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# Iridium-Catalyzed Asymmetric Ring-Opening of Oxabenzonorbornadienes with *N*-Substituted Piperazine Nucleophiles

**Wen Yang [1], Renshi Luo [2] and Dingqiao Yang [1,*]**

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[1] Key Laboratory of Theoretical Chemistry of Environment, Ministry of Education, School of Chemistry and Environment, South China Normal University, Guangzhou 510006, China; 18971194938@yeah.net
[2] School of Pharmaceutical Sciences, Gannan Medical University, Yi Xue Yuan Road, Ganzhou 341000, China; luorenshi2010@163.com
* Correspondence: yangdq@scnu.edu.cn; Tel.: +86-20-3931-0068; Fax: +86-20-3104-0403

**Abstract:** Iridium-catalyzed asymmetric ring-opening of oxabenzonorbornadienes with *N*-substituted piperazines was described. The reaction afforded the corresponding ring-opening products in high yields and moderate enantioselectivities in the presence of 2.5 mol % $[Ir(COD)Cl]_2$ and 5.0 mol % (*S*)-*p*-Tol-BINAP. The effects of various chiral bidentate ligands, catalyst loading, solvent, and temperature on the yield and enantioselectivity were also investigated. A plausible mechanism was proposed to account for the formation of the corresponding *trans*-ring opened products based on the X-ray structure of product **2i**.

**Keywords:** iridium catalyst; asymmetric ring-opening; oxabenzonorbornadiene; chiral bisphosphine ligand; *N*-substituted piperazines

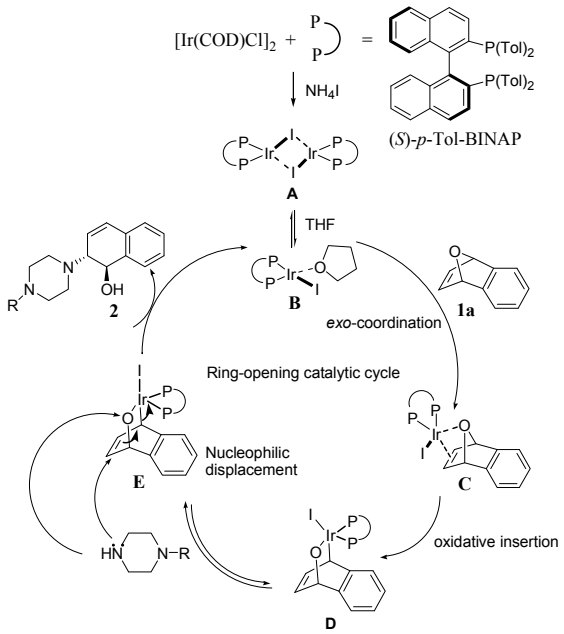
## 1. Introduction

The use of oxabicyclic templates to introduce *trans*-1,2-bifunctional groups to the carbocyclic molecule skeleton is an effective strategy for the synthesis of complex molecules. Pioneering work in this field was first described by Lautens and co-workers [1–17] who reported rhodium-catalyzed asymmetric ring-opening (ARO) of oxabicyclic alkenes to produce the corresponding products in high yields and excellent enantioselectivities (up to 99% *ee*). The asymmetric ring-opening has been extensively studied with a broad range of nucleophiles, including organomagnesium, organolithium, organozinc reagents, organoboronic acids, alcohols, phenols, carboxylic acids, terminal alkynes, and aromatic amines. In addition, many other transition metal catalysts have been tested, including Cu [18–23], Pd [24–35], Ni [36–42], Zr [43], Fe [44], Ru [45–52], and Pt [53–55] catalysts. For example, Cheng *et al*. [56–59] recently described asymmetric ring-opening of oxabenzonorbornadiene with alkyl- or alkenyl- or allylzirconium reagents and zinc powder under mild conditions catalyzed by $Ni(dppe)Br_2$ or $Pd((R)\text{-binap})Cl_2$, which yielded the corresponding 1,2-dihydronaphth-1-ols in good to excellent yields with high enantioselcetivities (up to 90% *ee*). Carretero *et al*. [60,61] reported a general copper-catalyzed ring-opening of oxabicylic alkenes with Grignard reagents. Hou *et al*. [30] investigated the asymmetric ring-opening of oxabicyclic alkenes with arylboronic acids catalyzed by the chiral phosphine-containing palladacycle, providing corresponding products in high yields and high *ee*. On the other hand, the different kinds of ligands previously used were bisphosphine ligands, including (*S*)-BINAP, (*R*)-(*S*)-PPF-P$^t$Bu$_2$ and DPPF. Halide and triflate salts such as $NH_4F$, $Et_3N{\cdot}HCl$, $NH_4Br$, $NH_4I$, $Bu_4NI$, and AgOTf were also used as additives to enhance the enantioselectivities of the ARO

reaction. Recently, our group demonstrated that iridium-catalyzed asymmetric ring-opening of oxa- and azabicyclic alkenes with nitrogen- or oxygen-based nucleophiles, such as amines, alcohols, phenols and Grignard reagents [62–74]. Furthermore, a new iridium-monophosphine catalyst was found to be efficient for asymmetric ring-opening of benzonorbornadiene with amines, providing a series of chiral substituted dihydronaphthalenes in high yields (up to 98%) and excellent enantioselectivities (>99% *ee*) [71]. To expand the scope of this novel Ir-catalyzed reaction, we are interested in studying the asymmetric ring-opening of oxabicyclic olefins with nitrogen-based nucleophiles in the presence of an iridium catalyst. Meanwhile, we also tried to optimize the catalytic system by using additive of $NH_4I$ in the reaction. Herein, we reported iridium-catalyzed asymmetric ring-opening of 1,4-dihydro-1,4-epoxynaphthalene (**1a**) or 1,4-dihydro-6,7-dimethoxy-1,4-epoxynaphthalene (**1b**) with *N*-substituted piperazine nucleophiles, which afforded the corresponding ring-opening products in good yields (up to 99%) with moderate enantioselectivities. This new method also offered potentially useful synthetic routes to optically active 2-*N*-substituted piperazine 1,2-dihydronaphthalen-1-ols.

