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Iridium-catalyzed asymmetric hydroalkynylation reactions of oxabenzonorbornadienes†

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Jun Hu,[a] Qingjing Yang,[a] Jianbin Xu,[a] Chao Huang,[a] Baomin Fan,*[a] Jun Wang,[b] Chengyuan Lin,[b] Zhaoxiang Bian[b,c] and Albert S. C. Chan*[c]

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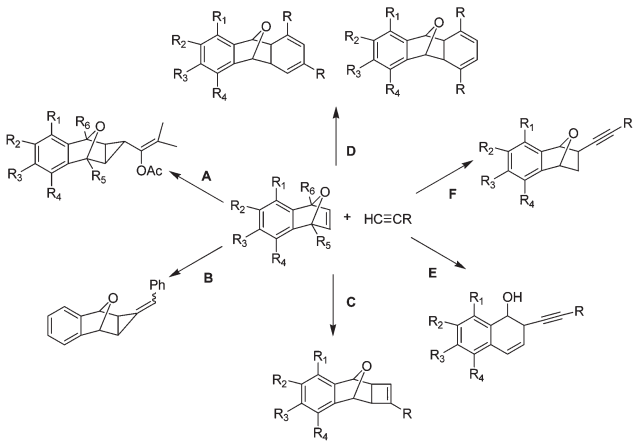
Oxabenzonorbornadienes were found to be suitable substrates for asymmetric hydroalkynylation reactions. Catalyzed by the complex of $[Ir(COD)Cl]_2$ and (*R*)-SYNPHOS, oxabenzonorbornadienes and terminal alkynes could react smoothly to give the alkynylated products in moderate to good yields (up to 93% yield) and enantioselectivities (up to 85% ee).

Introduction

Caused by the coexistence of a carbon–carbon double bond in the strained cycle and an oxygen bridge at the allylic position, oxabenzonorbornadienes have not only high chemical reactivities but also high reactive diversities. Promoted by different catalysts, the isomerization,[1,2] dimerization,[3,4] hydroamination,[5] carbometalation,[6] hydroarylation,[7] chloroacetonylation,[8] carbocyclization[9–15] and ring-opening[16] reactions of oxabenzonorbornadienes have been realized. Furthermore, the reactions of oxabenzonorbornadienes and terminal alkynes are particularly interesting. Under different reaction conditions, oxabenzonorbornadienes and terminal alkynes can undergo [2 + 1] (Scheme 1A and B),[17] [2 + 2] (Scheme 1C),[18] and [2 + 2 + 2] (Scheme 1D)[19] cycloaddition reactions respectively, leading to various cyclic products. In addition, some non-cyclization reactions can also take place between oxabenzonorbornadienes and terminal alkynes. For example, in the presence of $Ni(dppe)Cl_2$, PPh_3, $ZnCl_2$, and Zn powder in toluene at 90 °C, the reaction of oxabenzonorbornadienes with terminal acetylenes gives the ring-opening products in good yields (Scheme 1E).[20] When catalyzed by Herrmann–Beller phosphapalladacycle, addition of trimethylsilylethyne to the carbon–carbon double bond of 7-oxa-benzonorbornadiene (hydroalkynylation reaction) proceeds readily (Scheme 1F).[21] However,



Scheme 1 The catalytic reactions of oxabenzonorbornadienes and terminal alkynes.

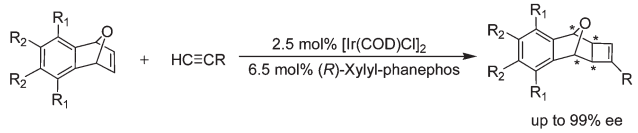
unlike the other reactions of oxabenzonorbornadienes,[3,16] few improvements have been achieved in the asymmetric version of these catalytic reactions between oxabenzonorbornadienes and terminal alkynes (Scheme 2).

Our group has been interested in the asymmetric reactions of norbornadienes and terminal alkynes for some time. We had found that the complex of iridium and chiral xylyl-phanephos is an efficient catalyst for the [2 + 2] cycloadditions of oxabenzonorbornadienes and terminal alkynes, with which the cyclobutene products can be constructed in a single step with up to 99% ee.[22] Recently, we also reported that changing the chiral diphosphine ligand from (*R*)-xylyl-phanephos to (*R*)-SYNPHOS (also named as BisbenzodioxanPhos), resulted in an iridium catalyst that can promote the asymmetric addition of the carbon–hydrogen bond of terminal alkynes to the carbon–carbon double bond of norbornadienes smoothly, and the hydroalkynylation products are generated with good yields (up to 92%) and high enantioselectivities (up to 97% ee).[23] During

