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Direct Construction of Axially Chiral 4-Arylquinoline via Acid-Promoted Dehydrative Cyclization/Oxidation of Diarylmethanols

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Abstract: Acid-promoted dehydrative cyclization/oxidation aromatization sequences from diarylmethanols was developed, providing a new family of axially chiral 4-arylquinolines in high yields (up to 81%). Importantly, both Lewis acid $Zn(OTf)_2$ and organic chiral phosphoric acid (CPA) are able to catalyzed this transformation and the asymmetric version was also primary investigated (up to 71 : 29 er).

Key words: chiral phosphoric acid; axially chiral; chiral quinoline

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Axiallychiral biaryls are important components omnipresent in natural products and synthetic bioactive molecules, as well as platforms for chiral catalyst and ligand[1-4]. Therefore, great interest and efforts have been devoted to prepare these synthetic targets. Compared with successful strategies developed for the construction of axially chiral biaryls, only a few routes available for atropisomericaza-heterocycles bearing pyridine units[5-11]. Pyridone and pyridine have been recognized as widespread microstructures of pharmaceutically active molecules such as oxytocin antagonist[12] and maxi K channel openers[13], and potential ligand in asymmetric catalysis (Scheme 1, a). Thus, the development of practical and straightforward routes for accessing novel atropisomeric aryl-pyridine is still in great demand. Among substituted axially chiral arylpyridine compounds, 4-aryl-pyridine was relatively less studied by virtue of the location of the N atom is far away from the reactive site and infertility in the C-H activation and chirality control process as a directing group[14-19]. In 2011, Tanaka group reported the catalytic intramolecular hydroarylation of alkynes for the synthesis of axiallychiral 4-aryl 2-quinolinones catalyzed by palladium (II)/(S)-xyl-H8-binap complex with yield of up to 97%[15]. Afterward, a stepwise installation of axially chiral 4-arylpyridine was realized by Rodriguez and coworkers, and a moderate yield obtained after three steps consistedof thiourea catalyzed Micheal addition, annulation and oxidative chirality retentionfrom centrally chirality to axially chirality (Scheme 1, b)[17]. Aza-quinonemethides (aza-QMs) have been emerged as useful and highly reactive species in organic synthesis and utilized as electrophilic alkylating reagents for the preparation of various optically active compounds containing centrally chirality[20-22]. We envisioned that this kind of aza-quinonemethides from simple diarylmethanols with suitable *ortho*-substituents could be regarded as the ideal feedstocks of axially chiral 4-arylpyridine

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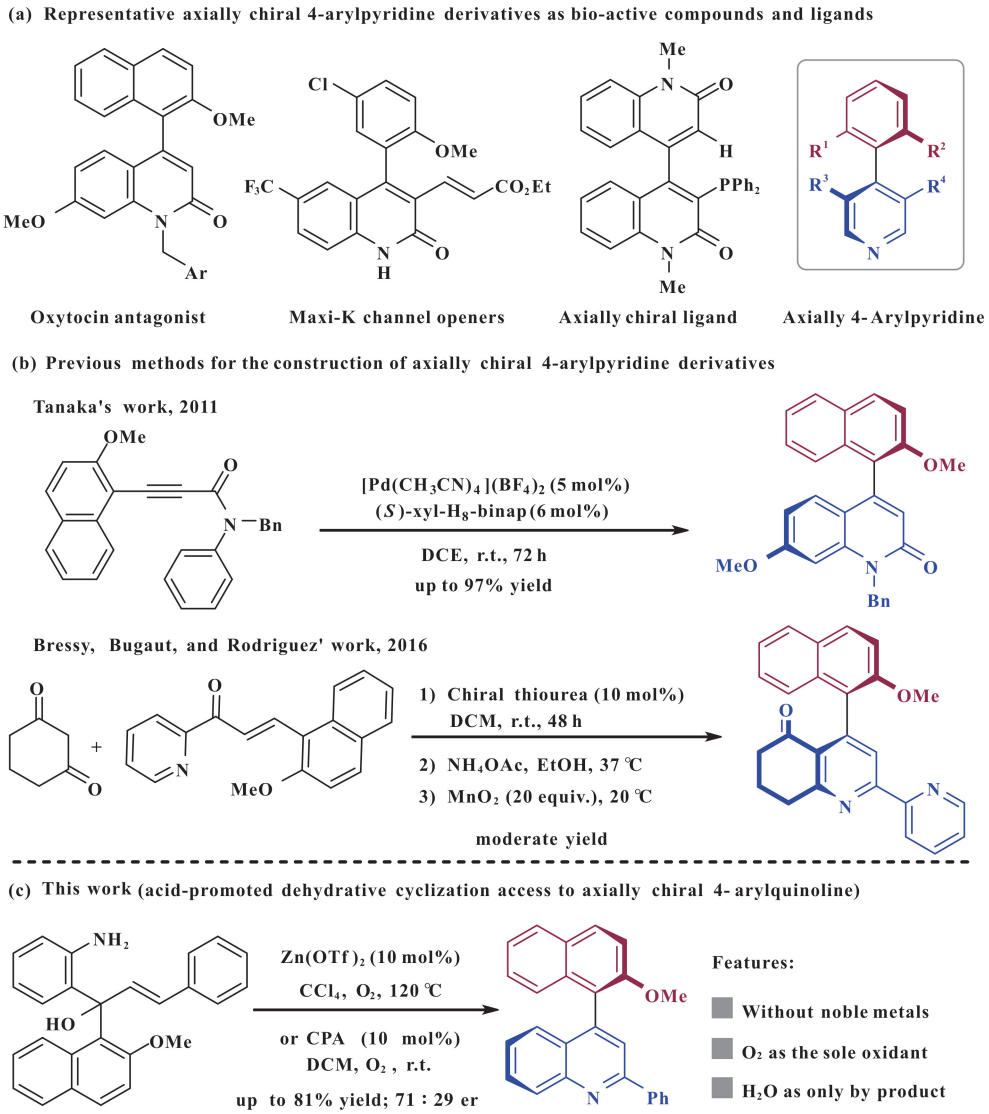
compounds. Importantly, low-toxic Lewis acid or Brønsted acid can readily promote this transformation with water as the only by-product in accordance with the demand of green chemistry[23-26]. Herein, we presented a new family of axially chiral 4-arylquinolines catalyzed by Lewis acid $Zn(OTf)_2$ or organic chiral phosphoric acid (CPA) in high yields of up to 81% and 71∶29 er (Scheme 1, c).