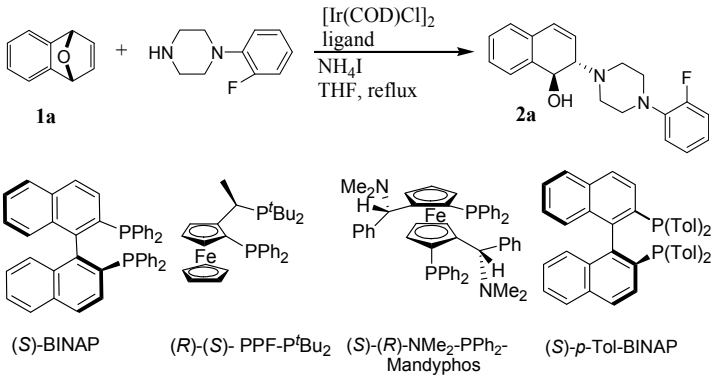
## 2. Results and Discussion

The substrates **1a**–**1b** were readily prepared by Diels-Alder reactions of benzynes with furan according to literature procedures [75]. To understand the nature of the catalytic ring-opening and optimize the reaction conditions, we first chose different chiral bisphosphine ligands, including (*S*)-BINAP, (*R*)-(*S*)-PPF-P$^{t-}$Bu$_2$, (*S*)-*p*-Tol-BINAP, and (*S*)-(*R*)-NMe$_2$-PPh$_2$-Mandyphos, to validate the catalytic activity of the iridium complexes. Consequently, a more efficient iridium catalyst system for the ring-opening reaction was explored. The different types of chiral ligands reacted with [Ir(COD)Cl]$_2$ to form iridium complexes to determine the viability of the enantioselectivity (Scheme 1). To probe the iridium-catalyzed asymmetric ring-opening of oxabicyclic alkene **1a** with 1-(2-fluorophenyl)piperazine, chiral bisphosphine ligand (*S*)-*p*-Tol-BINAP was used and 1 equivalent of $NH_4I$ was added as the additive. We found that the ring-opening product **2a** was obtained in high yield (up to 99%) with moderate enantioselectivity (54% *ee*) (Table 1, entry 4). However, the enantiomeric excess value was low (2%–58% *ee*) when (*S*)-BINAP and ferrocene bisphosphine ligands were used as the chiral ligands (Table 1, entries 1–3). The enantiomeric excess value was 55% *ee* when (*S*)-*p*-Tol-BINAP was used as the ligand in the presence of 1.25% mol [Ir(COD)Cl]$_2$ (Table 1, entry 5). Therefore, (*S*)-*p*-Tol-BINAP was chosen as the optimized ligand.




**Scheme 1.** The proposed mechanism for asymmetric ring-opening of **1a** with *N*-substituted piperazines.

**Table 1.** Effects of chiral bisphosphine ligands and catalyst loading [a].

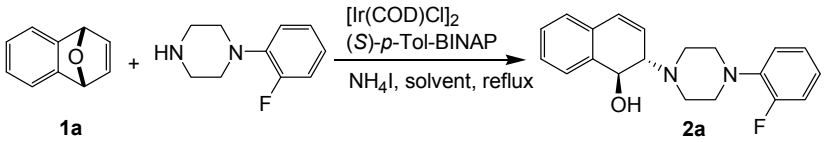



| Entry | Ligand (mol %) | $[Ir(COD)Cl]_2$ (mol %) | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 1 | (*S*)-BINAP(5.0) | 2.5 | 12 | 76 | 37 |
| 2 | (*R*)-(*S*)-PPF-P$^{t-}$Bu$_2$(5.0) | 2.5 | 12 | 76 | 2 |
| 3 | (*S*)-(*R*)-$NMe_2$-$PPh_2$-Mandyphos(5.0) | 2.5 | 12 | 30 | 58 |
| 4 | (*S*)-*p*-Tol-BINAP(5.0) | 2.5 | 12 | 99 | 54 |
| 5 | (*S*)-*p*-Tol-BINAP(2.5) | 1.25 | 12 | 83 | 55 |

[a] Conditions: $[Ir(COD)Cl]_2$ (2.5 mol %) and chiral ligand (5 mol %) were dissolved in 2.0 mL THF. $NH_4I$ (1 equiv.) was then added and stirred for another 10–20 min. Substrate **1a** (0.3 mmol, 1 equiv.) was added and the mixture was heated to reflux. 1-(2-Fluorophenyl)piperazine (2 equiv.) was added at the first sign of reflux; [b] Isolated yield; [c] *ee* was determined by HPLC with a Chiralcel OD or AD column.

With the catalyst system consisting of $[Ir(COD)Cl]_2$ and (*S*)-*p*-Tol-BINAP in hand, other reaction parameters were further optimized. We screened several commonly used solvents (Table 2, entries 1–9), the solvent effect on enantioselectivities of ring-opening reaction was remarkable, as seen from Table 2.

