

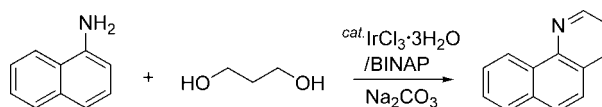
N-Heterocyclization of Naphthylamines with 1,2- and 1,3-Diols Catalyzed by an Iridium Chloride/BINAP System

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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 IrCl₃ 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 naphthylamines with 1,2-diols. A reaction mechanism for the *N*-heterocyclization of naphthylamines with 1,3-diols by IrCl₃ 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*-heterocyclization of anilines with diols leading to indoles and quinolines is developed by Tsuji and Watanabe et al.^{3a,b} Thereafter, the RuCl₃/SnCl₂ 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 RuCl₃ 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 IrCl₃ 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-naphthylamine (**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 IrCl₃·3H₂O (0.10 mmol), ligand (0.15 mmol), and Na₂CO₃ (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 IrCl₃·3H₂O 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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(3) (a) Tsuji, Y.; Huh, K.-T.; Watanabe, Y. *Tetrahedron Lett.* **1986**, 277, 377. (b) Tsuji, Y.; Huh, K.-T.; Watanabe, Y. *J. Org. Chem.* **1987**, *52*, 1673. (c) Cho, C. S.; Lee, J. W.; Lee, D. Y.; Shim, S. C.; Kim, T. *J. Chem. Commun.* **1996**, 2115. (d) Cho, C. S.; Lim, H. K.; Shim, S. C.; Kim, T. J.; Choi, H.-J. *Chem. Commun.* **1998**, 995.

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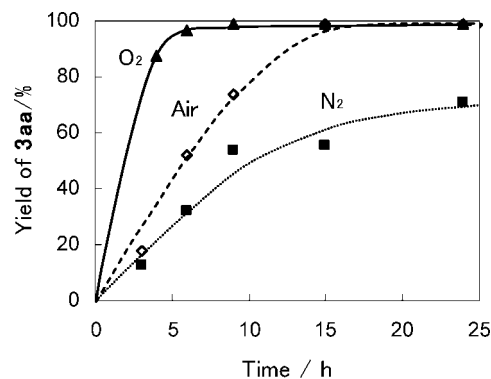
TABLE 1. Reaction of 1-Naphtylamine (**1a**) with 1,3-Propanediol (**2a**) by Ir-Catalyst under Various Conditions^a

| entry | ligand | temp/°C | yield of 3aa /% |
|-----------------|-----------------------------------|---------|------------------------|
| 1 | — | 169 | — |
| 2 | PPh ₃ | 169 | 44 |
| 3 | P ⁽ⁿ Oct) 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 Na₂CO₃. ^e Under N₂. ^f [IrCl(cod)]₂ (0.1 mmol) was used instead of IrCl₃.

monodentate ligand like PPh₃ or P⁽ⁿOct)₃ was added to the catalytic system under standard conditions, 6,7-benzoinidole (**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 IrCl₃·3H₂O 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 Na₂CO₃ 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 O₂ was compared with that under air or N₂ (Figure 1). It was found that the reaction under O₂ atmosphere promotes more rapidly than the reaction under

**FIGURE 1.** Time-dependence curve for the formation of **3aa** under N₂, air, and O₂ atmosphere (under the reaction conditions as shown in entry 6, Table 1).

air or N₂, 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 reaction⁹ of primary alcohols to esters. Among these three reactions, O₂ 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 O₂ to regenerate the Ir-catalyst. These observations indicate that O₂ 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-benzoinidole (**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 benzoinidole, 2,3-dimethyl-6,7-benzoinidole (**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 benzoinidole 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 PPh₃ 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).

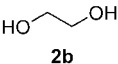
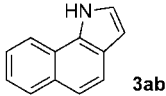
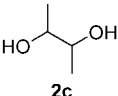
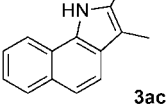
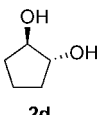
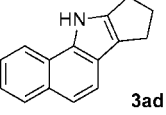
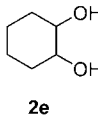
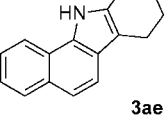
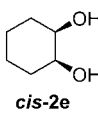