Scheme 1 Representative axially chiral 4-arylpyridine and synthetic strategies

1 Experimental

1.1 General

All reactions were set up under inert atmosphere utilizing glassware that was flame-dried and cooled under vacuum. All non-aqueous manipulations were using standard Schlenk techniques. Reactions were monitored using thin-layer chromatography (TLC) on silica gel plates. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain. Silica gel flash column chromatography was performed on SYNTHWARE 40~63 μm silica gel.

1.2 Instrumentation

All NMR spectra were run at 400 mol/LHz (^{1}H NMR) or 100 mol/LHz (^{13}C NMR/^{31}P NMR) in $CDCl_3$, solution. ^{1}H NMR spectra were internally referenced to TMS. ^{13}C NMR spectra were internally referenced to the residual solvent signal. Data for ^{1}H

NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (J) were reported in Hz. High resolution mass spectra (HRMS) were recorded on Bruker MicrOTOF-QII mass instrument (ESI).

1.3 Materials

Unless otherwise indicated, starting catalysts and materials were obtained from Sigma Aldrich, TCI, Alfa Aesar, Adamas or Acros, moreover, commercially available reagents were used without additional purification.

1.4 General procedure for the substrates

To a solution of NaOH (400 mg, 10 mmol) in ethanol (50 mL) at 0 ℃ was add aldehyde (1.06 g, 10 mmol) and 2′-aminoacetophenone (10 mmol) slowly. Allow the mixture to warm to room temperature for 3 h. Added water to the mixture and extracted with EA. Then remove the solvent under reduced pressure. Purified the crude residue by column chromatography (PE: EA = 20 ∶ 1) to obtain the product in 1.9 g (86% yield).

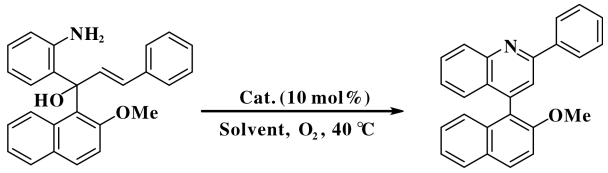
To a stirred solution of 1-bromo-2-methoxynaphthalene (1.18 g, 5 mmol) in THF (50 mL) was added dropwise a 2.5 mol/L solution of *n*-BuLi (2 mL, 5 mmol) in hexane at −78 ℃. After stirring was continued for 1 h at −78 ℃, (E)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one (446 mg, 2 mmol) in THF (10 mL) was added to this solution and stirring was continued for 2 h at ambient temperature. The reaction mixture was diluted with water and extracted with diethyl ethyl. The combined extracts was washed with brine and dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash chromatography (PE ∶ EA = 4 ∶ 1) to give the diarylmethanol 1 (594 mg, 76%) as a yellow foam.

A dry reaction tube equipped with a stir bar was charged withdiarylmethanol 1 (38.1 mg, 0.1 mmol), $Zn(OTf)_2$(3.6 mg, 0.01 mmol). It was capped with a rubber septum, evacuated and backfilled with oxygen. Then CCl_4 was added to the tube. The reaction mixture was stirred at 120 ℃ for 0.5 h. Upon completion, the mixture was directly subjected to silica gel flash chromatography to give the pure product 2.