**Table 2.** Effects of solvent on the ring-opening [a].




| Entry | Solvent | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|
| 1 | $ClCH_2CH_2Cl$ | 12 | nr | – |
| 2 | DMF | 12 | nr | – |
| 3 | DME | 12 | nr | – |
| 4 | THF | 12 | 99 | 54 |
| 5 | THP | 12 | 81 | 53 |
| 6 | toluene | 12 | 79 | 52 |
| 7 | $CH_3CN$ | 12 | 88 | 52 |
| 8 | $CH_2Cl_2$ | 12 | 15 | 56 |
| 9 | 1,4-dioxane | 12 | 95 | 50 |

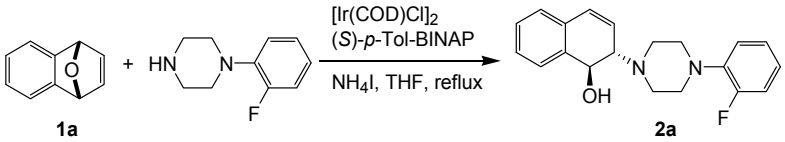
[a] Conditions: $[Ir(COD)Cl]_2$ (2.5 mol %) and (*S*)-*p*-Tol-BINAP (5.0 mol %) were dissolved in 2.0 mL solvent. $NH_4I$ (1 equiv.) was then added and stirred for another 10–20 min. Substrate **1a** (0.3 mmol, 1 equiv.) was added and the mixture was heated to reflux. 1-(2-Fluorophenyl)piperazine (2 equiv.) was added at the first sign of reflux; [b] Isolated yield; [c] *ee* was determined by HPLC with a Chiralcel OD or AD column.

It was found that in 1,4-dioxane, $CH_3CN$, toluene, tetrahydropyran (THP) and tetrahydrofuran (THF), the reactions were much faster than in any other solvents, and the reactions were completed in 12 h (Table 2, entries 4–7, and 9). However, the enantioselectivity was found to be 54% *ee* (Table 2, entry 4). There were no ring-opening products formed when the reactions were performed in dimethylformamide (DMF), 1,2-dimethoxyethane (DME) or 1,2-dichloroethane (Table 2, entries 1–3). Reactions in $CH_2Cl_2$ afforded the ring-opening products in a low yield (15%) with moderate

enantioselectivity (56% *ee*) (Table 2, entry 8). Among several solvents examined, THF turned out to be the best, yielding the corresponding ring-opening product **2a** in 99% yield with 54% *ee*.

The influence of temperature was also investigated in the iridium-catalyzed asymmetric ring-opening reaction of oxabicyclic alkene **1a** with 1-(2-fluorophenyl)piperazine. No product was obtained when the reaction mixture was stirred at 25 °C for 12 h (Table 3, entry 1). It was further found that the temperature had little effect on the enantioselectivity (Table 3, entries 2–4). The product **2a** was obtained in 50% yield with 40% *ee* when the reaction mixture was stirred at 50 °C for 12 h (Table 3, entry 2). Furthermore, the product **2a** was obtained in 99% yield with 54% *ee* when the reaction mixture was stirred at reflux (80 °C) (Table 3, entry 3). Consequently, the optimum reaction conditions were determined to be as follows: 2.5 mol % $[Ir(COD)Cl]_2$, 5.0 mol % (*S*)-*p*-Tol-BINAP, 2 equiv. of 1-(2-fluorophenyl)piperazine, and 1 equiv. of $NH_4I$ to oxabicyclic alkene **1a** as additive in THF at 80 °C.

**Table 3.** Effects of the temperature on the ring-opening [a].




**1a** **2a**

| Entry | Temperature (°C) | Product | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 1 | 25 | **2a** | 12 | nr | – |
| 2 | 50 | **2a** | 12 | 50 | 40 |
| 3 | 80 | **2a** | 12 | 99 | 54 |
| 4 | 100 | **2a** | 12 | 82 | 48 |

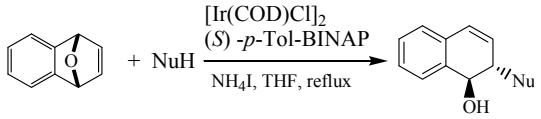
[a] Conditions: $[Ir(COD)Cl]_2$ (2.5 mol %) and (*S*)-*p*-Tol-BINAP (5.0 mol %) were dissolved in 2.0 mL THF. $NH_4I$ (1 equiv.) was then added and stirred for another 10–20 min. Substrate **1a** (0.3 mmol, 1 equiv.) was added and the mixture was heated. 1-(2-Fluorophenyl)piperazine (2 equiv.) was added at the first sign of reflux; [b] Isolated yield; [c] *ee* was determined by HPLC with a Chiralcel OD or AD column.

Under the optimized reaction conditions, the iridium-catalyzed ring-opening reaction of **1a** with different *N*-substituted piperazines was demonstrated to be an efficient method for the synthesis of *trans*-1,2-*N*-substituted piperazines 1,2-dihydronaphthalen-1-ols in high yields with moderate enantioselectives (Table 4). For example, various *N*-phenylpiperazines with either electron-donating or electron-withdrawing substituents at the phenyl position afforded the corresponding products in high yields (up to 99%) and good enantioselectivity in the presence of 2.5 mol % $[Ir(COD)Cl]_2$ and 5.0 mol % (*S*)-*p*-Tol-BINAP (Table 4, entries 1–16, 18–19, and 22–24). 1,4-Dihydro-1,4-epoxynaphthalene (**1a**) with 1-(2-methoxyphenyl)piperazine however afforded the corresponding ring-opening product **2f** in high yield with poor enantioselectivity (Table 4, entry 6).

To further extend the scope of this transformation, the reaction of dimethoxy substituted oxabenzonorbornadiene **1b** with various *N*-substituted piperazines were also examined. It was found that the reactions of 1,4-dihydro-6,7-dimethoxy-1,4-epoxynaphthalene (**1b**), a less reactive substrate, with *N*-substituted piperazines offered the desired products in good yields with moderate enantioselectivity (Table 5, entries 1–9).

Unfortunately, the reaction of 1,4-dihydro-6,7-dimethoxy-1,4-epoxynaphthalene (**1b**) with 1-(3,4-dichlorophenyl)piperazine afforded the corresponding ring-opening product **3e** in a lower yield (47%) with poor enantioselectivity (16% *ee*) (Table 5, entry 5).

**Table 4.** Iridium-catalyzed asymmetric ring-opening of oxabenzonorbornadiene **1a** with *N*-substituted piperazines [a].