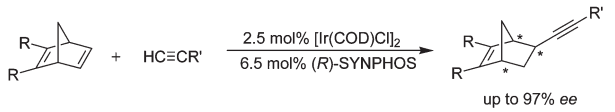
[a]*Key Laboratory of Chemistry in Ethnic Medicinal Resources, State Ethnic Affairs Commission and Ministry of Education, Yunnan University of Nationalities, Kunming, 650500, China. E-mail: adams.bmf@hotmail.com; Fax: (+86)-871-5910017*
[b]*School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China*
[c]*Institute of Creativity, Hong Kong Baptist University, Hong Kong, China. E-mail: ascchan@hkbu.edu.hk; Fax: +852-34112123*

†Electronic supplementary information (ESI) available: Copies of ^1H and ^{13}C NMR spectra of new compounds, and HPLC chromatograms. See DOI: 10.1039/c2ob26775f

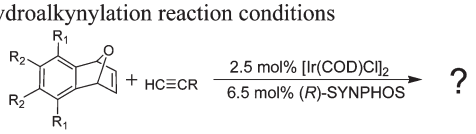
(A) Iridium-catalyzed asymmetric [2+2] cycloaddition reaction of oxabenzonorbornadienes and terminal alkynes



(B) Iridium-catalyzed asymmetric hydroalkynylation of norbornadienes



(C) Reaction of oxabenzonorbornadienes under asymmetric hydroalkynylation reaction conditions



Scheme 2 The Ir catalyzed asymmetric reactions of norbornadiene derivatives and terminal alkynes.

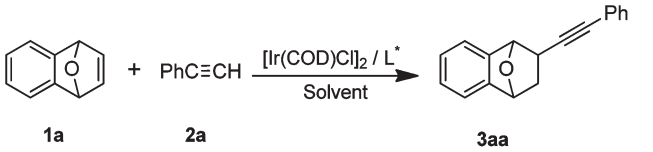
the course of our further investigation on this iridium-catalyzed asymmetric hydroalkynylation reaction, we wondered if oxabenzonorbornadienes can serve as substrates for this reaction, and how the oxygen atom at the bridge chain would affect the reaction. Herein, we wish to report the results of our exploration of oxabenzonorbornadienes as substrates in the iridium-catalyzed asymmetric hydroalkynylation reactions.

Results and discussion

In our initial trial, oxabenzonorbornadiene **1a** was treated with phenylacetylene **2a** (2 equiv.) under the conditions which had been optimized for the asymmetric hydroalkynylation reaction of norbornadienes. Using the complex of $[Ir(COD)Cl]_2$ and (*R*)-SYNPHOS **4** as catalyst, DCE as solvent, the reaction was completed after 24 hours' stirring at 70 °C, and the hydroalkynylation product **3aa** was separated with 63% yield and 77% ee (Table 1, entry 1). Just like in the iridium-catalyzed [2 + 2] cycloaddition reaction of oxabenzonorbornadienes and terminal alkynes, only the carbon–carbon double bond in oxabenzonorbornadiene **1a** was involved here, and the oxygen bridge chain was maintained without any transformation.! After one simple recrystallization, the ee value of **3aa** could be increased to 96%.

Since the catalytic reactions of oxabenzonorbornadienes and terminal alkynes are quite sensitive to reaction conditions, it is necessary to investigate the effect of various reaction parameters on this iridium-catalyzed asymmetric hydroalkynylation reaction of oxabenzonorbornadiene **1a**. The chiral ligand was the main focus, and several types of chiral ligands were examined (Fig. 1). As shown in Table 1, the monodentate chiral ligands, (*R*)-MONOPHOS **6** and (*S*)-NMDPP **8**, were proved useless in this reaction (Table 1, entries 3 and 5), since

Table 1 Iridium-catalyzed asymmetric addition of phenylacetylene **2a** to 7-oxabenzonorbornadiene **1a** with different chiral ligands[a]



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

Entry	Temp (°C)	Solvent	Ligand	Time (h)	Yield[b] (%)	ee[c] (%)
1	70	DCE	**4**	24	63	77 (96)[d]
2	90	DCE	**5**	18	Trace	N.D.
3	90	DCE	**6**	18	6	N.D.
4	90	DCE	**7**	18	NR	/
5	90	DCE	**8**	24	Complex result	/
6	90	DCE	**9**	18	Trace	N.D.
7	90	DCE	**10**	18	22	<10
8	90	DCE	**11**	18	80	43
9	90	DCE	**12**	12	70	48
10	90	DCE	**13**	12	64	38
11	90	DCE	**14**	18	51	67
12	90	DCE	**15**	18	69	66
13	90	DCE	**16**	18	48	61
14	90	DCE	**17**	12	68	70
15	90	DCE	**4**	6	67	73
16	50	DCE	**4**	60	47	76
17	rt	DCE	**4**	60	<10	/
18	70	THF	**4**	24	68	66
19	70	DME	**4**	24	52	68
20	70	Toluene	**4**	24	27	62
21	70	^{i}PrOH	**4**	24	50	69

[a] Reaction conditions: **1a** (0.3 mmol), **1a** : **2a**:$[Ir(COD)Cl]_2$: bidentate ligand (1 : 2 : 0.025 : 0.065) and **1a** : **2a**:$[Ir(COD)Cl]_2$: monodentate ligand (1 : 2 : 0.025 : 0.13), in solvent (2 mL) under Ar for indicated period of time. [b] Isolated yield by column chromatography. [c] ee % were determined by chiral HPLC using a Chiralcel OD-H column. [d] The ee value was determined after one simple recrystallization.