2 Result and dicussion

Initially, diaryl methanol **1a** was selected as reaction substrate to examine catalytic activities of diverse acid catalysts including Brønsted acids and Lewis acids in DCM solvent at 40 ℃ under O_2 atmosphere. The results in table 1 showed Lewis acid $Zn(OTf)_2$ afforded

Table 1 Optimization of the Reaction Conditions[a]



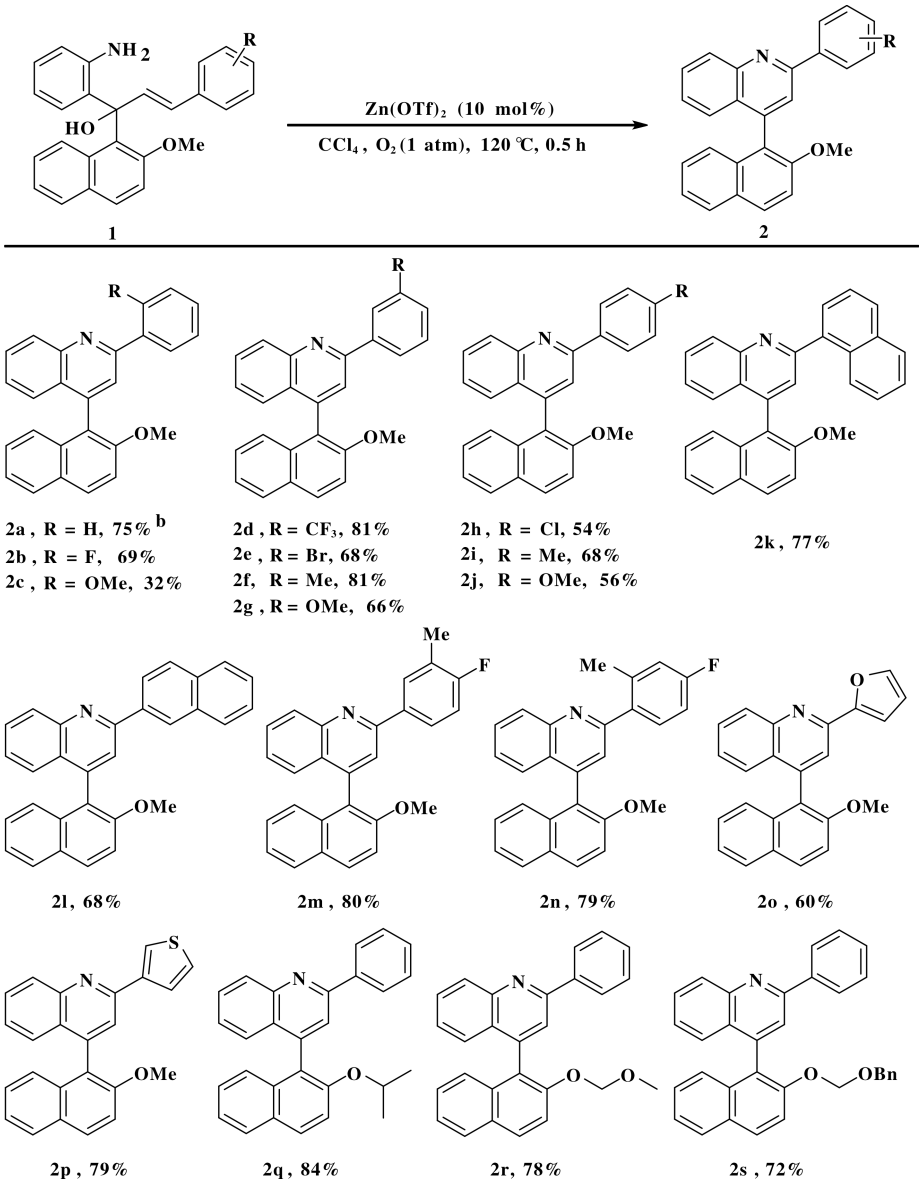
1a　　2a

Entry	Cat.	Solvent	Time/h	Yield/%[b]
1	$(PhO)_2PO_2H$	DCM	12	36
2	CF_3CO_2H	DCM	12	31
3	TsOH	DCM	12	24
4	$B(C_6F_5)_3$	DCM	12	34
5	$Zn(OTf)_2$	DCM	4	56
6	$Dy(OTF)_3$	DCM	4	37
7	$In(OTf)_3$	DCM	4	41
8	$Zn(OTf)_2$	DCM	4	52
9	$Zn(OTf)_2$	DCM	4	21
10	$Zn(OTf)_2$	$CHCl_3$	4	33
11	$Zn(OTf)_2$	Tol	4	35
12	$Zn(OTf)_2$	DMF	4	N.R
13	$Zn(OTf)_2$	CCl_4	4	60
14	$Zn(OTf)_2$	CCl_4	1	65
15	$Zn(OTf)_2$	CCl_4	0.5	71
16	$Zn(OTf)_2$	CCl_4	0.5	75
17	$Zn(OTf)_2$	CCl_4	0.5	50

a. Reaction conditions: **1a** (0.1 mmol), catalyst (10 mol %) in solvent (2.0 mL) at 40 ℃ for indicated time; b. Isolated yield; c. The reaction proceeded at 80 ℃; d. The reaction proceeded at 100 ℃; e. The reaction proceeded at 120 ℃; f. The reaction proceeded at 140 ℃.

a higher yield of 56% (entries 1-9). Next screening of solvent indicated that CCl_4 was superior than other reaction media, providing the desired product **2a** in 60% yield (entries 10-13). Temperature increasing from 40 to 120 ℃ could benefit the outcomes and an isolated yield of 75% was finally acquired for a very shorter 0.5 hours (entries 14-17).

