.; Houghton, K. S.; Koleter, G. *J. Org. Chem.* **1973**, *38*, 3004.

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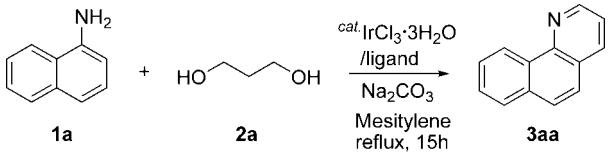
TABLE 1. Reaction of 1-Naphtylamine (1a) with 1,3-Propanediol (2a) by Ir-Catalyst under Various Conditions[a]



1a **2a** **3aa**

entry	ligand	temp/°C	yield of **3aa**/%[b]
1	–	169	–
2	PPh_3	169	44
3	$P(^nOct)_3$	169	66
4	dppe	169	14
5	dppp	169	13
6	BINAP	169	99 (96)
7[c]	BINAP	169	58
8	BINAP	150	3
9[d]	BINAP	169	79
10[e]	BINAP	169	55
11[f]	BINAP	169	–

[a] See text. [b] GLC yields based on **2a** used. The number in parentheses shows isolated yield. [c] **1a** (2 mmol) was used. [d] The reaction was performed in the absence of Na_2CO_3. [e] Under N_2. [f] $[IrCl(cod)]_2$ (0.1 mmol) was used instead of $IrCl_3$.

monodentate ligand like PPh_3 or $P(^nOct)_3$ was added to the catalytic system under standard conditions, 7,8-benzoquinoline (**3aa**) was obtained in 44% or 66% yield, respectively (entries 1 and 2). Typical bidentate phosphine ligands such as 1,2-bis(diphenylphosphino)ethane (dppe) and 1,3-bis(diphenylphosphino)propane (dppp) were less efficient than monodentate ligands to lead to **3aa** in low yields (entries 4 and 5). It was found that *rac*-2,2′-bis(diphenylphosphino)-1,1′-binaphtyl (BINAP) is a very efficient ligand for the $IrCl_3 \cdot 3H_2O$ catalyst to form **3aa** in almost quantitative yield (96% isolated yield) (entry 6). This method provides a simple efficient route to **3aa**, since the precedent Ru-catalyzed reaction gave **3aa** in low yield (37%).[3b] The reaction was strongly dependent on a starting molar ratio of **1a** to **2a**, and the yield of **3aa** was decreased with decreasing the molar ratio of **1a** to **2a**. Thus, the yield of **3aa** decreased to 58% in a stoichiometric reaction of **1a** and **2a** (entry 7). When the reaction temperature was lowered from 169 to 150 °C, the reaction gave **3aa** in poor yield (3%) (entry 8). In this reaction, however, as the diol **2a** was completely consumed, the dehydrogenation of the diol **2a** to an aldehyde by the Ir complex seems to take place easily at this temperature. Consequently, the cyclization step would call for higher temperature than 150 °C. The reaction in the absence of Na_2CO_3 led to **3aa** in slightly lower yield (79%) (entry 9). Hence the base is not an essential component in this reaction. The reaction under nitrogen atmosphere proceeded slowly to give **3aa** in 55% yield as discussed later (entry 10). $[IrCl(cod)]_2$ complex was inert in this reaction, although this complex serves as an efficient catalyst for the alkylation reaction of methyl ketones with primary alcohols (entry 11).[7] Probably under such higher temperature the complex may be decomposed to an inactive Ir compound.

To reveal the effect of oxygen on the present cyclization, the reaction of **1a** with **2a** under O_2 was compared with that under air or N_2 (Figure 1). It was found that the reaction under O_2 atmosphere promotes more rapidly than the reaction under

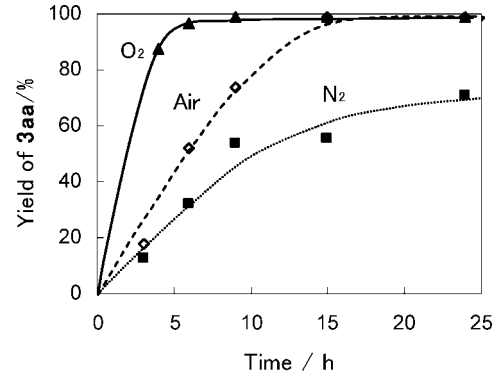


FIGURE 1. Time-dependence curve for the formation of **3aa** under N_2, air, and O_2 atmosphere (under the reaction conditions as shown in entry 6, Table 1).