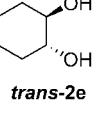
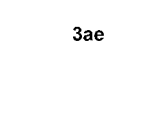
The reaction of 4-methyl-1-naphtylamine (**1b**) with **2a** or **2c** afforded 6-methylbenzo[*h*]quinoline (**3ba**) (90%) or 2,3,5-trimethyl-1*H*-benzo[*g*]indole (**3bc**) (88%) in high isolated yields, respectively (entries 1 and 2). Similarly, 7-methoxy-1-naphtylamine (**1c**) and 5-methoxy-1-naphtylamine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

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

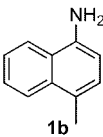
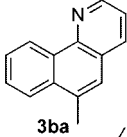
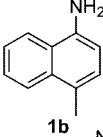
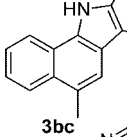
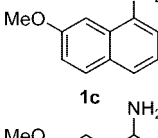
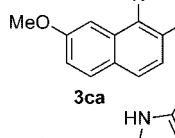
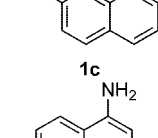
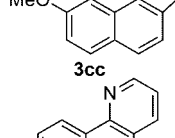
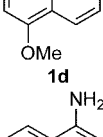
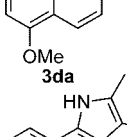
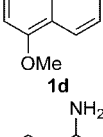
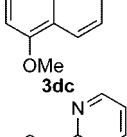
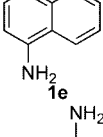
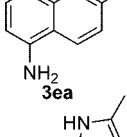
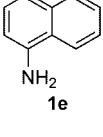
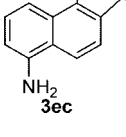
| $ \begin{array}{c} \text{NH}_2 \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{C}_6\text{H}_4 \\ \text{1a} \end{array} + \text{HO}-(\text{CH}_2)_n-\text{OH} \xrightarrow[\text{Mesitylene (3 mL), reflux (169 }^\circ\text{C), under Air, 15 h}]{\text{IrCl}_3 \cdot 3\text{H}_2\text{O (5 mol\%), BINAP (7.5 mol\%), Na}_2\text{CO}_3 \text{ (8 mol\%)}} \begin{array}{c} \text{NH} \\ \\ \text{C}_6\text{H}_4 \\ \\ \text{C}_6\text{H}_4 \\ \text{3} \end{array} $ | | | |
|--|---|---|------------------------|
| Entry | 2 | Product (3) | Yield (%) ^b |
| 1 |  |  | 56 (47) |
| 2 |  |  | 99 (96) |
| 3 ^{c,d} |  |  | 90 (84) |
| 4 ^{c,d} |  |  | 99 (88) |
| | (cis/trans = 64/36) | | |
| 5 ^{c,d} |  |  | 98 (90) |
| 6 ^{c,d} |  |  | 96 (88) |

^a **1a** (5 mmol) was allowed to react with **2** (2 mmol) in the presence of IrCl₃·3H₂O (0.1 mmol, 5 mol % based on **2**), ligand (0.15 mmol, 7.5 mol %), and Na₂CO₃ (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 PPh₃ (0.2 mmol, 10 mol % based on **2**) was used instead of BINAP.

8-methoxy-2,3-dimethyl-1H-benzo[g]indole (**3cc**) (78%), 7-methoxy-benzo[h]quinoline (**3da**) (72%), and 6-methoxy-2,3-dimethyl-1H-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-1H-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 IrCl₃.⁴ 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

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 |  | 2a |  | 95 (90) |
| 2 |  | 2c |  | 90 (88) |
| 3 |  | 2a |  | 78 (72) |
| 4 |  | 2c |  | 80(78) |
| 5 |  | 2a |  | 76 (72) |
| 6 |  | 2c |  | 79(76) |
| 7 |  | 2a |  | 66 (59) |
| 8 |  | 2c |  | 58 (52) |