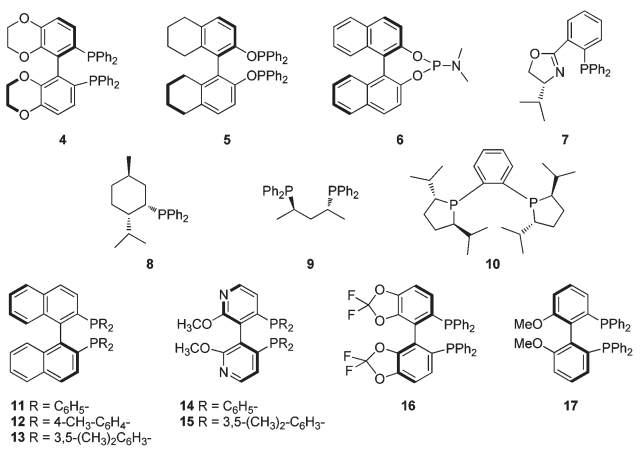


Fig. 1 Chiral ligands tested in the addition of terminal alkynes to 7-oxabicyclic alkenes.

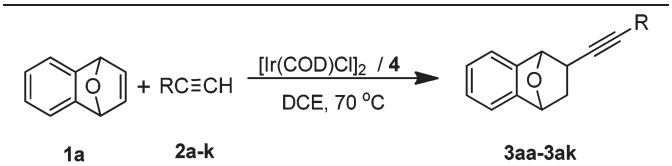
the former gave the desired product in a very poor yield and the latter resulted a quite complex mixture. The chiral diphosphinite ligand **5**, N,P-ligand (*R*)-^{i}Pr-PHOX **7** and diphosphine ligand (*R*,*R*)-BDPP **9** were also invalid in this reaction (Table 1,

entries 2, 4 and 6). (*R*,*R*)-^{i}Pr-DUPHOS **10** showed low efficiency in this reaction (Table 1, entry 7). However, we determined that biaryl diphosphine ligands were more efficient in this reaction (Table 1, entries 8–15). The BINAP ligands **11–13**, PyPhos ligands **14** and **15**, (*R*)-DIFLUORPHOS **16** and (*S*)-MeO-BIPHEP **17** could all make the desired product **3aa** in moderate to good yields and enantioselectivities. (*R*)-SYNPHOS **4** was optimal in all of these chiral ligands tested and could promote the best enantioselectivity along with good yield. Just like in the asymmetric hydroalkynylation reaction of norbornadienes, the screening of temperature and solvent showed 70 °C and DCE were the best ones (Table 1, entries 1 and 15–21).

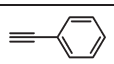
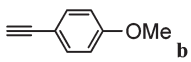
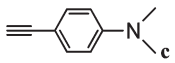
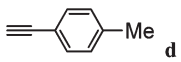
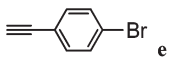
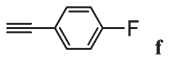
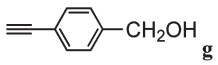
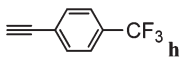
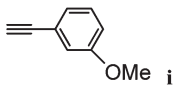
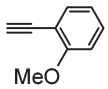
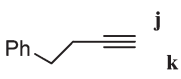
Under the best reaction conditions for asymmetric hydroalkynylation reaction of oxabenzonorbornadiene **1a**, which are the same as those for asymmetric hydroalkynylation reaction of norbornadienes, a series of terminal alkynes **2a–k** were tested, and the results are summarized in Table 2. Generally, all terminal aromatic alkynes could react with **1a** smoothly to provide the corresponding products in moderate to good yields and enantioselectivities (Table 2, entries 1–10). Substituents with different electronic and steric properties on the aromatic rings of terminal alkynes **2b–j** were well tolerated by this addition reaction. It should be noted that the terminal alkyne with CH_2OH on the aromatic ring afforded the hydroalkynylation product in good enantioselectivity (73% ee) and moderate yield (54%) (entry 7), and no competitive reactions of the hydroxy group adding to oxabenzonorbornadiene **1a** were observed. In addition, the aliphatic terminal alkyne **2k** could also be used in this catalytic system with **1a**, giving the corresponding hydroalkynylation product with comparable yield and ee value (entry 11).