With the optimized reaction conditions in hand, we next carried out to investigate the substrate generality and the results depicted in Scheme 2. Delightingly,



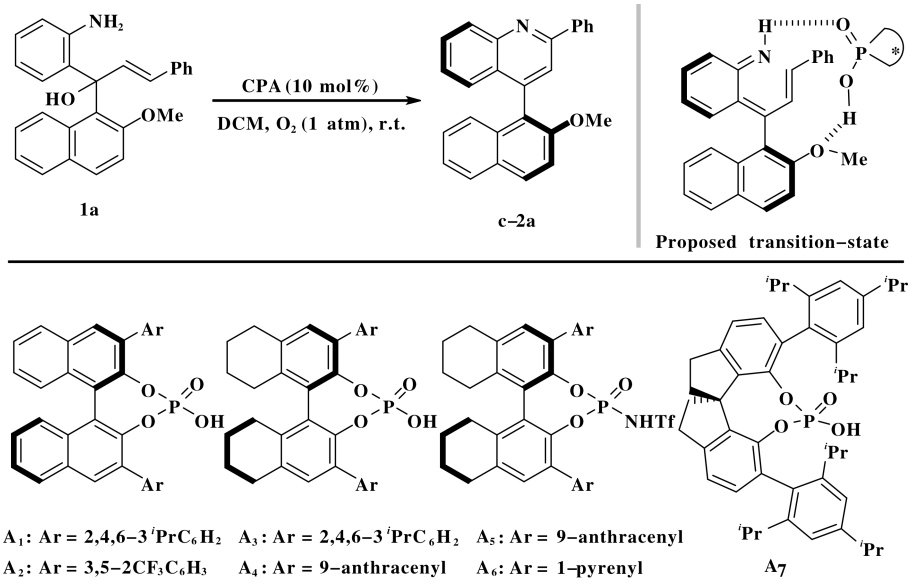
Scheme 2 a Reaction condition: 1a (0.1 mmol), $Zn(OTf)_2$ (10 mol%) in CCl_4 (2.0 mL) at 120 ℃ under O_2 atmosphere for 0.5 h; b. Isolated yield was given.

a vast range of substituted diarylmethanols **1** wereamenable to this reaction regardless of electronic characteristics and position of the substituents. Accordingly, starting materials with halide, methoxyl, methyl and trifluoromethyl group in the aromatic ring were all tolerated to deliver the correspondingproducts **2b-j** with moderate to high yield (54%~81%), except the 2-OMe substituted **2c** with an only 32% yield. 1-/2-Naphthyl-substituted **2k-l** and di-substituted substrates **2m-o** were also easily obtained with good outcomes (68%~80%). Heteroatom aromatic groups such as furan 1o and thiophen 1p were compatible with the stand-

ard reaction conditions as well, providing the desired products 2o-p in good yields of 60% and 79%, respectively. Moreover, protecting group of the oxygen atom at the 2-position in naphthol was explored and the same excellent yields (72% ~ 84%) was obtained for the compounds **2p-s** .

Finally, we want to develop an asymmetric version for this acid-promoted transformation. After a lot of attempted trials in Zn-chiral ligands catalytic system (see SI), we turned our attention to chiral phosphoric acid catalysts. The preliminary results were showed in Table 2. The asymmetric conversion of substrate **1a** to

Table 2 Condition optimization for the asymmetric dehydrativecyclyzation [a]



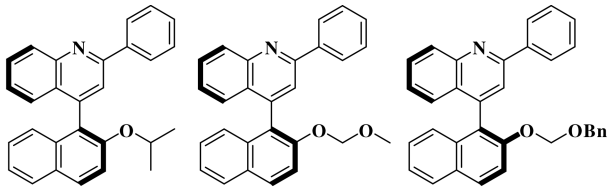
Entry	Cat.	Solvent	Yield/%[b]	Er
1	A1	DCM	16	52 : 48
2	A2	DCM	41	51 : 49
3	A3	DCM	24	52 : 48
4	A4	DCM	37	62 : 38
5	A5	DCM	47	59 : 41
6	A6	DCM	45	59 : 41
7	A7	DCM	11	52 : 48
8	A4	Toluene	44	64 : 36
9	A4	Xylene	43	60 : 40
10	A4	CyH	25	64 : 36
11	A4	MTBE	13	60 : 40

a. Reaction condition: **1a** (0.1 mmol), CPA (10 mol%) in DCM (1.0 mL) at room temperature overnight under O_2 atmosphere; b. Isolated yield; c. Determined by chiral HPLC analysis.

the desired product *c*- **2a** was catalyzed by a series of chiral phosphoric acids. 44% Yield and 64 : 36 er value was gained by A4 in toluene at room temperature. Main challenge in catalytic asymmetric process might be resulted from the fast reaction of the highly reactive intermediate than tough chirality inversion in proposed

transition state from racemic substrate **1a** into chiral product *c*- **2a** was catalyzed by a series of chiral phosphoric acids. 44% Yield and 64 ∶ 36 er value was gained by A4 in toluene at room temperature. Main challenge in catalytic asymmetric process might be resulted from the fast reaction of the highly than tough chirality inversion in proposed transition from racemic substrate **1a** into chiral product *c*- **2a**.