air or N_2, which shows that the oxidation step is involved as an important step in the present cyclization as discussed later. In previous papers, we reported several Ir-catalyzed reactions of alcohols including the dehydrogenation to aldehydes as a key step, i.e., the alkylation of ketones with alcohols and diols,[7] the Guerbet reaction of alcohols,[8] and the dimerization reaction[9] of primary alcohols to esters. Among these three reactions, O_2 is needed to promote the reaction of primary alcohols to esters. In this reaction, since the hydrogenation step by an Ir-hydride generated by the hydrogen transfer from alcohols to Ir catalyst is not involved, it is necessary to remove the hydride from the Ir-hydride with O_2 to regenerate the Ir-catalyst. These observations indicate that O_2 is not necessary in the Ir-catalyzed reactions including the hydrogenation step with the Ir-hydride generated in the reaction course.

On the basis of these results, the reaction of **1a** with several diols was examined under the standard conditions (Table 2). The reaction of **1a** with ethylene glycol (**2b**) afforded 6,7-benzoindole (**3ab**) in 47% isolated yield (entry 1). The cyclization of **1a** with a secondary 1,2-diol like 2,3-butanediol (**2c**) proceeded more selectively than that with primary 1,2-diol **2b** to give the corresponding benzoindole, 2,3-dimethyl-6,7-benzoindole (**3ac**), in 96% isolated yield (entry 2). The reaction with a cyclic diol like *trans*-1,2-cyclopentanediol (**2d**) or 1,2-cyclohexanediol (**2e**) (*cis*-**2e**/*trans*-**2e** = 64/36) afforded the corresponding benzoindole derivatives, **3ad** (84%) and **3ae** (88%), respectively (entries 3 and 4). Although the reactions of **1a** with pure *cis*-**2e** and *trans*-**2e** were examined, the reactivity between *cis*-**2e** and *trans*-**2e** was found to be almost the same (entries 5 and 6). In these reactions, the cyclization promoted smoothly even by the use of PPh_3 ligand in place of BINAP ligand.

The *N*-heterocyclization of several substituted naphthylamines with 1,2- and 1,3-diols was examined under optimized reaction conditions (Table 3).

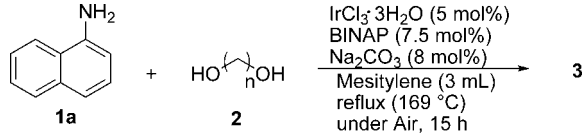
The reaction of 4-methyl-1-naphtylamine (**1b**) with **2a** or **2c** afforded 6-methylbenzo[*h*]quinoline (**3ba**) (90%) or 2,3,5-trimethyl-1*H*-benzo[*g*]indole (**3bc**) (88%) in high isolated yields, respectively (entries 1 and 2). Similarly, 7-methoxy-1-naphtylamine (**1c**) and 5-methoxy-1-naphtylamine (**1d**) reacted with **2a** and **2c** under these conditions to give the corresponding cyclization products, 9-methoxy-benzo[*h*]quinoline (**3ca**) (72%),

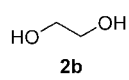
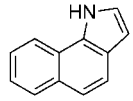
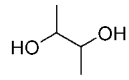
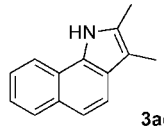
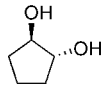
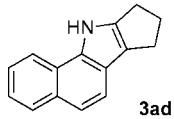
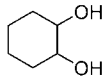
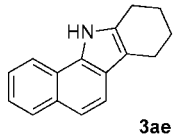
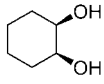
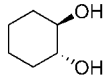
(7) (a) Taguchi, K.; Nakagawa, H.; Hirabayashi, T.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2004**, *126*, 72. (b) Maeda, K.; Obora, Y.; Sakaguchi, S.; Ishii, Y. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 689.

(8) Matsu-ura, T.; Sakaguchi, S.; Obora, Y.; Ishii, Y. *J. Org. Chem.* **2006**, *71*, 8306.

(9) Izumi, A.; Obora, Y.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **2006**, *47*, 9199.