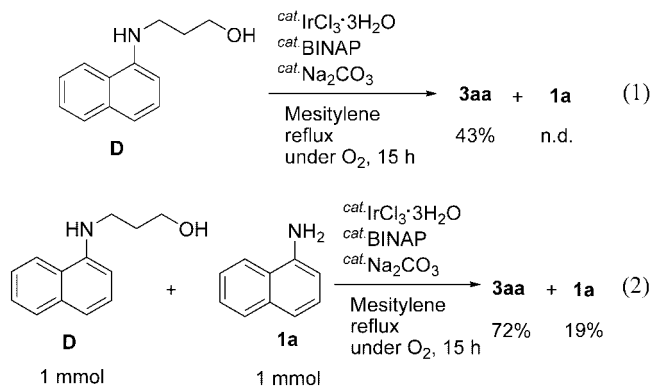
^a **1a** (5 mmol) was allowed to react with **2** (2 mmol) in the presence of IrCl₃·3H₂O (0.1 mmol, 5 mol % based on **2**), BINAP (0.15 mmol, 7.5 mol %), and Na₂CO₃ (0.16 mmol, 8 mol %) under O₂ (1 atm) at refluxing temperature (169 °C) in mesitylene (3 mL) for 15 h. ^b GLC yields based on **2** used. The numbers in parentheses show isolated yields.

synthesized from aniline and 1,3-diols by RuCl₃ 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 RuCl₃·*n*H₂O combined with PPh₃. 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).

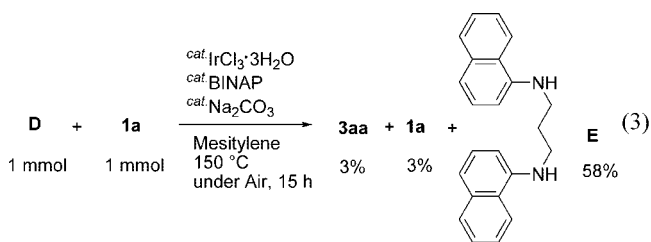
In our Ir-catalyzed benzoquinoline synthesis from **1a** and **2a**, the reaction seems to proceed through a similar reaction pathway

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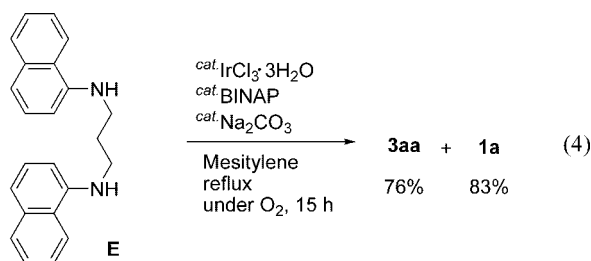
proposed by Watanabe.^{3b} Thus, we prepared 3-(1-naphthylamino)-1-propanol (**D**) and tried the cyclization of **D** itself and the reaction of **D** with **1a** under the influence of $\text{IrCl}_3 \cdot 3\text{H}_2\text{O}$ and BINAP (eqs 1 and 2). In contrast to the Ru-catalyzed reaction where 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).



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.

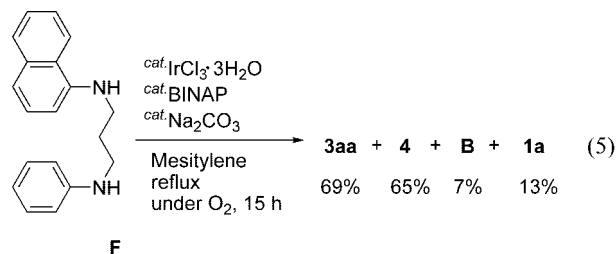


Thus, to obtain further information on the reaction path in the present cyclization reaction, diamine **E** was prepared and allowed to react under the same conditions to produce an approximately equimolar amount of **3aa** (76%) and **1a** (83%) (eq 4).



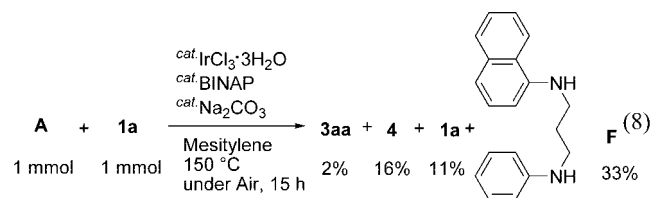
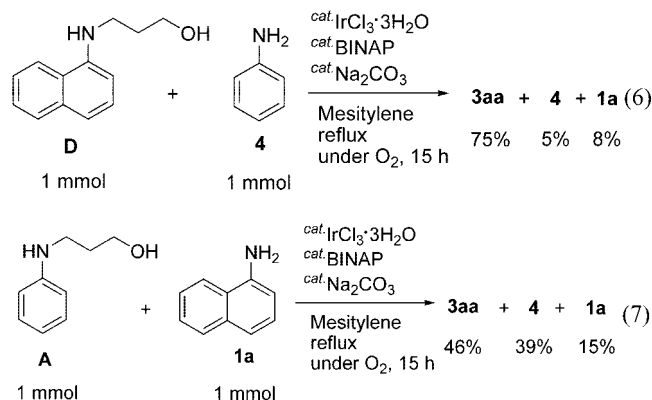
In addition, to investigate the reactivity and selectivity of the diamine intermediates, *N*-(naphthalene-1-yl)-*N'*-phenylpropane-1,3-diamine (**F**) was prepared and allowed to react under these reaction conditions (eq 5). As a result, a selective *N*-heterocyclization reaction took place to produce **3aa** in 69% yield