To extend the substrate scope of this transformation, several substituted oxabenzonorbornadiene derivatives **1b–i** were also examined (Table 3). It can be seen that the electronic properties of the substituents on the phenyl ring have obvious effect on the enantioselectivities of the reactions. Electron-withdrawing groups are preferred in this catalytic system, since higher enantioselectivities can be obtained. For example, when employing dibromo-oxabenzonorbornadiene **1d**, an 85% ee was achieved, which represented the highest enantioselectivity for the asymmetric hydroalkynylation reaction of oxabenzonorbornadienes (entry 3). However, electron-donating groups slightly decrease the enantioselectivities of the reactions (entry 2, and entries 4–6). Bulky substituents in oxabenzonorbornadiene derivatives have a negative effect on the reactions, and the closer the substituents to the carbon–carbon double bonds, the greater the negative effect on the reactions. This was proved by the fact that the methoxy groups in **1b** caused the decrease of the reaction's enantioselectivity (entry 1), however the methyl groups on the bridgeheads in **1h** and **1i** blocked the reactions completely (entry 7 and entry 8).

Table 2 Iridium-catalyzed asymmetric addition of various alkynes **2a–k** to 7-oxabenzonorbornadiene **1a**[a]



1a **2a-k** **3aa-3ak**

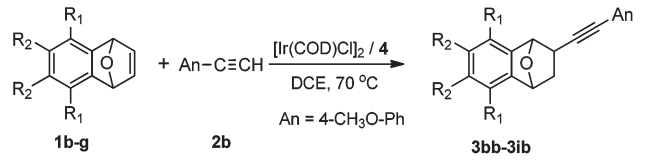
Entry	Alkyne	Time (h)	Yield[b] (%)	ee[c] (%)
1	 **a**	24	63	77
2	 **b**	24	87	78
3	 **c**	10	90	74
4	 **d**	30	90	69
5	 **e**	60	82	62
6	 **f**	60	89	75
7	 **g**	15	54	73
8	 **h**	60	51	73
9	 **i**	48	76	74
10	 **j**	36	93	75
11	 **k**	48	61	67

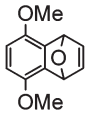
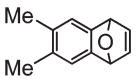
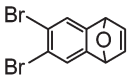
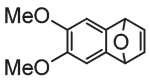
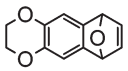
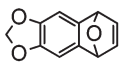
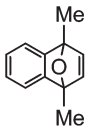
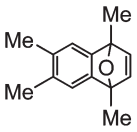
[a] Reaction conditions: **1a** (0.3 mmol), **1a** : **2a**:[Ir(COD)Cl]$_2$: **4** = 1 : 1.5 : 0.025 : 0.065, in DCE (2 mL) at 70 °C under Ar for indicated period of time. [b] Isolated yield by column chromatography. [c] ee % were determined by chiral HPLC using a Chiralcel OD-H or AD-H column.

Conclusions

In summary, it was found that oxabenzonorbornadienes could also be served as substrates for the iridium-catalyzed asymmetric hydroalkynylation reactions. Under the best reaction conditions, which were same as those for norbornadienes, most of the tested oxabenzonorbornadienes reacted with terminal alkynes smoothly, generating the addition products of carbon–hydrogen bonds in terminal alkynes across the carbon–carbon double bonds in oxabenzonorbornadienes. Though the oxygen bridges were maintained without any transformation in these reactions, compared with carbon bridges,[23] they did affect the enantioselectivities of the reactions negatively. Generally, moderate to good ee values (up to 85%) were obtained. The influence of the electronic and steric properties of substituents in substrates was also investigated. Further improvements of this type of catalytic reactions and detailed study of the reaction mechanism are still in progress.

Table 3 Iridium-catalyzed asymmetric addition of 4-methoxy-phenyl-acetylene **2b** to substituted oxabenzonorbornadiene derivatives **1b–g**[a]



Entry	Substituted oxabenzonorbornadiene	Time (h)	Yield[b] (%)	ee[c] (%)
1	 **b**	19	92	67 (87)[d]
2	 **c**	19	81	75
3	 **d**	19	84	85[e]
4	 **e**	60	66	76 (98)[d]
5	 **f**	65	75	73
6	 **g**	46	70	72
7	 **h**	60	NR	/
8	 **i**	60	NR	/

[a] Reaction conditions: **1a** (0.3 mmol), **1a** : **2a**:$[Ir(COD)Cl]_2$: **4** = 1 : 1.5 : 0.025 : 0.065, in DCE (2 mL) at 70 °C under Ar for indicated period of time. [b] Isolated yield by column chromatography. [c] ee % were determined by chiral HPLC using a Chiralcel OD-H, OJ-H or AD-H column. [d] The ee value was determined after one simple recrystallization. [e] The other two repeated experiments showed 84% and 84.5% ee values respectively.