TABLE 2. Reaction of 1-Naphtylamine (1a) with Various Diols (2a) with Ir-Catalyst[a]



Entry	2	Product (3)	Yield (%)[b]
1	 **2b**	 **3ab**	56 (47)
2	 **2c**	 **3ac**	99 (96)
3[c,d]	 **2d**	 **3ad**	90 (84)
4[c,d]	 **2e** (*cis*/*trans* = 64/36)	 **3ae**	99 (88)
5[c,d]	 ***cis*-2e**	**3ae**	98 (90)
6[c,d]	 ***trans*-2e**	**3ae**	96 (88)

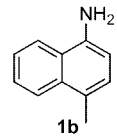
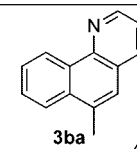
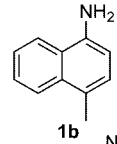
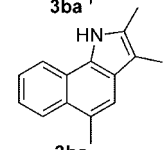
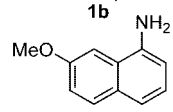
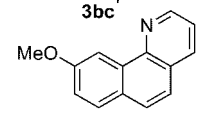
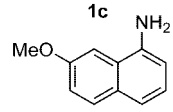
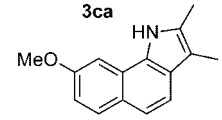
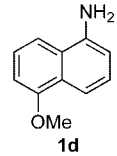
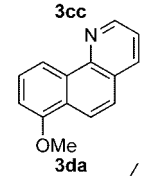
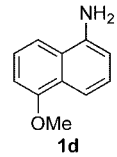
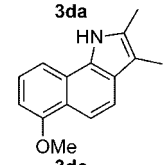
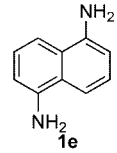
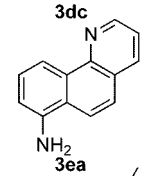
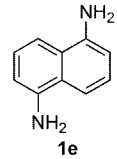
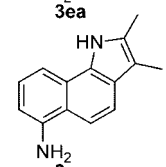
[a] **1a** (5 mmol) was allowed to react with **2** (2 mmol) in the presence of $IrCl_3 \cdot 3H_2O$ (0.1 mmol, 5 mol % based on **2**), ligand (0.15 mmol, 7.5 mol %), and Na_2CO_3 (0.16 mmol, 8 mol %) under air at refluxing temperature (169 °C) in mesitylene (3 mL) for 15 h. [b] GLC yields based on **2** used. The numbers in parentheses show isolated yields. [c] **1a** (10 mmol) was used. [d] PPh_3 (0.2 mmol, 10 mol % based on **2**) was used instead of BINAP.

8-methoxy-2,3-dimethyl-1*H*-benzo[*g*]indole (**3cc**) (78%), 7-methoxy-benzo[*h*]quinoline (**3da**) (72%), and 6-methoxy-2,3-dimethyl-1*H*-benzo[*g*]indole (**3dc**) (76%), respectively (entries 3−6). To obtain double *N*-heterocyclization product, 1,5-diaminonaphthalene (**1e**) was allowed to react with **2a** and **2c** under the same conditions; however, double-cyclization products were not obtained, but monocyclization products, 7-amino-benzo[*h*]quinoline (**3ea**) (59%) and 6-amino-2,3-dimethyl-1*H*-benzo[*g*]indole (**3ec**) (52%), were formed from **2a** and **2c**, respectively (entries 7 and 8).

In a previous paper, we reported the quinoline synthesis from ketones and aminobenzyl alcohols by $IrCl_3$.[4] Recently, cyclic amines were synthesized by the reaction of primary amines with diols by Ir complex, and the reaction is shown to proceed via the dehydrogenation of diols to aldehydes which then react with amines to form Schiff-base imines followed by hydrogenation by an Ir-hydride generated in the reaction course to give cyclic amines in good yields.[10] On the other hand, quinolines are

(10) Fujita, K.; Fujii, T.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 3525.

TABLE 3. Reaction of Various Naphtylamines (1) with 1,2- or 1,3-Diols (2) with Ir-Catalyst[a]

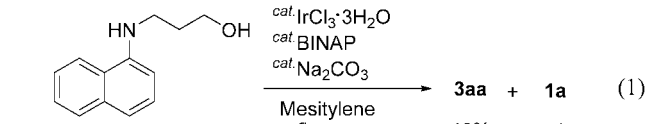
Entry	1	2	Product (3)	Yield (%)[b]
1	 **1b**	**2a**	 **3ba**	95 (90)
2	 **1b**	**2c**	 **3bc**	90 (88)
3	 **1c**	**2a**	 **3ca**	78 (72)
4	 **1c**	**2c**	 **3cc**	80(78)
5	 **1d**	**2a**	 **3da**	76 (72)
6	 **1d**	**2c**	 **3dc**	79(76)
7	 **1e**	**2a**	 **3ea**	66 (59)
8	 **1e**	**2c**	 **3ec**	58 (52)

[a] **1a** (5 mmol) was allowed to react with **2** (2 mmol) in the presence of $IrCl_3 \cdot 3H_2O$ (0.1 mmol, 5 mol % based on **2**), BINAP (0.15 mmol, 7.5 mol %), and Na_2CO_3 (0.16 mmol, 8 mol %) under O_2 (1 atm) at refluxing temperature (169 °C) in mesitylene (3 mL) for 15 h. [b] GLC yields based on **2** used. The numbers in parentheses show isolated yields.