Including **1a** , other substrates with different protected groups such as 1q-s also smoothly underwent the CPA-catalyzed asymmetric dehydrative aromatization. The corresponding products c- **2q-s** were obtained in moderate yields with up to 71 ∶ 29 er (Scheme 3).



c- **2q**, 44%, 60:40 er *c*- **2r**, 37%, 71:29 er *c*- **2s**, 26%, 54.5:45.5 er

Scheme 3 Results for 1q-s to undertake the CPA-catalysis

3 Conclusion

We have realized $Zn(OTf)_2$-promoted dehydrative cyclization/aerobic oxidation aromatization for the direct and practical synthesis of novel axially chiral 4-arylquinolines in high yields (up to 81%). Furthermore, organic chiral phosphoric acid (CPA) are also able to catalyze this transformation and the preliminary results (71 ∶ 29 er) was also obtained. Further efforts will be devoted to the improvement of the enantiomeric excess of this kind of 4-arylquinolines in our laboratory.

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Experimental characterization data:

4-(2-methoxynaphthalen-1-yl)-2-phenylquinoline(2a): Light yellow solid, mp 89 ~ 91 ℃, 27.1 mg, 75% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.28 (d, J = 8.3 Hz, 1H), 8.20 (d, J = 7.3 Hz, 2H), 8.00 (d, J = 9.0 Hz, 1H), 7.86 (s, 2H), 7.68 (t, J = 7.1 Hz, 1H), 7.49 (t, J = 7.1 Hz, 2H), 7.43 (d, J = 8.9 Hz, 2H), 7.31 (dd, J = 14.1, 8.3 Hz, 3H), 7.27 - 7.21 (m, 1H), 7.19 (d, J = 8.3 Hz, 1H), 3.75 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 157.12, 154.37, 148.75, 144.86, 139.86, 133.46, 130.44, 130.12, 129.61, 129.35, 128.95, 128.89, 128.10, 127.76, 127.39, 127.03, 126.28, 125.97, 125.00, 123.93, 121.52, 120.62, 113.44, 56.60. The enantiomeric purity of the product was determined by HPLC analysis: 20% ee (Chiralcel IA, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_r(major) = 5.485 min, t_r(minor) = 5.162 min.

2-(2-fluorophenyl)-4-(2-methoxynaphthalen-1-yl)quinoline(2b): Yellow solid, mp 74 ~ 76 ℃, 26.2 mg, 69% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.33 - 8.24 (m, 1H), 8.20 (t, J = 7.3 Hz, 1H), 8.01 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.1 Hz, 2H), 7.71 (t, J = 6.6 Hz, 1H), 7.44 (d, J = 9.1 Hz, 1H), 7.42 - 7.38 (m, 1H), 7.38 - 7.31 (m, 3H), 7.29 (d, J = 8.2 Hz, 1H), 7.24 (t, J = 9.2 Hz, 2H), 7.20 - 7.11 (m, 1H), 3.78 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 160.85 (d, J = 250.1 Hz), 154.42, 148.72, 144.20, 133.42, 131.70, 131.68, 130.75 (d, J = 8.4 Hz), 130.41, 130.06, 129.49, 128.98, 128.02, 127.36, 126.96, 126.53, 125.98, 124.98, 124.88, 124.80, 124.67 (d, J = 3.1 Hz), 123.89, 120.59, 116.26 (d, J = 22.9 Hz), 113.59, 56.69.

4-(2-methoxynaphthalen-1-yl)-2-(2-methoxyphenyl)quinoline(2c): Yellow foam, mp 78 ~ 79 ℃, 12.6 mg, 32% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.27 (d, J = 8.3 Hz, 1H), 7.99 (dd, J = 16.2, 8.2 Hz, 2H), 7.89 (d, J = 6.8 Hz, 2H), 7.68 (t, J = 7.0 Hz, 1H), 7.45 (d, J = 9.1 Hz, 1H), 7.37 (dd, J = 16.8, 8.6 Hz, 4H), 7.30 (d, J = 5.8 Hz, 2H), 7.15 (t, J = 7.3 Hz, 1H), 6.99 (d, J = 8.1 Hz, 1H), 3.78 (s, 6H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 157.37, 156.74, 154.43, 148.67, 142.69, 133.56, 131.60, 130.27, 130.22, 129.96, 129.04, 127.97, 127.07, 126.77,

126.04, 125.98, 125.87, 125.22, 123.85, 121.30, 113.70, 111.53, 56.71, 55.75.

4-(2-methoxynaphthalen-1-yl)-2-(3-(trifluoromethyl)phenyl)quinoline(2d): Light yellow solid, mp 68~69 ℃, 34.3 mg, 81% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.51 (s, 1H), 8.40 (d, J = 7.4 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 10.3 Hz, 2H), 7.76 - 7.66 (m, 2H), 7.61 (t, J = 7.6 Hz, 1H), 7.46 (d, J = 9.0 Hz, 1H), 7.36 (s, 3H), 7.27 (t, J = 7.4 Hz, 1H), 7.16 (d, J = 8.3 Hz, 1H), 3.78 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 155.34, 154.33, 148.71, 145.41, 140.54, 133.36, 130.90, 130.57, 130.17, 129.89, 129.30, 128.92, 128.14, 127.60, 127.10, 126.73, 125.99, 125.88, 125.84, 124.81, 124.57, 124.53, 123.95, 121.02, 120.24, 113.32, 56.54.