together with aniline **4** (65%), and the yield of quinoline **B** was very low (7%).



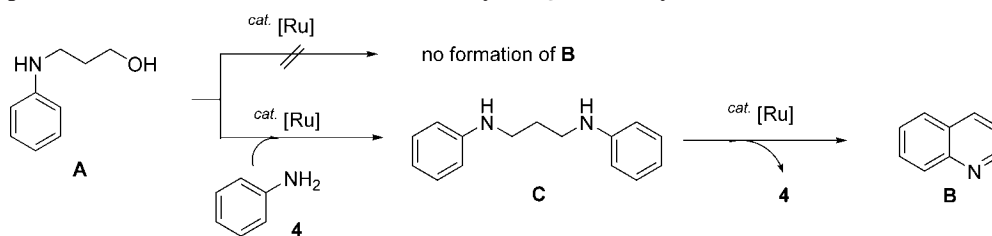
We next investigated the reactivity and selectivity of the **D** as an intermediate in the present reaction. Thus, the **D** was reacted with **4** under these conditions, giving **3aa** in 75% yield as the sole *N*-heterocyclization product without formation of **B** (eq 6). In this reaction, **4** 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.

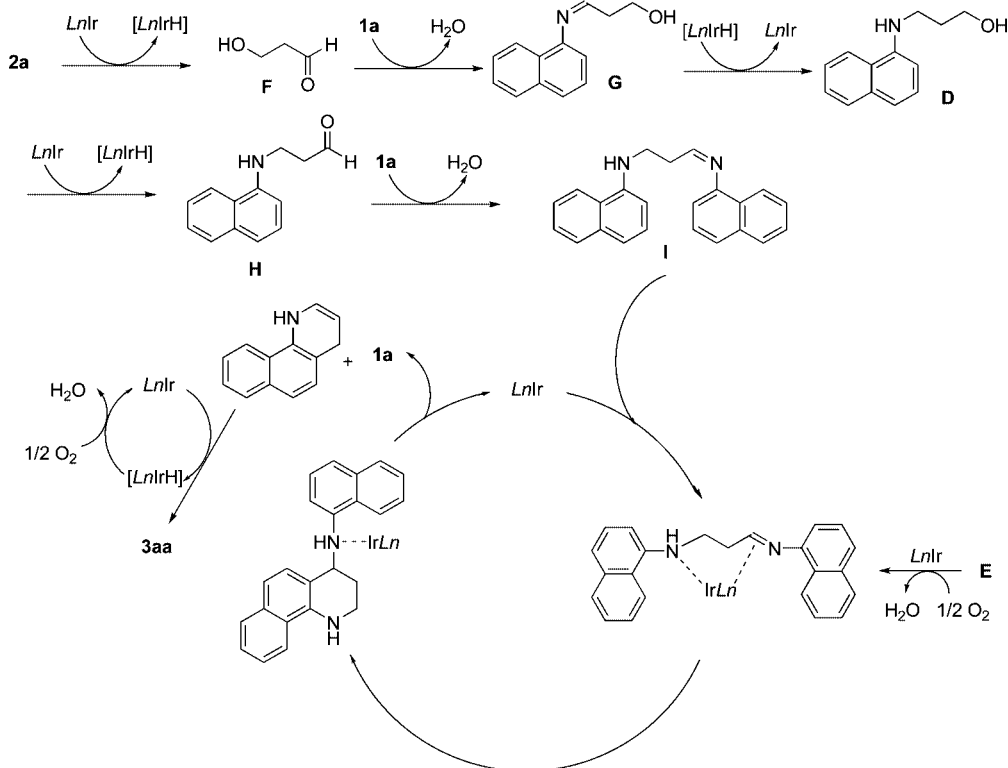


From these results, it is rather hazardous to predict a reaction pathway in detail at the present stage, but the following two possible reaction pathways may be proposed for the formation of **3aa** by the present Ir-catalyzed reaction (Schemes 2 and 3).