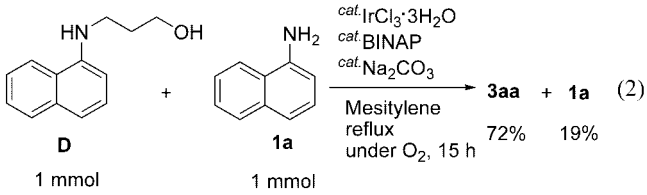
synthesized from aniline and 1,3-diols by $RuCl_3$ catalyst, and the reaction mechanism is studied in detail. [3b] 3-Anilino-1-propanol (**A**), which is predictable as a precursor to a quinoline (**B**), is prepared and the intra- and intermolecular cyclization of **A** and of **A** with aniline (**4**), respectively, is studied in the presence of $RuCl_3 \cdot nH_2O$ combined with PPh_3. They obtained **B** in 73% yield by intermolecular cyclization, but not by intramolecular cyclization, and concluded that **B** is formed through the cyclization of *N*,*N*′-diphenylpropane-1,3-diamine (**C**) derived from **A** and **4**, since **C**, prepared independently, leads to **B** and **4** (Scheme 1).

In our Ir-catalyzed benzoquinoline synthesis from **1a** and **2a**, the reaction seems to proceed through a similar reaction pathway

proposed by Watanabe.[3b] Thus, we prepared 3-(1-napthtylamino)-1-propanol (**D**) and tried the cyclization of **D** itself and the reaction of **D** with **1a** under the influence of $IrCl_3 \cdot 3H_2O$ and BINAP (eqs 1 and 2). In contrast to the Ru-catalyzed reaction where the intramolecular cyclization of **A** to **B** does not occur, the Ir-catalyzed reaction of **D** produced **3aa** in 43% yield (eq 1). In addition, the reaction of **D** with **1a** led to **3aa** in higher yield (72%), and **1a** was recovered in 19% (eq 2).

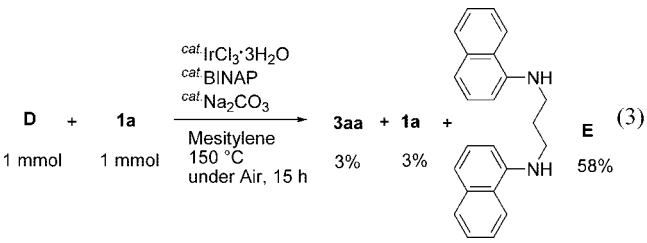


(1)



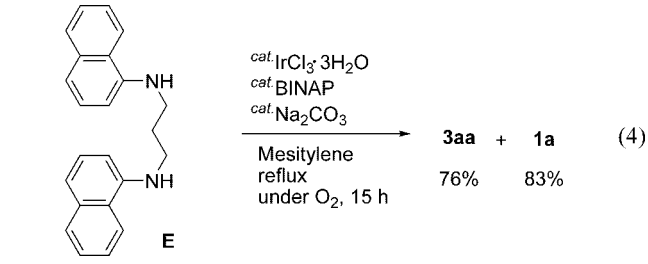
(2)

The product distribution derived from **D** itself was found to be different from that derived from **D** and **1a**. These results suggest that a reaction mechanism for the formation of **3aa** from **D** (as shown in eq 1) seems to be different from that from **D** and **1a** (as shown in eq 2). Indeed, when the reaction of **D** with **1a** was performed under low reaction temperature (150 °C), the yield of **3aa** was only 3%, but *N*,*N*′-di(naphthalene-1-yl)propane-1,3-diamine (**E**) was obtained in 58% yield (eq 3). This result suggested that diamine **E** would also be a probable intermediate in the present reaction.



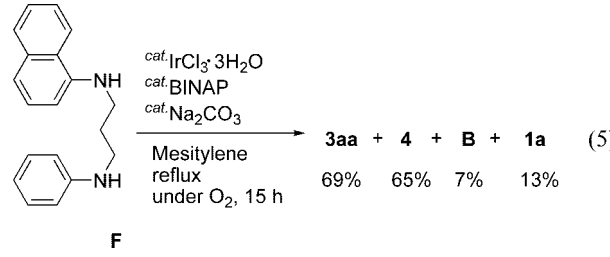
(3)

Thus, to obtain further information on the reaction path in the present cyclization reaction, diamine **E** was prepared and allowed to react under the same conditions to produce an approximately equimolar amount of **3aa** (76%) and **1a** (83%) (eq 4).