Experimental section

General remarks

The reactions and manipulations were performed under an atmosphere of argon by using standard Schlenk techniques and Drybox (Mikrouna, Supper 1220/750). Anhydrous toluene, DME and THF were distilled from sodium benzophenone ketyl prior to use. Anhydrous DCE was distilled from calcium hydride and stored under argon. Absolute isopropyl alcohol was distilled from magnesium and stored under argon. Alkynes were purchased from Sigma-Aldrich company, chiral ligands were purchased from Strem company, and oxabenzonorbornadienes were synthesized according to the reported procedures in literatures.[24] ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker-Avance 400 or 500 MHz spectrometer. $CDCl_3$ was used as solvent. Chemical shifts (δ) were reported in ppm with tetramethylsilane as internal standard, and J values were given in Hz. The enantioselective excesses were determined by Agilent 1260 Series HPLC using Daicel AD-H, OD-H, or OJ-H chiral columns eluted with a mixture of isopropyl alcohol and hexane. Melting points were measured on X-4 melting point apparatus and uncorrected. High resolution mass spectra (HRMS) were performed on a VG Autospec-3000 spectrometer. Column chromatography was performed with silica gel (200–300 mesh).

Typical procedure for the iridium-catalyzed asymmetric hydroalkynylations of oxabenzonorbornadienes

Under the protection of argon, $[Ir(COD)Cl]_2$ (5.1 mg, 0.0075 mmol), (*R*)-SYNPHOS **4** (12.5 mg, 0.0195 mmol) and 1.0 mL 1,2-dichloroethane were added to a Schlenk tube. The solution obtained was stirred at room temperature. 30 minutes later, 7-oxa-benzonorbornadiene **1a** (43.2 mg, 0.3 mmol) and another 1.0 mL 1,2-dichloroethane were added, and the stirring was continued for additional 20 minutes. After the addition of phenylacetylene **2a** (61.2 mg, 0.6 mmol), the Schlenk tube was sealed with a rubber septum and moved to an oil bath. The mixture was stirred at 70 °C (bath temperature) until the reaction was complete. After vacuum evaporation of the reaction solvent, the residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (15 : 1), and a white solid was obtained as product **3aa** (46.5 mg, 63% yield). The enantioselective excess of the product was determined to be 77% by chiral HPLC. After one simple recrystallization, the ee value increased to 96%.

2-(Phenylethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3aa). White solid, 63% yield, mp 96–97 °C, 77% ee (96% ee after one simple recrystallization). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.43 (m, 2H), 7.29–7.27 (m, 5H), 7.25–7.22 (m, 2H), 5.52–5.51 (d, J = 4.9 Hz, 1H), 5.47 (s, 1H), 2.75–2.72 (dd, J = 8.36, 4.00 Hz, 1H), 2.29–2.24 (dt, J = 11.56, 4.78 Hz, 1H), 1.95–1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 144.4, 131.6, 128.2, 127.8, 127.1, 126.8, 123.5, 119.3, 119.1, 92.0, 84.4, 81.3, 79.2, 36.7, 32.3; HRMS (ESI) calcd for $C_{18}H_{14}ONa$ $[M + Na]^+$, 269.0942, found 269.0948; HPLC (Chiralcel OD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 8.0 min, t_{major} = 18.9 min.

2-((4-Methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ab). White solid, 87% yield, mp 124–125 °C, 78% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.31 (m, 2H), 7.30–7.17 (m, 4H), 6.85–6.82 (m, 2H), 5.54–5.53 (d, J = 4.9 Hz, 1H), 5.47 (s, 1H), 3.81 (s, 3H), 2.75–2.72 (dd, J = 8.38, 4.12 Hz, 1H), 2.29–2.24 (dt, J = 11.54, 4.46 Hz, 1H), 1.97–1.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 145.3, 144.4, 133.0, 127.1, 126.8, 119.3, 119.1, 115.7, 113.8, 90.4, 84.5, 81.1, 79.2, 55.2, 36.8, 32.3; HRMS (ESI) calcd for $C_{19}H_{16}O_2Na$ $[M + Na]^+$, 299.1048, found 299.1062; HPLC (Chiralcel OD-H, i-propanol/

hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 10.1 min, t_{major} = 19.7 min.

***N*,*N*-Dimethyl-4-((1,2,3,4-tetrahydro-1,4-epoxynaphthalen-2-yl)ethynyl)aniline (3ac).** White solid, 92% yield, mp 115–116 °C, 74% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.21 (m, 4H), 7.16–7.14 (m, 2H), 6.60–6.58 (d, J = 8.8 Hz, 2H), 5.50–5.49 (d, J = 4.8 Hz, 1H), 5.43 (s, 1H), 2.94 (s, 6H), 2.73–2.70 (dd, J = 8.00, 4.00 Hz, 1H), 2.26–2.21 (dt, J = 11.56, 4.78 Hz, 1H), 1.93–1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.8, 145.4, 144.6, 132.7, 127.1, 126.8, 119.3, 119.1, 111.8, 110.6, 89.4, 84.6, 82.0, 79.2, 40.3, 36.9, 32.5; HRMS (ESI) calcd for $C_{20}H_{19}NONa$ $[M + Na]^+$, 312.1364, found 312.1360; HPLC (Chiralcel AD-H, *i*-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 9.7 min, t_{minor} = 11.2 min.