**1a** **2a~2x**

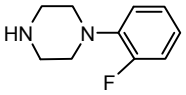
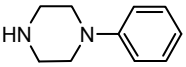
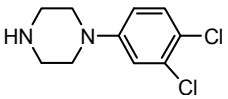
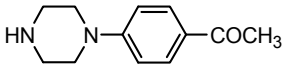
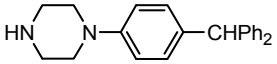
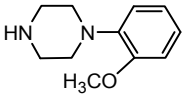
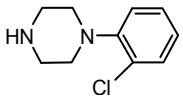
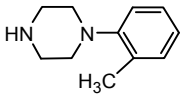
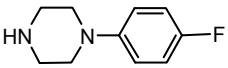
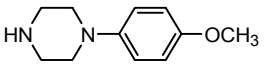
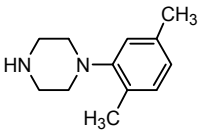
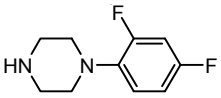
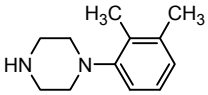
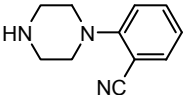
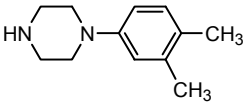
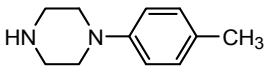
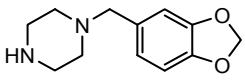
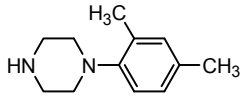
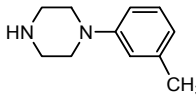
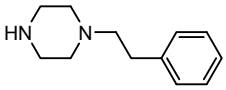
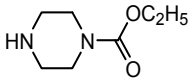
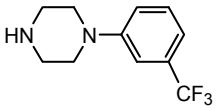
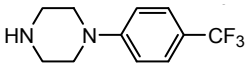
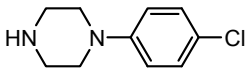
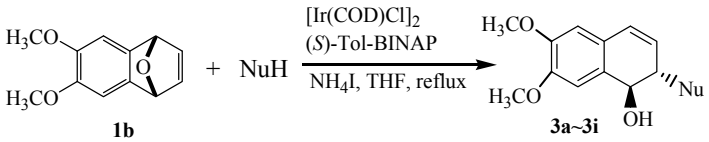
| Entry | NuH | Product | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 1 |  | **2a** | 12 | 99 | 54 |
| 2 |  | **2b** | 12 | 87 | 36 |
| 3 |  | **2c** | 12 | 86 | 67 |
| 4 |  | **2d** | 8 | 87 | 38 |
| 5 |  | **2e** | 8 | 98 | 49 |
| 6 |  | **2f** | 8 | 81 | 33 |
| 7 |  | **2g** | 8 | 89 | 50 |
| 8 |  | **2h** | 8 | 87 | 54 |
| 9 |  | **2i** | 10 | 91 | 45 |
| 10 |  | **2j** | 10 | 85 | 54 |
| 11 |  | **2k** | 10 | 98 | 36 |
| 12 |  | **2l** | 10 | 97 | 43 |
| 13 |  | **2m** | 12 | 88 | 47 |
| 14 |  | **2n** | 10 | 95 | 54 |
| 15 |  | **2o** | 10 | 96 | 58 |
| 16 |  | **2p** | 10 | 85 | 27 |
| 17 |  | **2q** | 12 | 86 | 57 |

**Table 4.** *Cont.*

| Entry | NuH | Product | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 18 |  | **2r** | 12 | 89 | 59 |
| 19 |  | **2s** | 10 | 90 | 59 |
| 20 |  | **2t** | 8 | 78 | 50 |
| 21 |  | **2u** | 6 | 85 | 51 |
| 22 |  | **2v** | 7 | 83 | 54 |
| 23 |  | **2w** | 8 | 76 | 56 |
| 24 |  | **2x** | 8 | 82 | 39 |

[a] Conditions: $[Ir(COD)Cl]_2$ (2.5 mol %) and (*S*)-*p*-Tol-BINAP (5.0 mol %) were dissolved in 2.0 mL THF and stirred for 10–20 min. $NH_4I$ (1 equiv.) was then added and stirred for another 10–20 min. Substrate **1a** (0.3 mmol, 1 equiv.) was added and the mixture was heated to reflux. *N*-Substituted piperazine nucleophiles (2 equiv.) were added at the first sign of reflux; [b] Isolated yield; [c] *ee* was determined by HPLC with a Chiralcel OD or AD column.

**Table 5.** Substrate scope of the iridium-catalyzed asymmetric ring-opening reaction [a].




**1b** **3a~3i**

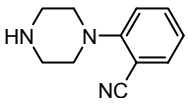
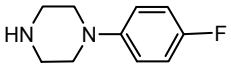
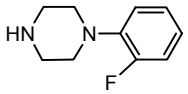
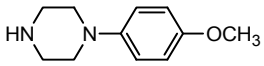
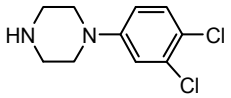
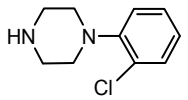
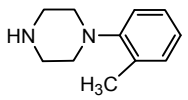
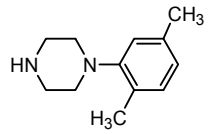
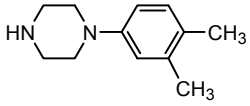
| Entry | NuH | Product | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 1 |  | **3a** | 24 | 77 | 37 |
| 2 |  | **3b** | 24 | 73 | 49 |
| 3 |  | **3c** | 24 | 79 | 38 |
| 4 |  | **3d** | 24 | 62 | 59 |
| 5 |  | **3e** | 24 | 47 | 16 |
| 6 |  | **3f** | 24 | 51 | 43 |
| 7 |  | **3g** | 24 | 76 | 38 |

**Table 5.** *Cont.*

| Entry | NuH | Product | Time (h) | Yield [b] (%) | *ee* [c] (%) |
|---|---|---|---|---|---|
| 8 |  | **3h** | 24 | 86 | 35 |
| 9 |  | **3i** | 24 | 81 | 45 |

[a] Conditions: $[Ir(COD)Cl]_2$ (2.5 mol %) and (*S*)-*p*-Tol-BINAP (5.0 mol %) were dissolved in 2.0 mL THF. $NH_4I$ (1 equiv.) was then added and stirred for another 10–20 min. Substrate **1b** (0.3 mmol, 1 equiv.) was added and the mixture was heated to reflux. *N*-Substituted piperazine nucleophiles (2 equiv.) were added at the first sign of reflux; [b] Isolated yield; [c] *ee* was determined by HPLC with a Chiralcel OD or AD column.