(4)

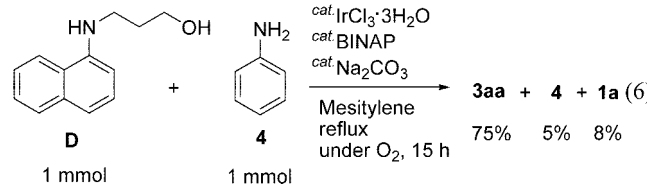
In addition, to investigate the reactivity and selectivity of the diamine intermediates, *N*-(naphthalene-1-yl)-*N*′-phenylpropane-1,3-diamine (**F**) was prepared and allowed to react under these reaction conditions (eq 5). As a result, a selective *N*-heterocyclization reaction took place to produce **3aa** in 69% yield together with aniline **4** (65%), and the yield of quinoline **B** was very low (7%).



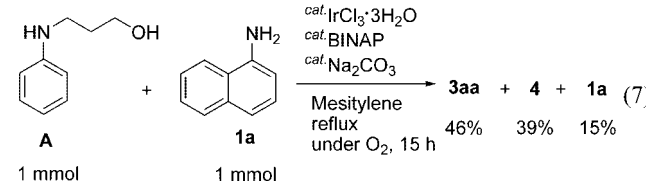
(5)

We next investigated the reactivity and selectivity of the **D** as an intermediate in the present reaction. Thus, the **D** was reacted with **4** under these conditions, giving **3aa** in 75% yield as the sole *N*-heterocyclization product without formation of **B** (eq 6). In this reaction, **4** was recovered in only 5%. On the other hand, the reaction of **A** with **1a** afforded the same *N*-heterocyclization product **3aa** in 46% yield together with **4** (39%), and **1a** was recovered in 15% (eq 7). Furthermore, the reaction of **A** with **1a** was performed at 150 °C, and the yield of cyclization product **3aa** was only 2%, but the corresponding diamine, **F**, was formed in 33% yield (eq 8).

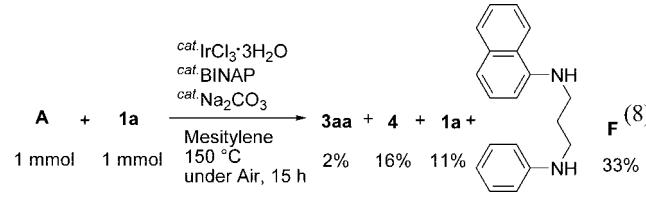
These results may indicate that the cyclization step would be a rate-determining step and the formation to the **3aa** is a kinetically and thermodynamically favored process. Furthermore, the fact that the product distribution of **3aa** and **4** in eqs 6 and 7 was considerably different suggests that **3aa** is not formed via a common reaction intermediate, which implies that both the aminoalcohol (**D**) and the diamines (**E** and **F**) can be intermediates of the present cyclization reaction.



(6)



(7)

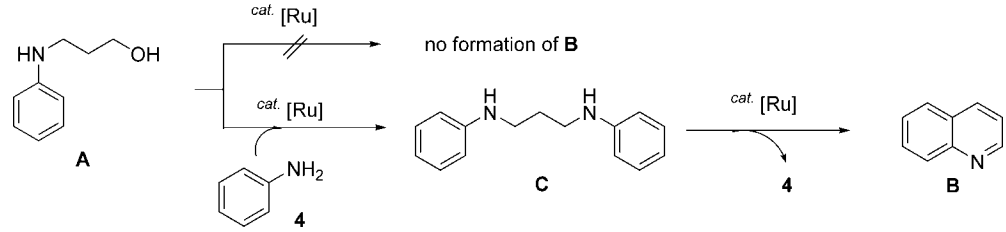


(8)