2-(*p*-Tolylethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ad). White solid, 90% yield, mp 107–108 °C, 69% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36–7.35 (m, 2H), 7.32–7.21 (m, 4H), 7.20–7.11 (m, 2H), 5.55–5.54 (d, J = 5.0 Hz, 1H), 5.48 (s, 1H), 2.76–2.74 (dd, J = 8.50, 4.50 Hz, 1H), 2.35 (s, 3H), 2.30–2.26 (dt, J = 11.50, 4.88 Hz, 1H), 1.97–1.93 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.6, 144.7, 138.1, 131.8, 129.2, 127.4, 127.1, 120.7, 119.6, 119.3, 91.5, 84.7, 81.7, 79.5, 37.0, 32.6, 21.7; HRMS (ESI) calcd for $C_{19}H_{17}O$ $[M + 1]^+$, 261.1279, found 261.1283; HPLC (Chiralcel OD-H, i-propanol/hexane = 5/95, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 8.5 min, t_{major} = 14.1 min.

2-((4-Bromophenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ae). White solid, 82% yield, mp 88–89 °C, 62% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.44 (m, 2H), 7.33–7.28 (m, 4H), 7.22–7.20 (m, 2H), 5.56 (d, J = 4.8 Hz, 1H), 5.49 (s, 1H), 2.76–2.73 (dd, J = 8.37, 4.10 Hz, 1H), 2.31–2.26 (dt, J = 11.58, 4.8 Hz, 1H), 2.00–1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 144.3, 133.1, 131.5, 127.3, 126.9, 122.5, 122.0, 119.3, 119.1, 93.3, 84.3, 80.4, 79.2, 36.7, 32.4; HRMS (ESI) calcd for $C_{18}H_{13}BrONa$ $[M + Na]^+$, 347.0047, found 347.0050; HPLC (Chiralcel OD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 6.7 min, t_{minor} = 8.5 min.

2-((4-Fluorophenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3af). White solid, 89% yield, mp 128–129 °C, 75% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.31–7.25 (m, 2H), 7.21–7.18 (m, 2H), 7.01–6.98 (m, 2H), 5.54–5.53 (d, J = 5.0 Hz, 1H), 5.47 (s, 1H), 2.74–2.72 (dd, J = 8.52, 4.02 Hz, 1H), 2.28–2.25 (dt, J = 9.52, 4.50 Hz, 1H), 1.97–1.93 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4, 161.5, 145.5, 144.6, 133.8, 133.7, 127.5, 127.1, 119.9, 119.8, 119.6, 119.3, 115.8, 115.6, 91.92, 91.91, 84.6, 80.5, 79.4, 37.0, 32.5; HRMS (ESI) calcd for $C_{18}H_{14}OF$ $[M + 1]^+$, 265.1029, found 265.1045; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 6.8 min, t_{minor} = 9.8 min.

(4-((1,2,3,4-Tetrahydro-1,4-epoxynaphthalen-2-yl)ethynyl)phenyl)methanol (3ag). White solid, 54% yield, mp 88–89 °C, 73% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.36 (m, 2H), 7.25–7.19 (m, 4H), 7.16–7.12 (m, 2H), 5.48–5.47 (d, J = 5.0 Hz, 1H), 5.42 (s, 1H), 4.63–4.62 (d, J = 6.4 Hz, 2H), 2.71–2.68 (dd, J = 8.40, 4.16 Hz, 1H), 2.25–2.19 (dt, J = 11.56, 4.52 Hz, 1H), 1.92–1.87 (m, 1H), 1.74–1.71 (t, J = 5.96 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 144.3, 140.5, 131.9, 127.2, 126.9, 126.7, 122.8, 119.3, 119.1, 92.1, 84.4, 81.1, 79.2, 65.0, 36.8, 32.4; HRMS (ESI) calcd for $C_{19}H_{16}O_2Na$ $[M + Na]^+$, 299.1048, found 299.1050; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 18.0 min, t_{minor} = 22.0 min.

2-((4-(Trifluoromethyl)phenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ah). White solid, 51% yield, mp 129–130 °C, 73% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.50 (m, 4H), 7.31–7.24 (m, 2H), 7.21–7.17 (m, 2H), 5.54–5.53 (d, J = 4.2 Hz, 1H), 5.48 (s, 1H), 2.76–2.73 (dd, J = 8.37, 4.00 Hz, 1H), 2.30–2.25 (dt, J = 11.56, 4.76 Hz, 1H), 1.98–1.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.3, 144.2, 131.9, 129.7, 129.4, 127.4, 127.3, 126.9, 125.20, 125.16, 125.13, 125.09, 122.6, 119.3, 119.2, 94.8, 84.3, 80.2, 79.2, 36.7, 32.4; HRMS (ESI) calcd for $C_{19}H_{13}F_3ONa$ $[M + Na]^+$, 337.0816, found 337.0813; (Chiralcel OD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 6.1 min, t_{minor} = 7.9 min.