2-(3-bromophenyl)-4-(2-methoxynaphthalen-1-yl)quinoline(2e): Yellow solid, mp 86~88 ℃, 31.9 mg, 68% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.46 (s, 1H), 8.33 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 7.6 Hz, 1H), 8.09 (d, J = 9.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.88 (s, 1H), 7.82 - 7.74 (m, 1H), 7.63 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 9.0 Hz, 1H), 7.42 (s, 4H), 7.36 - 7.28 (m, 1H), 7.22 (d, J = 8.4 Hz, 1H), 3.84 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 155.36, 154.33, 148.66, 145.20, 133.37, 132.17, 130.74, 130.50, 130.31, 130.14, 129.77, 128.93, 128.09, 127.55, 127.05, 126.59, 126.22, 125.95, 124.84, 123.92, 123.14, 121.12, 120.36, 113.37, 56.57.

4-(2-methoxynaphthalen-1-yl)-2-(3-methylphenyl)quinoline(2f): Light yellow solid, mp 84~86 ℃, 30.4 mg, 81% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.28 (d, J = 8.3 Hz, 1H), 8.08 - 8.00 (m, 2H), 7.97 (d, J = 7.5 Hz, 1H), 7.92 - 7.83 (m, 2H), 7.70 (t, J = 6.9 Hz, 1H), 7.45 (d, J = 9.0 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 11.4 Hz, 3H), 7.27 (s, 2H), 7.19 (d, J = 8.4 Hz, 1H), 3.77 (s, 3H), 2.46 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 157.28, 148.71, 144.70, 139.81, 138.48, 133.44, 130.35, 130.07, 130.06, 129.50, 128.94, 128.73, 128.39, 128.04, 127.34, 126.96, 126.15, 125.90, 124.99, 124.87, 123.88, 121.61, 120.70, 113.46, 56.61, 21.60.

4-(2-methoxynaphthalen-1-yl)-2-(3-methoxyphenyl)quinoline(2g): Light yellow foam, mp 83~85℃, 25.8 mg, 66% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.28 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.84 (d, J = 11.1 Hz, 2H), 7.74 (d, J = 7.5 Hz, 1H), 7.72 - 7.66 (m, 1H), 7.45 (d, J = 9.1 Hz, 1H), 7.43 - 7.37 (m, 1H), 7.34 (s, 3H), 7.25 (d, J = 9.8 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.00 (d, J = 7.3 Hz, 1H), 3.91 (s, 3H), 3.77 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 160.18, 156.87, 154.36, 148.67, 144.79, 141.34, 133.43, 130.41, 130.12, 129.81, 129.56, 128.93, 128.07, 127.45, 127.00, 126.28, 125.93, 124.98, 123.90, 121.57, 120.61, 120.20, 115.52, 113.44, 112.72, 56.60, 55.48.

2-(4-chlorophenyl)-4-(2-methoxynaphthalen-1-yl)quinoline(2h): Yellow foam, mp 79~81℃, 25.4 mg, 54% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.25 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.2 Hz, 2H), 8.03 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.82 (s, 1H), 7.74 - 7.67 (m, 1H), 7.51 - 7.42 (m, 3H), 7.34 (s, 4H), 7.30 - 7.21 (m, 1H), 7.17 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 155.74, 154.33, 148.68, 145.09, 138.24, 135.50, 133.39, 130.48, 130.05, 129.73, 128.99, 128.55, 128.09, 127.41, 127.03, 126.44, 125.95, 124.88, 123.92, 121.01, 120.45, 113.39, 56.58.

4-(2-methoxynaphthalen-1-yl)-2-(4-methylphenyl)quinoline(2i): Pale yellow foam, mp 81~82 ℃, 25.4 mg, 68% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.26 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 7.7 Hz, 2H), 8.01 (d, J = 9.0 Hz, 1H), 7.93 - 7.81 (m, 2H), 7.68 (t, J = 6.9 Hz, 1H), 7.45 (d, J = 9.0 Hz, 1H), 7.32 (p, J = 8.9, 7.9 Hz, 5H), 7.25 (d, J = 6.7 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H), 3.77 (s, 3H), 2.41 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.35,

148.72, 144.62, 139.35, 137.03, 133.45, 130.33, 130.00, 129.56, 129.46, 128.94, 128.03, 127.59, 127.25, 126.95, 126.02, 125.89, 125.01, 123.87, 121.31, 120.75, 113.48, 56.61, 21.37.

4-(2-methoxynaphthalen-1-yl)-2-(4-methoxyphenyl)quinoline(2j): Yellow solid, mp 142~144 ℃, 21.9 mg, 56% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.24 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.82 (s, 1H), 7.67 (t, J = 7.0 Hz, 1H), 7.45 (d, J = 9.0 Hz, 1H), 7.36 (d, J = 6.8 Hz, 1H), 7.33 - 7.27 (m, 2H), 7.25 (d, J = 6.5 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 3.86 (s, 3H), 3.77 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 160.82, 156.62, 148.70, 144.59, 133.45, 132.42, 130.32, 129.85, 129.46, 129.03, 128.95, 128.02, 127.07, 126.94, 125.87, 125.02, 123.87, 120.99, 114.21, 113.49, 56.62, 55.42.