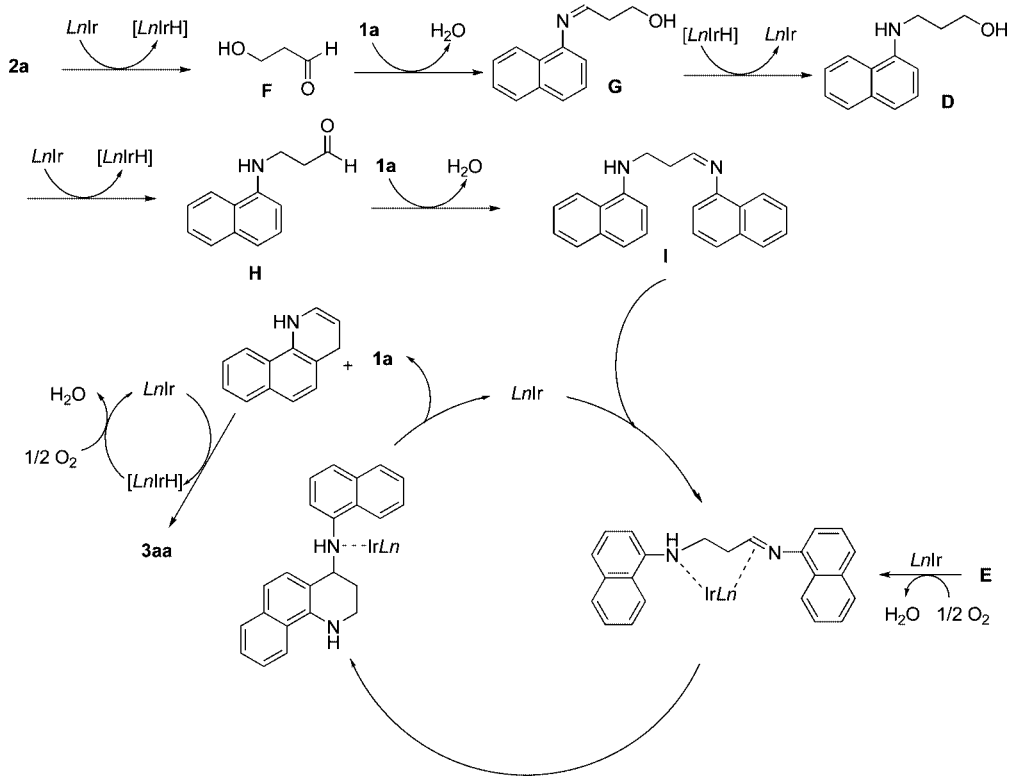
From these results, it is rather hazardous to predict a reaction pathway in detail at the present stage, but the following two possible reaction pathways may be proposed for the formation of **3aa** by the present Ir-catalyzed reaction (Schemes 2 and 3).

It is probable that the reaction is initiated by the Ir-catalyzed dehydrogenation of diol **2a** to aldehyde (**F**), which readily reacts with **1a** to give an imine intermediate (**G**) followed by hydrogenation by the in situ generated Ir-hydride leading to **D**. One plausible reaction pathway is that the resulting **D** reacts

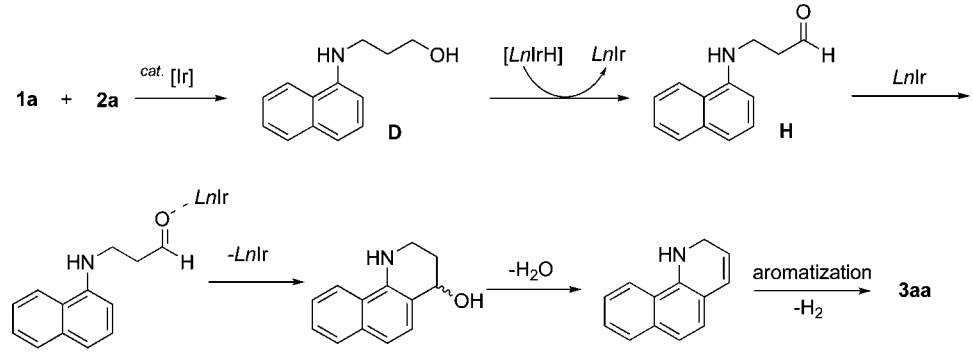
SCHEME 1. Reported Reaction Mechanism for the Ru-Catalyzed Quinoline Synthesis[3d]



SCHEME 2. A Plausible Reaction Mechanism through Diamine Intermediate (E)



SCHEME 3. Another Plausible Reaction Pathway through Aminoalcohol Intermediate (D)



further with **1a** after the formation of aldehyde **H** to give imine **I**. The formation of **3aa** from **I** may be explained by a similar reaction path proposed by Watanabe et al. (Scheme 2).[3b] However, another possible reaction pathway involving the direct intramolecular cyclization of **D** to afford **3aa** would also be plausible (Scheme 3).