2-((3-Methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ai). White solid, 76% yield, mp 100–101 °C, 74% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.25 (m, 2H), 7.22–7.14 (m, 4H), 7.02–6.99 (m 1H), 6.83–6.80 (m, 1H), 5.51–5.50 (d, J = 4.8 Hz, 1H), 5.45 (s, 1H), 3.77 (s, 3H), 2.73–2.70 (dd, J = 8.40, 4.16 Hz, 1H), 2.26–2.21 (dt, J = 11.60, 4.56 Hz, 1H), 1.92–1.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 145.3, 144.4, 129.3, 127.2, 126.9, 124.6, 124.2, 119.3, 119.1, 116.4, 114.6, 91.9, 84.4, 81.3, 79.2, 55.3, 36.8, 32.4; HRMS (ESI) calcd for $C_{19}H_{16}O_2Na$ $[M + Na]^+$, 299.1048, found 299.1045; (Chiralcel OD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 10.3 min, t_{major} = 25.2 min.

2-((2-Methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3aj). White solid, 93% yield, mp 109–110 °C, 75% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (m, 1H), 7.25–7.19 (m, 3H), 7.14–7.12 (m, 2H), 6.87–6.81 (m, 2H), 5.49 (d, J = 4.8 Hz, 1H), 5.46 (s, 1H), 3.84 (s, 3H), 2.77 (dd, J = 8.36, 4.16 Hz, 1H), 2.29–2.23 (dt, J = 11.56, 4.68 Hz, 1H), 1.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9, 145.4, 144.5, 133.8, 129.3, 127.1, 126.8, 120.4, 119.3, 119.1, 112.6, 110.5, 96.2, 84.5, 79.3, 55.8, 36.9, 32.7; HRMS (ESI) calcd for $C_{19}H_{16}O_2Na$ $[M + Na]^+$, 299.1048, found 299.1043; (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 14.2 min, t_{minor} = 15.6 min.

2-(4-Phenylbut-1-yn-1-yl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3ak). Colorless oil, 61% yield, 67% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34–7.16 (m, 9H), 5.49–5.48 (d, J = 5.5 Hz, 1H), 5.33 (s, 1H), 2.88–2.85 (t, J = 7.50 Hz, 2H), 2.54–2.49 (m, 3H), 2.14–2.10 (m, 1H), 1.87–1.83 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.6, 144.7, 141.2, 128.8, 128.6, 127.3, 127.0, 126.5, 119.5, 119.2, 84.8, 83.4, 80.9, 79.4, 37.0, 35.7, 31.9, 21.4; HRMS (EI) calcd for $C_{20}H_{18}O$ $[M]^+$, 274.1358, found 274.1350; HPLC (Chiralcel AD-H, i-propanol/hexane = 1/99, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 10.7 min, t_{minor} = 12.8 min.

5,8-Dimethoxy-2-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3bb). White solid, 92% yield,

mp 105–107 °C, 67% ee (87% ee after one simple recrystallization). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.39 (m, 2H), 6.85–6.83 (m, 2H), 6.69–6.68 (d, J = 0.7 Hz, 2H), 5.71–5.70 (d, J = 4.8 Hz, 1H), 5.64 (s, 1H), 3.84–3.82 (m, 9H), 2.78–2.75 (dd, J = 8.45, 4.16 Hz, 1H), 2.27–2.23 (dt, J = 11.52, 4.52 Hz, 1H), 2.00–1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 146.7, 146.6, 134.6, 133.6, 133.0, 115.8, 113.8, 111.5, 111.2, 90.6, 82.4, 81.0, 56.1, 55.3, 36.4, 31.9; HRMS (ESI) calcd for $C_{21}H_{20}O_4Na$ $[M + Na]^+$, 359.1259, found 359.1256; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 11.0 min, t_{major} = 16.3 min.

2-((4-Methoxyphenyl)ethynyl)-6,7-dimethyl-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3cb). White solid, 81% yield, mp 136–137 °C, 75% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.37 (d, J = 8.5 Hz, 2H), 7.08 (br, 1H), 7.03 (br, 1H), 6.84–6.82 (d, J = 8.5 Hz, 2H), 5.47–5.46 (d, J = 5 Hz, 1H), 5.40 (s, 1H), 3.81 (s, 3H), 2.72–2.69 (dd, J = 8.00, 4.00 Hz, 1H), 2.25–2.21 (m, 7H), 1.93–1.89 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.4, 143.5, 142.6, 135.4, 135.1, 133.3, 120.8, 120.6, 116.0, 114.0, 91.0, 84.7, 81.2, 79.4, 55.5, 37.5, 32.9, 20.23, 20.20; HRMS (ESI) calcd for $C_{21}H_{21}O_2$ $[M + 1]^+$, 305.1542, found 305.1551; HPLC (Chiralcel OD-H, i-propanol/hexane = 20/80, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{minor} = 8.2 min, t_{major} = 11.9 min.