The stereochemistry of 1,2-*trans* ring-opened product **2i** was unambiguously confirmed by X-ray crystallography. The single crystal of **2i** was achieved by solvent evaporation from a mixture of dichloromethane, petroleum ether and ethyl acetate. Its configuration was assigned as (1*S*, 2*S*) and confirmed as 1,2-*trans* configuration, as shown in Figure 1 (See Supplementary Materials for details). It is obvious that the ring-opening reaction favors the formation of *trans*-2-*N*-substituted piperazine 1,2-dihydro-naphthalen-1-ol products.

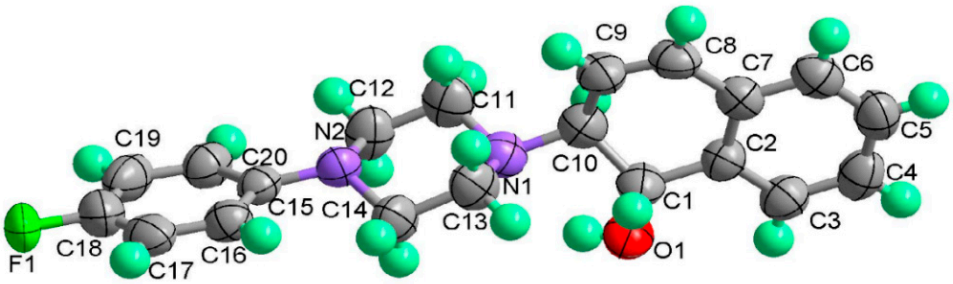



**Figure 1.** ORTEP plot for **2i** [a]. [a] Crystal data. $C_{20}H_{21}FN_2O$, *M* = 342.39. Monoclinic *a* = 9.572 (3), *b* = 10.034 (3), *c* = 17.732 (5), *alpha* = 90, *beta* = 90 (8), *gamma* = 90, *T* =296 K, space group. Orthorhombic, P 21 21 21, *Z* = 4. wR2 (reflections) = 0.1882 (3432). The Cambridge Crystallographic Data Centre (CCDC) 1415336 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

Based on our findings above, we propose a mechanism, outlined in Scheme 1. When $[Ir(COD)Cl]_2$ was used as the iridium source, and reacted with (*S*)-*p*-Tol-BINAP to form the complex of $[Ir(S)$-*p*-Tol-BINAP$)I]_2$ **A** in the presence of $NH_4I$, which is then cleaved by solvent to give the monomeric iridium complex **B**. Reversible *exo* coordination of oxabenzonorbornadiene **1a** leads to iridium complex **C**, followed by oxidative insertion with retention to form a bridgehead C–O bond and produce the π-allyl iridium alkoxide complex **D**. We further propose that the oxidative cleavage of the C–O bond is the enantioselectivity discriminating step in the catalytic cycle. Once iridium complex **C** is formed, the iridium alkoxide complex could be protonated by the *N*-substituted piperazine nucleophiles to generate cationic iridium complex **E**. This proton transfer has two effects. First, the iridium species are made more electrophilic as a result of the positive charge, and the nucleophile is rendered more nucleophilic by deprotonation. Second, the positioning of the iridium metal on the π-allyl moiety will influence the regioselectivity of nucleophilic attack. Nucleophilic attack with inversion is proposed to occur adjacent to the alkoxy group in an $S_N2$ fashion relative to the iridium metal. Finally, product **2** is subsequently liberated and the iridium monomer is regenerated, which will either reform the dimer or continue the catalytic cycle.

## 3. Experimental Section

### *3.1. Chemistry*

#### 3.1.1. General

Solvents and solutions were transferred with syringes. $^{1}$H-NMR spectra were recorded at 400 MHz using a Varian XL (Palo Alto, CA, USA) 400 spectrometer with $CDCl_3$ as reference standard (7.27 ppm). Spectral features are tabulated in the following order: Chemical shift (ppm); number of protons; multiplicity (s—singlet, d—doublet, t—triplet, q—quartet, m—multiplet, br—broad); coupling constants (*J*, Hz), $^{13}$C-NMR spectra were recorded at 400 MHz with $CDCl_3$ as reference standard (77.23 ppm). IR spectra were obtained using a Nicolet DX (Madison, WI, USA) FT-IR spectrometer. High resolution mass was obtained from a VG 70-250S (double focusing) mass spectrometer at 70 ev (Waters, Milford, MA, USA). The enantiomeric excess value was measured by HPLC with CHIRALCEL OD or AD columns (Chiral Technologies, Minato-ku, Japan). Melting points were taken with a Tai-Ke melting point apparatus (Beijing, China). Analytical TLC was performed using EM separations percolated silica gel 0.2 mm layer UV 254 nm fluorescent sheets (Beijing, China). Column chromatography was performed as "Flash chromatography" as reported by using (200–300 mesh) Merck grade silica gel (Merck, Beijing, China). The THF, toluene, DME, and THP was distilled from sodium benzophenone ketyl immediately prior to use. DMF, $CH_2Cl_2$, $CH_3CN$, $ClCH_2CH_2Cl$, and 1,4-dioxane were distilled from calcium hydride. Furan was distilled prior to use. All other reagents were obtained from Alfa Aesar (Shanghai, China) and *J* & K (Guangzhou, China) and used as received unless otherwise stated.