4-(2-methoxynaphthalen-1-yl)-2-(naphthalen-1-yl)quinoline(2k): pale yellow foam, mp 184~187 ℃, 31.5 mg, 77% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.34 (d, J = 7.4 Hz, 2H), 8.00 (d, J = 8.9 Hz, 1H), 7.88 (dt, J = 23.3, 7.3 Hz, 4H), 7.73 (d, J = 11.8 Hz, 2H), 7.58 (t, J = 7.5 Hz, 1H), 7.53 - 7.46 (m, 2H), 7.44 (d, J = 9.2 Hz, 2H), 7.37 (dd, J = 19.5, 7.6 Hz, 2H), 7.29 (d, J = 5.3 Hz, 2H), 7.23 (s, 1H), 3.81 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 148.53, 144.28, 138.78, 134.10, 133.38, 131.40, 130.47, 130.04, 129.66, 129.18, 128.91, 128.47, 128.12, 128.05, 127.16, 127.02, 126.63, 126.53, 126.10, 125.96, 125.92, 125.80, 125.47, 124.96, 123.89, 120.34, 113.40, 56.57.

4-(2-methoxynaphthalen-1-yl)-2-(naphthalen-2-yl)quinoline(2l): White foam, mp 193~196 ℃, 28.0 mg, 68% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.64 (s, 1H), 8.44 (d, J = 8.4 Hz, 1H), 8.32 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 5.6 Hz, 2H), 7.98 (d, J = 8.6 Hz, 1H), 7.95 - 7.83 (m, 3H), 7.71 (t, J = 7.1 Hz, 1H), 7.52 - 7.41 (m, 3H), 7.35 (dt, J = 15.2, 8.0 Hz, 3H), 7.28 - 7.20 (m, 2H), 3.78 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 156.89, 154.39, 144.88, 133.91, 133.57, 133.48, 130.44, 130.12, 129.64, 128.97, 128.87, 128.57, 128.09, 127.76, 127.43, 127.27, 127.04, 126.70, 126.32, 125.97, 125.27, 125.01, 123.93, 121.59, 120.66, 113.45, 56.62.

2-(4-fluoro-3-methylphenyl)-4-(2-methoxynaphthalen-1-yl)quinoline(2m): Yellow solid, mp 157~159 ℃, 31.4 mg, 80% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.32 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 6.8 Hz, 1H), 8.11 - 8.01 (m, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.87 (s, 1H), 7.76 (t, J = 6.8 Hz, 1H), 7.52 (d, J = 9.0 Hz, 1H), 7.40 (p, J = 10.4, 8.5 Hz, 3H), 7.32 (d, J = 7.8 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.18 (t, J = 8.9 Hz, 1H), 3.84 (s, 3H), 2.44 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 162.42 (d, J = 247.7 Hz), 156.25, 154.33, 148.66, 144.89, 135.63 (d, J = 3.5 Hz), 133.41, 130.97 (d, J = 5.6 Hz), 130.41, 129.95, 129.62, 128.94, 128.07, 127.22, 126.99, 126.83 (d, J = 8.4 Hz), 126.19, 125.92, 124.92, 123.90, 121.17, 120.57, 115.35 (d, J = 22.6 Hz), 113.42, 56.59, 14.76.

2-(4-fluoro-2-methylphenyl)-4-(2-methoxynaphthalen-1-yl)quinoline(2n): Yellow solid, mp 130~132 ℃, 30.9 mg, 79% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.25 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 9.0 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 6.9 Hz, 1H), 7.64 - 7.55 (m, 1H), 7.51- 7.42 (m, 2H), 7.36 (q, J = 7.8, 7.4 Hz, 3H), 7.28 (t, J = 7.3 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H), 7.00 (t, J = 8.9 Hz, 2H), 3.79 (s, 3H), 2.49 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 162.78 (d, J = 247.0 Hz), 158.92, 154.37, 148.35, 144.14, 138.80 (d, J = 8.0 Hz), 133.36, 131.72, 131.64, 130.45, 129.88, 129.57, 128.92, 128.11, 126.99, 126.87, 126.41, 125.99, 124.81, 124.78, 123.88, 120.32, 117.39 (d, J = 21.1 Hz), 113.41, 112.90 (d, J = 21.3 Hz), 56.56, 20.66.

2-(furan-2-yl)-4-(2-methoxynaphthalen-1-yl)quinoline(2o): Yellow solid, mp 91~92 ℃, 21.1 mg, 60% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.24 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 9.0

Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.80 (s, 1H), 7.67 (s, 1H), 7.60 (s, 1H), 7.44 (d, J = 9.0 Hz, 1H), 7.38 - 7.32 (m, 1H), 7.32 - 7.23 (m, 3H), 7.23 - 7.20 (m, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.57 (s, 1H), 3.77 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.32, 153.93, 148.85, 144.80, 144.08, 133.34, 130.41, 129.71, 128.91, 128.03, 127.40, 126.98, 126.14, 125.94, 124.90, 123.89, 120.39, 119.89, 113.43, 112.20, 110.18, 56.61.