To obtain information about the role of O_2 in the intramolecular cyclization of **D**, the reaction of **D** under O_2 was compared with those under air and Ar. The yield of **3aa** under O_2 (see eq 1), air, and Ar decreased in order of 43% (O_2), 25% (air), and 13% (Ar). The fact that the intramolecular cyclization is accelerated under O_2 indicates that the reaction step promoted by O_2 is included in the reaction course from **D** to **3aa** and **E**. In addition, the effect of O_2 on the reaction of diamine **E** was similarly examined. As a result, the yield of **3aa** was 83% under O_2 (see, eq 3), 62% under air, and 43% under Ar. In the presence of O_2 in the reaction system, the Ir-hydride generated during the reaction is trapped by O_2 to regenerate Ir species liberating H_2O. Under the present higher temperature (169 °C) condition, however, the resulting Ir-hydride seems to liberate hydrogen to

regenerate Ir species even in the absence of O_2. It is probable that the aromatization step is prompted by the existence of O_2. Thus, the cyclization of **D** to **3aa** is thought to progress smoothly under the influence of O_2.

In conclusion, we have developed a facile approach to benzoquinoline and benzoindole derivatives from naphtylamines and 1,2- and 1,3-diols catalyzed by $IrCl_3$ combined with BINAP ligand. The reaction gave the desired products in good yields.

Experimental Section

All starting materials except **A**,[3d] **D**,[11] and **E**[12] were commercially available and used without any purification.

Compounds **3aa**,[3b] **3ab**,[6a]**3ac**,[13] **3ad**,[14] **3ae**,[6a] **3ba**,[15] **3ca**,[16] and **3ea**[17] were reported previously. Compound **F** was prepared according to a literature method.[18]

A Typical Reaction Procedure for the Formation of 7,8-Benzoquinoline Is As Follows (Table 1, entry 6). A mixture of $IrCl_3 \cdot H_2O$ (35 mg, 0.10 mmol), BINAP (93 mg, 0.15 mmol), and Na_2CO_3 (17 mg, 0.16 mmol) was added to the mixture of **1a** (716 mg, 5 mmol) and **2a** (152 mg, 2 mmol) in mesitylene (3 mL) under open air. The reaction mixture was stirred at the refluxing temperature of mesitylene (169 °C) for 15 h. The yield of the product was estimated from the peak area based on the internal standard technique using GC. The product (**3aa**) was isolated by column chromatography (70−230 mesh Alumina, *n*-hexane/ethyl acetate = 15: 1) in 96% yield (344 mg).

Reaction of 3-(1-Naphtylamino)propanol (D) in the Presence of Ir-Catalyst (Eq 1). A mixture of $IrCl_3 \cdot H_2O$ (18 mg, 0.05 mmol), BINAP (47 mg, 0.075 mmol), and Na_2CO_3 (9 mg, 0.08 mmol) was added to 3-(1-naphtylamino)-1-propanol (201 mg, 1 mmol) in mesitylene (1.5 mL) under O_2 (1 atm). The reaction mixture was stirred at the refluxing temperature of mesitylene (169 °C) for 15 h. GC analysis of the reaction mixture showed that **3aa** was formed in 43% yield.

3bc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.43 (s, 3H), 2.76 (s, 3H), 7.43−7.53 (m, 3H), 7.91(d, J = 7 Hz, 1H), 8.07 (d, J = 8 Hz, 1H), 8.27 (br, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 8.6 (CH_3), 11.6 (CH_3), 20.0 (CH_3), 108.5 (C), 118.9 (CH), 119.5 (CH), 121.5 (C), 122.9 (CH), 124.5 (C), 124.8 (CH), 125.2 (C), 125.3 (CH), 128.3 (C), 128.6 (C), 129.2 (C); GC-MS (EI) *m*/*z* (rel intensity) 209 (100) $[M]^+$, 194 (30); HRMS (EI) *m*/*z* calcd for $C_{15}H_{15}N$ $[M]^+$ 209.1204, found 209.1199.

3cc. ^{1}H NMR (400 MHz,$CDCl_3$) δ 2.32 (s, 3H), 2.45 (s, 3H), 3.96 (s, 3H), 7.08 (tt, J = 5 Hz, 2 Hz, 1H), 7.24 (d, J = 2 Hz, 1H), 7.49 (dd, J = 19 Hz, 8 Hz, 2H), 7.84 (d, J = 9 Hz, 1H), 8.34 (br, 1H); ^{13}C NMR (400 MHz,$CDCl_3$) δ 8.6 (CH_3), 11.6 (CH_3), 55.3 (CH_3), 99.1 (CH), 108.9 (C), 114.4 (CH), 116.2 (CH), 119.5 (CH), 122.0 (C), 125.1 (C), 125.4 (C),128.9 (C), 129.0 (C), 130.5 (CH), 157.4 (C); GC-MS (EI) *m*/*z* (rel intensity) 225 (100) $[M]^+$, 210 (15), 182 (31); HRMS (EI) *m*/*z* calcd for $C_{15}H_{15}NO$ $[M]^+$ 225.1154, found 225.1148.