#### 3.1.2. Preparation of 1,4-Dihydro-1,4-epoxynaphthalene (**1a**)

To a 100 mL round-bottomed flask with a reflux condenser tube, 10 mL furan and 10 mL DME were added. Taking two 25 mL dropping bottles, one with 4 mL iso-amyl nitrite and 10 mL DME (A), another with 2-aminobenzoic acid (2.75 g, 0.02 mol) dissolved by 10 mL DME (B). Then 1 mL A and 1 mL B were added to the refluxing furan solution per 4 minute. Firstly, the A was added, then the B. The solution became red brown, giving off gas when the reagents were added. Let the mixture refluxing until the solution did not release gas after all the reactants were added (about 15 min). After completion 2% sodium hydroxide (25 mL) was added to the mixture and transferred to separating funnel to rinse, which we can get the organic phase and the aqueous solution extracted three times by 15 mL petroleum ether (bp. 30–60 °C). Then the extractive solution and the organic phase were mixed together. The mixture was washed by water (15 mL × 4) and dried by anhydrous magnesium sulfate. After completion the reaction mixture was concentrated in *vacuo* and the solvents were removed, the crude mixture was purified by flash chromatography gave **1a** a yellow solid (1.72 g, 60%). $R_f$ = 0.45 on silica gel (25% ethyl acetate in petroleum ether). m.p.: 55–56 °C. IR (thin film, $cm^{-1}$) 3125 (s), 3040 (s), 3020 (s), 1958 (s), 1916 (s), 1814 (s), 1620 (s), 1562 (s), 1449 (s), 1345 (s), 1278 (s), 1195 (s), 1164 (s), 1128 (s), 1073 (s), 986 (s), 938 (s), 844 (s), 765 (s), 689 (s), 635 (s). $^{1}$H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.20 (m, 1H), 7.05 (t, *J* = 1.0 Hz, 1H), 7.02–6.94 (m, 1H), 5.74 (s, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.0, 143.0, 125.0, 120.3, 82.3.

#### 3.1.3. Preparation of 1,4-Dihydro-6,7-dimethoxy-1,4-epoxynaphthalene (**1b**)

A stirred solution of 1,2-dibromo-4,5-dimethoxybenzene (2.0 g, 6.8 mmol) and furan (20 mL) in anhydrous THF (20 mL) was maintained at −78 °C under $N_2$ and was treated dropwise with *n*-butyl lithium (1.29 mol/L) in hexane (5.3 mL). The solution was stirred at −78 °C for 0.5 h and then allowed to room temperature during 2 h. The work-up yielded a crude product was purified by flash chromatography (30% ethyl acetate in hexanes) to give **1b** a white solid (0.9 g, 65%). $R_f$ = 0.21 on silica gel (30% ethyl acetate in hexanes); m.p.: 128–130 °C; IR (thin film, $cm^{-1}$) 2926 (s), 2924 (s), 2839 (s), 1599 (s), 1485 (s), 1467 (s), 1325 (s), 1285 (s), 1063 (s); $^{1}$H-NMR (400 MHz, $CDCl_3$) δ 7.04 (2H, t,

*J* = 0.91 Hz, Ar-H), 6.97 (2H, s, =CH), 5.68 (2H, s, CH), 3.85 (6H, s, $CH_3O$); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 146.1, 143.6 141.9, 107.0, 82.8, 56.7.

3.1.4. General Procedure for the Asymmetric Ring-Opening of **1a** with *N*-Substituted Piperazines

A 5.0 mL round-bottomed flask was equipped with a reflux condenser, 2.5 mol % chloro(1,5-cyclooctadiene)iridium (I) dimer $[Ir(COD)Cl]_2$ and 5.0 mol % (*S*)-*p*-Tol-BINAP were added and followed by addition of anhydrous tetrahydrofuran (2.0 mL). After they were stirred for 10 min to produce a yellow solution. 1,4-Dihydro-1,4-epoxynaphthalene **1a** (50 mg, 0.3468 mmol) was added; then 10 min later, additive of ammonium iodide (1.0 equiv. to **1a**) was added and heated to reflux. At the first sign of reflux, *N*-substituted piperazine nucleophiles (2.0 equiv. to **1a**) were added. The reaction mixture was stirred at reflux and monitored by TLC until completion (typically 6–12 h). The solvent was removed in *vacuo* and the crude mixture was purified by column chromatography on silica gel to afford the desired products.

*(1S,2S)-2-[4-(2-Fluoro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2a**). Prepared according to general procedure. **2a** was obtained as a white solid (111.9 mg, 99%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.21 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 54% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 19.0 min (major) and 20.9 min (minor). m.p.: 125–126 °C; $[\alpha]_D^{25}$ = +83.2° (*c* = 68.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3510 (br), 3054 (w), 2977 (s), 2934 (s), 2862 (s), 1490 (s), 1445 (s), 1383 (s), 1351 (s), 1077 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.2 Hz), 7.31–7.23 (2H, m), 7.11–6.93 (5H, m), 6.58 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.17 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.93 (1H, 11.6), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.4 Hz), 3.22 (1H, br), 3.21–3.05 (4H, m), 3.02–2.98 (2H, m), 2.78–2.73 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 157.1, 154.7, 140.2, 137.2, 131.9, 129.6, 128.1, 127.6, 126.4, 124.8, 124.7, 122.8, 119.2, 116.4, 67.9, 67.7, 51.3, 49.2. MS (ESI): calcd *m*/*z* for $C_{20}H_{21}FN_2O$ ($M^+$) 324.16, found: 325.12 $[M + H]^+$. Anal. Calcd for $C_{20}H_{21}FN_2O$: C, 74.05; H, 6.53; N, 8.64. Found: C, 74.29; H, 6.74; N, 8.56.