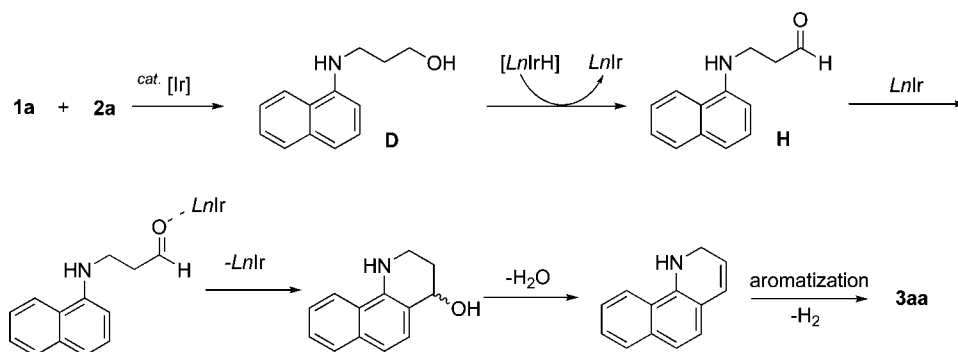
It is probable that the reaction is initiated by the Ir-catalyzed dehydrogenation of diol **2a** to aldehyde (**F**), which readily reacts with **1a** to give an imine intermediate (**G**) followed by hydrogenation by the in situ generated Ir-hydride leading to **D**. One plausible reaction pathway is 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 O₂ in the intramolecular cyclization of **D**, the reaction of **D** under O₂ was compared with those under air and Ar. The yield of **3aa** under O₂ (see eq 1), air, and Ar decreased in order of 43% (O₂), 25%

(air), and 13% (Ar). The fact that the intramolecular cyclization is accelerated under O₂ indicates that the reaction step promoted by O₂ is included in the reaction course from **D** to **3aa** and **E**. In addition, the effect of O₂ on the reaction of diamine **E** was similarly examined. As a result, the yield of **3aa** was 83% under O₂ (see, eq 3), 62% under air, and 43% under Ar. In the presence of O₂ in the reaction system, the Ir-hydride generated during the reaction is trapped by O₂ to regenerate Ir species liberating H₂O. 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 O₂. It is probable that the aromatization step is prompted by the existence of O₂. Thus, the cyclization of **D** to **3aa** is thought to progress smoothly under the influence of O₂.

In conclusion, we have developed a facile approach to benzoquinoline and benzoindole derivatives from naphthylamines and 1,2- and 1,3-diols catalyzed by IrCl₃ 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 IrCl₃·H₂O (35 mg, 0.10 mmol), BINAP (93 mg, 0.15 mmol), and Na₂CO₃ (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 IrCl₃·H₂O (18 mg, 0.05 mmol), BINAP (47 mg, 0.075 mmol), and Na₂CO₃ (9 mg, 0.08 mmol) was added to 3-(1-naphtylamino)-1-propanol (201 mg, 1 mmol) in mesitylene (1.5 mL) under O₂ (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. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 8.6 (CH₃), 11.6 (CH₃), 20.0 (CH₃), 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 C₁₅H₁₅N [M]⁺ 209.1204, found 209.1199.

3cc. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 8.6 (CH₃), 11.6 (CH₃), 55.3 (CH₃), 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 C₁₅H₁₅NO [M]⁺ 225.1154, found 225.1148.

3da. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 55.7 (CH₃), 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 C₁₄H₁₁NO [M]⁺ 209.0841, found 209.0842.

3dc. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 8.6 (CH₃), 11.6 (CH₃), 55.5 (CH₃), 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 (CH₃); GC-MS (EI) *m/z* (rel intensity) 225 (100) [M]⁺, 210 (15), 182 (43); HRMS (EI) *m/z* calcd for C₁₄H₁₁NO [M]⁺ 225.1154, found 225.1157.

3ec. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 8.6 (CH₃), 11.6 (CH₃), 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 C₁₄H₁₄N₂ [M]⁺ 210.1157, found 210.1158.

F: ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (400 MHz, CDCl₃) δ 28.8 (CH₂), 42.2 (CH₂), 42.3 (CH₂), 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 C₁₉H₂₀N₂ [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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