3da. ^{1}H NMR (400 MHz,$CDCl_3$) δ 4.02 (s, 3H), 7.07 (d, J = 8 Hz, 1H), 7.48 (dd, J = 8 Hz, 4 Hz, 1H), 7.62−7.66 (m, 2H), 8.14 (dd, J = 8 Hz, 2 Hz, 1H), 8.28 (d, J = 9 Hz, 1H), 8.88 (d, J = 9 Hz, 1H), 8.98 (dd, J = 4 Hz, 2 Hz, 1H); ^{13}C NMR (400 MHz,$CDCl_3$) δ 55.7 (CH_3), 107.3 (CH), 116.4 (CH), 121.4 (CH), 121.8 (CH), 124.4 (CH), 124.8 (C), 126.5 (C), 127.2 (CH), 132.6 (C), 135.8 (CH), 146.2 (C), 148.7 (CH), 155.4 (C); GC-MS (EI) *m*/*z* (rel intensity) 209 (100) $[M]^+$, 194 (50), 166 (65); HRMS (EI) *m*/*z* calcd for $C_{14}H_{11}NO$ $[M]^+$ 209.0841, found 209.0842.

3dc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.43 (s, 3H), 4.02 (s, 3H), 6.77 (d, J = 8 Hz, 1H), 7.40 (t, J = 8 Hz, 1H), 7.50 (d, J = 8 Hz, 1H), 7.60 (d, J = 9 Hz, 1H), 7.94 (d, J = 9 Hz, 1H), 8.32 (br, 1H); ^{13}C NMR (400 MHz,$CDCl_3$) δ 8.6 (CH_3), 11.6 (CH_3), 55.5 (CH_3), 102.1 (CH), 108.8 (C), 111.8 (C), 113.3 (C), 117.7 (CH), 121.3 (CH), 122.2 (C), 125.3 (CH), 125.4 (C), 129.0 (C), 129.4 (C), 156.5 (CH_3); GC-MS (EI) *m*/*z* (rel intensity) 225 (100) $[M]^+$, 210 (15), 182 (43); HRMS (EI) *m*/*z* calcd for $C_{14}H_{11}NO$ $[M]^+$ 225.1154, found 225.1157.

3ec. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.37 (s, 3H), 4.11 (br, 2H), 7.18−7.24 (m, 2H), 7.30−7.33 (m, 1H), 7.38 (dd, J = 9 Hz, 1 Hz, 1H), 7.51 (d, J = 9 Hz, 1H), 8.29 (br, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 8.6 (CH_3), 11.6 (CH_3), 108.0 (CH), 108.8 (C), 110.1 (CH), 112.3 (CH), 117.5 (CH), 119.2 (C), 122.1 (C), 124.9 (CH), 125.7 (C), 129.0 (C), 129.8 (C), 143.2 (C); GC-MS (EI) *m*/*z* (rel intensity) 210 (100) $[M]^+$, 195 (19); HRMS (EI) *m*/*z* calcd for $C_{14}H_{14}N_2$ $[M]^+$ 210.1157, found 210.1158.

F: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81−1.87 (s, 2H), 3.12 (t, J = 7 Hz, 2H), 3.20 (t, J = 7 Hz, 2H), 3.92 (br, 2H), 6.45−6.49 (m, 3H), 6.61 (dq, J = 11 Hz, 3 Hz, 1H), 7.09 (dt, J = 19 Hz, 6 Hz, 3H), 7.21−7.33 (m, 3H), 7.60 (d, J = 9 Hz, 1H), 7.67 (d, J = 2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 28.8 (CH_2), 42.2 (CH_2), 42.3 (CH_2), 104.2 (CH), 112.9 (CH), 117.3 (CH), 117.5 (CH), 119.8 (CH), 123.4 (C), 124.6 (CH), 125.7 (CH), 126.5 (CH), 128.6 (CH), 129.2 (CH), 134.2 (C), 143.3 (C), 148.1 (C); GC-MS (EI) *m*/*z* (rel intensity) 276 (100) $[M]^+$, 156 (43), 143 (21); HRMS (EI) *m*/*z* calcd for $C_{19}H_{20}N_2$ $[M]^+$ 276.1626, found 276.1625.

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Supporting Information Available: Experimental procedure and NMR spectral data of **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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