*(1S,2S)-2-(4-Phenyl-piperazin-1-yl)-1,2-dihydro-naphthalen-1-ol* (**2b**). Prepared according to general procedure. **2b** was obtained as a white solid (93 mg, 87%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.42 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 36% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 2% 2-propanol in hexanes were 31.3 min (minor) and 35.9 min (major). m.p.: 162–163 °C; $[\alpha]_D^{25}$ = + 62.8° (*c* = 39.5 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3345 (br), 3016 (w), 2928 (s), 2824 (s), 1597 (m), 1492 (s), 1452 (s), 1369 (m), 1226 (s), 1169 (s), 1133 (m), 1045 (m), 763 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.56 (1H, d, *J* = 7.2 Hz), 7.26–7.19 (4H, m), 7.05 (1H, dd, *J* = 4.2 Hz, *J* = 2.8 Hz), 6.91–6.82 (3H, m), 6.52 (1H, dd, *J* = 2.8 Hz, *J* = 2.8 Hz), 6.08 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.89 (1H, *J* = 7.6 Hz), 3.50 (1H, *J* = 2.8 Hz), 3.37 (1H, br), 3.23–3.13 (4H, m), 2.95–2.89 (2H, m), 2.70–2.65 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.4, 137.2, 131.9, 129.6, 129.3, 128.1, 127.6, 126.4, 125.0, 124.5, 120.1, 116.4, 67.9, 67.6, 49.9, 49.1. MS (ESI): calcd *m*/*z* for $C_{20}H_{22}N_2O$ ($M^+$) 306.17, found: 307.16 $[M + H]^+$. Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.21; H, 7.31; N, 9.28.

*(1S,2S)-2-[4-(3,4-Dichloro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2c**). Prepared according to general procedure. **2c** was obtained as a white solid (112 mg, 86%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.37 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 67% using HPLC analysis on a CHIRALCEL. AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 33.9 min (major) and 36.9 min (minor). m.p.: 142–143 °C; $[\alpha]_D^{25}$ = +100.4° (*c* = 45.6 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3456 (br), 3027 (w), 2936 (m), 2836 (s), 1594 (s), 1552 (m), 1483 (s), 1452 (m), 1237 (s), 1139 (m), 1044 (s), 782 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.51 (1H, d, *J* = 7.2 Hz), 7.30–7.20 (3H, m), 7.05 (1H, d, *J* = 6.8 Hz), 6.91 (1H, d, *J* = 2.8 Hz), 6.72 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 6.46 (1H, dd, *J* = 2.0 Hz, *J* = 1.6 Hz), 6.02 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.83 (1H, d, *J* = 11.6 Hz), 3.42 (1H, d, *J* = 10.8 Hz), 3.22–3.05 (5H, m), 2.98–2.85

(2H, m), 2.70–2.61 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 150.7, 137.0, 132.9, 131.8, 130.6, 129.7, 128.1, 127.7, 126.4, 125.1, 124.3, 122.4, 117.5, 115.6, 67.9, 67.5, 49.4, 48.8. MS (ESI): calcd $m/z$ for $C_{20}H_{20}Cl_2N_2O$ ($M^+$) 374.10, found: 375.05 $[M + H]^+$. Anal. Calcd for $C_{20}H_{20}Cl_2N_2O$: C, 64.01; H, 5.37; N, 7.46. Found: C, 63.82; H, 5.69; N, 7.47.

*(1S,2S)-1-{4-(1-Hydroxy-1,2-dihydro-naphthalen-2-yl)-piperazin-1-yl]-phen-yl}-ethanone* (**2d**). Prepared according to general procedure. **2d** was obtained as a white solid (105 mg, 87%) by flash chromatography (ethyl acetate: petroleum ether = 2:1, *v*/*v*). $R_f$ = 0.40 on silica gel (ethyl acetate: petroleum ether = 2:1, *v*/*v*). The *ee* was determined to be 38% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 2% 2-propanol in hexanes were 30.3 min (minor) and 34.9 min (major). m.p.: 202–203 °C; $[\alpha]_D^{25} = -3.0^\circ$ (*c* = 26.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3396 (br), 3018 (w), 2923 (s), 2841 (s), 1739 (m), 1643 (s), 1597 (s), 1388 (s), 1245 (s), 1086 (s), 817 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.88 (2H, d, *J* = 8.8 Hz), 7.58 (1H, d, *J* = 6.8 Hz), 7.27 (2H, td, *J* = 7.6 Hz, *J* = 7.2 Hz), 7.10 (1H, d, *J* = 6.8 Hz), 6.88 (2H, d, *J* = 7.6 Hz), 6.57 (1H, d, *J* = 6.0 Hz), 6.08 (1H, d, *J* = 9.6 Hz), 4.93 (1H, d, *J* = 11.2 Hz), 3.54 (1H, d, *J* = 2.0 Hz), 3.41–3.35 (4H, m), 3.19 (1H, br), 2.97–2.94 (2H, m), 2.73–2.71 (2H, m), 2.52 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 196.7, 154.3, 137.0, 131.9, 130.6, 129.8, 128.2, 128.0, 127.8, 126.5, 125.2, 124.3, 113.7, 68.0, 67.6, 48.9, 48.1, 26.3. MS (ESI): calcd $m/z$ for $C_{22}H_{24}N_2O_2$ ($M^+$) 348.18, found: 349.15 $[M + H]^+$. Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04. Found: C, 75.65; H, 7.34; N, 8.01.