6,7-Dibromo-2-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3db). White solid, 92% yield, mp 190–192 °C, 85% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (s, 1H), 7.51 (s, 1H), 7.38–7.26 (m, 2H), 6.84–6.81 (m, 2H), 5.48–5.47 (d, J = 5 Hz, 1H), 5.40 (s, 1H), 3.79 (s, 3H), 2.75–2.72 (dd, J = 8.00, 3.96 Hz, 1H), 2.28–2.24 (dt, J = 9.50, 4.50, Hz, 1H), 1.95–1.91 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.6, 146.6, 145.7, 133.3, 125.0, 124.8, 123.4, 123.0, 115.6, 114.1, 89.6, 84.1, 81.9, 79.0, 55.5, 36.7, 32.4; HRMS (ESI) calcd for $C_{19}H_{14}O_2Br_2$ $[M]^+$, 431.9361, found 431.9363; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 11.9 min, t_{minor} = 13.1 min.

6,7-Dimethoxy-2-((4-methoxyphenyl)ethynyl)-1,2,3,4-tetrahydro-1,4-epoxynaphthalene (3eb). White solid, 66% yield, mp 125–127 °C, 76% ee (98% ee after one simple recrystallization). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38–7.35 (m, 2H), 6.90–6.81 (m, 4H), 5.48–5.47 (d, J = 4.5 Hz, 1H), 5.41 (s, 1H), 3.89–3.87 (s, 6H), 3.80 (s, 3H), 2.68–2.65 (dd, J = 8.50, 4.00 Hz, 1H), 2.24–2.20 (dt, J = 11.50, 5.00 Hz, 1H), 1.90–1.86 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.4, 148.5, 148.2, 137.9, 137.0, 133.2, 116.0, 114.0, 104.2, 104.1, 90.8, 85.0, 81.2, 79.7, 56.53, 56.5, 55.5, 37.5, 32.9; HRMS (ESI) calcd for $C_{21}H_{21}O_4$ $[M + 1]^+$, 337.1440, found 337.1460; HPLC (Chiralcel OJ-H, i-propanol/hexane = 50/50, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 42.5 min, t_{minor} = 68.2 min.

7-((4-Methoxyphenyl)ethynyl)-2,3,6,7,8,9-hexahydro-6,9-epoxynaphtho[2,3-b][1,4]dioxine (3fb). White solid, 75% yield, mp 178–180 °C, 73% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.35 (m, 2H), 6.83–6.80 (m, 3H), 6.77 (s, 1H), 5.43–5.42 (d, J = 5.2 Hz, 1H), 5.36 (s, 1H), 4.22 (s, 4H), 3.80 (s, 3H), 2.71–2.68 (dd, J = 8.40, 4.00 Hz, 1H), 2.24–2.18 (dt, J = 11.60, 4.80 Hz, 1H), 1.93–1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 142.3, 142.0, 138.4, 137.5, 133.0, 115.7, 113.8, 109.2, 108.9, 90.6, 84.4, 81.0, 79.1, 64.3, 55.3, 37.4, 32.8; HRMS (ESI) calcd for $C_{21}H_{19}O_4$ $[M + 1]^+$, 335.1278, found 335.1272; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 27.8 min, t_{minor} = 33.6 min.

6-((4-Methoxyphenyl)ethynyl)-5,6,7,8-tetrahydro-5,8-epoxynaphtho[2,3-d][1,3]dioxole (3gb). White solid, 70% yield, mp 189–190 °C, 72% ee. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.38 (m, 2H), 6.85–6.82 (m, 3H), 6.78 (s, 1H), 5.99 (d, J = 1.2 Hz, 1H), 5.96–5.95 (d, J = 1.2 Hz, 1H), 5.46–5.45 (d, J = 4.8 Hz, 1H), 5.39 (s, 1H), 3.83 (s, 3H), 2.70–2.67 (dd, J = 8.40, 4.00 Hz, 1H), 2.26–2.21 (dt, J = 11.60, 4.80 Hz, 1H), 1.92–1.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 146.7, 146.4, 139.1, 138.1, 133.0, 115.7, 113.8, 101.6, 101.4, 101.2, 90.4, 84.6, 81.0, 79.3, 55.3, 37.0, 32.5; HRMS (ESI) calcd for $C_{20}H_{16}O_4Na$ $[M + Na]^+$, 343.0946, found 343.0941; HPLC (Chiralcel AD-H, i-propanol/hexane = 10/90, flow rate 1.0 mL min^{-1}, λ = 254 nm): t_{major} = 22.3 min, t_{minor} = 27.4 min.

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