4-(2-methoxynaphthalen-1-yl)-2-(thiophen-3-yl) quinoline (2p): Yellow foam, mp 86 ~ 87 ℃, 28.9 mg, 79% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.21 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 11.2 Hz, 2H), 7.89 (t, J = 7.4 Hz, 2H), 7.75 (s, 1H), 7.67 (t, J = 6.6 Hz, 1H), 7.42 (dd, J = 10.7, 6.2 Hz, 2H), 7.37 - 7.31 (m, 1H), 7.29 (d, J = 7.0 Hz, 2H), 7.24 (d, J = 6.9 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 3.76 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.33, 153.09, 148.68, 144.74, 142.87, 133.40, 130.39, 129.82, 129.57, 128.92, 128.05, 127.31, 127.02, 127.00, 126.30, 126.04, 125.90, 124.96, 124.73, 123.91, 121.46, 120.53, 113.44, 56.60.

4-(2-isopropoxynaphthalen-1-yl)-2-phenylquinoline (2q): Pale yellow foam, mp 77 ~ 78 ℃, 32.7 mg, 84% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.36 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 7.3 Hz, 2H), 8.05 (d, J = 9.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 2H), 7.77 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 7.1 Hz, 2H), 7.55 - 7.48 (m, 2H), 7.44 (t, J = 7.8 Hz, 2H), 7.41 - 7.36 (m, 2H), 7.32 (d, J = 6.7 Hz, 1H), 7.27 (d, J = 8.3 Hz, 1H), 4.60 (dt, J = 11.6, 5.7 Hz, 1H), 1.16 (d, J = 5.8 Hz, 3H), 1.08 (d, J = 5.8 Hz, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 156.86, 153.04, 148.65, 145.19, 133.65, 130.11, 129.97, 129.48, 129.31, 129.10, 128.87, 128.76, 128.01, 127.65, 127.42, 126.81, 126.25, 126.04, 125.16, 124.00, 121.47, 116.89, 72.02, 22.35, 22.23. The enantiomeric purity of the product was determined by HPLC analysis: 20% ee (Chiralcel OD-H, hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 254 nm), t_r(major) = 4.547 min, t_r(minor) = 5.085 min.

4-(2-(methoxymethoxy) naphthalen-1-yl)-2-phenylquinoline (2r): Pale yellow foam, mp 105 ~ 107 ℃, 30.4 mg, 78% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.28 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 7.3 Hz, 2H), 7.99 (d, J = 9.0 Hz, 1H), 7.89 (s, 2H), 7.70 (t, J = 7.2 Hz, 1H), 7.58 (d, J = 9.0 Hz, 1H), 7.51 (t, J = 7.1 Hz, 2H), 7.47 - 7.41 (m, 1H), 7.38 (d, J = 7.7 Hz, 2H), 7.33 (d, J = 6.9 Hz, 1H), 7.31 - 7.24 (m, 1H), 7.21 (d, J = 8.3 Hz, 1H), 5.06 (s, 2H), 3.15 (s, 3H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 156.98, 152.04, 144.77, 133.41, 130.32, 130.07, 129.64, 129.38, 128.89, 128.05, 127.66, 127.37, 126.95, 126.27, 125.97, 125.22, 124.42, 122.35, 121.32, 116.53, 95.02, 56.13. The enantiomeric purity of the product was determined by HPLC analysis: 42% ee (Chiralcel IA, hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 254 nm), t_r(major) = 4.673 min, t_r(minor) = 28.722 min.

4-(2-((benzyloxy)methoxy)naphthalen-1-yl)-2-phenylquinoline (2s): Pale yellow foam, mp 144 ~ 146 ℃, 33.7 mg, 72% yield. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.29 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 7.3 Hz, 2H), 8.00 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 8.7 Hz, 2H), 7.50 (t, J = 7.1 Hz, 2H), 7.45 (d, J = 6.9 Hz, 1H), 7.38 (t, J = 7.8 Hz, 2H), 7.28 (d, J = 7.5 Hz, 2H), 7.25 - 7.17 (m, 4H), 7.08 (s, 2H), 5.19 (q, J = 7.0 Hz, 2H), 4.38 (s, 2H). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 157.03, 151.97, 148.74, 139.73, 137.00, 133.43, 130.36, 130.13, 129.66, 129.63, 129.38, 128.89, 128.41, 128.08, 127.83, 127.69, 127.37, 126.98, 126.31, 125.98, 125.22, 124.41, 122.13, 121.35, 116.28, 92.55, 70.06. The enantiomeric purity of the product was determined by HPLC analysis: 9% ee (Chiralcel IA, hexane/*i*-PrOH = 99/1, flow rate 1.0 mL/min, λ = 254 nm), t_r(major) = 16.388 min, t_r(minor) = 23.424 min.

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酸催化的二芳基甲醇脱水环化氧化芳构化直接构筑 4-芳基喹啉

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摘要：我们发展了酸催化的二芳基甲醇的脱水环化氧化芳构化的方法，直接高产率（高达 81%）的合成轴手性的 4-芳基喹啉. 而且，**Lewis** 酸 **Zn**（**OTf**）$_2$和手性膦酸都能催化这个反应，初步的不对称研究可以用 **er** 71∶29 得到产物.

关键词：手性膦酸；轴手性；手性喹啉