*(1S,2S)-2-(4-Benzhydryl-piperazin-1-yl)-1,2-dihydro-naphthalen-1-ol* (**2e**). Prepared according to general procedure. **2e** was obtained as a white solid (135 mg, 98%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.22 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 49% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 2% 2-propanol in hexanes were 18.2 min (major) and 19.8 min (minor). m.p.: 160–161 °C; $[\alpha]_D^{25} = +150.2^\circ$ (*c* = 33.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3429 (br), 3027 (w), 2923 (s), 2807 (m), 1594 (s), 1487 (m), 1451 (s), 1383 (m), 1133 (s), 1040 (s), 741 (s), 697 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.66 (1H, d, *J* = 7.2 Hz), 7.52 (4H, d, *J* = 7.6 Hz), 7.39–7.25 (8H, m), 7.15 (1H, d, *J* = 7.2 Hz), 6.62 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.26 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.94 (1H, *J* = 11.6 Hz), 4.34 (1H, s), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.4 Hz), 3.45 (1H, br), 2.98–2.84 (2H, m), 2.69–2.61 (2H, m), 2.49–2.42 (4H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 142.8, 137.3, 132.0, 129.3, 128.7, 128.5, 128.1, 127.9, 127.5, 127.1, 126.3, 125.0, 124.9, 67.8, 67.3, 52.5, 49.2. MS (ESI): calcd $m/z$ for $C_{27}H_{28}N_2O$ ($M^+$) 396.22, found: 397.19 $[M + H]^+$. Anal. Calcd for $C_{27}H_{28}N_2O$: C, 81.87; H, 7.12; N, 7.06. Found: C, 81.52; H, 7.43; N, 7.02.

*(1S,2S)-2-[4-(2-Methoxy-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (2f). Prepared according to general procedure. 2f was obtained as a white solid (95 mg, 81%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.17 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*); The *ee* was determined to be 33% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 2% 2-propanol in hexanes were 27.6 min (minor) and 29.3 min (major); m.p.: 148–149 °C; $[\alpha]_D^{25} = +53.8^\circ$ (*c* = 69.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3519 (br), 3089 (w), 2978 (s), 2934 (s), 2863 (s), 2805 (s), 1490 (s), 1445 (s), 1415 (s), 1383 (s), 1351 (s), 1297 (m), 1076 (s), 1044 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.61 (1H, d, *J* = 7.2 Hz), 7.29–7.25 (2H, m), 7.10 (1H, d, *J* = 7.2 Hz), 7.02 (1H, dt, *J* = 8.0 Hz, *J* = 2.4 Hz), 6.98–6.95 (2H, m), 6.88 (1H, d, *J* = 8.0 Hz), 6.57 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.20 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.95 (1H, d, *J* = 11.6 Hz), 3.88 (3H, s), 3.54 (1H, *J* = 6.4 Hz), 3.41 (1H, br), 3.18–3.01 (4H, m), 3.01–2.98 (2H, m), 2.79–2.70 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 152.4, 141.3, 137.3, 132.0, 129.4, 128.0, 127.6, 126.3, 125.0, 124.9, 123.2, 121.1, 118.4, 111.2, 67.8, 67.7, 55.5, 51.4, 49.3. MS (ESI): calcd $m/z$ for $C_{21}H_{24}N_2O_3$ ($M^+$) 336.18, found: 337.10 $[M + H]^+$. Anal. Calcd for $C_{21}H_{24}N_2O_3$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.89; H, 7.44; N, 8.56.

*(1S,2S)-2-[4-(2-Chloro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2g**). Prepared according to general procedure. **2g** was obtained as a white solid (105 mg, 89%) by flash chromatography (ethyl acetate: petroleum ether = 1:3, *v*/*v*). $R_f$ = 0.25 on silica gel (ethyl acetate: petroleum ether = 1:3, *v*/*v*). The *ee* was determined to be 50% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 19.4 min (major) and 20.3 min (minor). m.p.: 122–123 °C; $[\alpha]_D^{25}$ = +91.6° (*c* = 29.7 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3468 (br), 3060 (w), 2927 (s), 2828 (s), 1588 (s), 1480 (s), 1453 (s), 1377 (m), 1230 (s), 1123 (s), 1040 (s), 781 (s), 749 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.61 (1H, d, *J* = 7.2 Hz), 7.37 (1H, d, *J* = 7.2 Hz), 7.31–7.22 (3H, m), 7.11–6.99 (2H, m), 6.97 (1H, d, *J* = 8.4 Hz), 6.58 (1H, dd, *J* = 2.8 Hz, *J* = 2.8 Hz), 6.21 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 4.95 (1H, 11.6), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.4 Hz), 3.34 (1H, br), 3.15–3.09 (4H, m), 3.05–2.95 (2H, m), 2.79–2.74 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.3, 137.3, 132.0, 130.9, 129.6, 129.0, 128.1, 127.8, 127.6, 126.4, 124.9, 124.0, 120.6, 67.9, 67.8, 51.9, 49.4. MS (ESI): calcd *m*/*z* for $C_{20}H_{21}ClN_2O$ ($M^+$) 340.13, found: 341.11 $[M + H]^+$. Anal.Calcd for $C_{20}H_{21}ClN_2O$: C, 70.48; H, 6.21; N, 8.22. Found: C, 70.20; H, 6.49; N, 8.49.

*(1S,2S)-2-[4-o-Toyl-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2h**). Prepared according to general procedure. **2h** was obtained as a white solid (97 mg, 87%) by flash chromatography (ethyl acetate: petroleum ether = 1:3, *v*/*v*). $R_f$ = 0.2 on silica gel (ethyl acetate: petroleum ether = 1:3, *v*/*v*). The *ee* was determined to be 54% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 14.7 min (major) and 16.4 min (minor). m.p.: 115–116 °C; $[\alpha]_D^{25}$ = +95.9° (*c* = 49.1 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3461 (br), 3019 (m), 2949 (s), 2878 (s), 2816 (w), 1596 (w), 1490 (s), 1453 (s), 1256 (m), 1224 (s), 1195 (m), 1132 (m), 1049 (s), 781 (s), 768 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.69 (1H, d, *J* = 7.2 Hz), 7.38–7.25 (4H, m), 7.19–7.07 (3H, m), 6.66 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.29 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 5.03 (1H, *J* = 12.0 Hz), 3.60 (1H, dt, *J* = 12.0 Hz, *J* = 2.8 Hz), 3.39 (1H, br), 3.11–3.02 (6H, m), 2.83–2.79 (2H, m), 2.42 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.6, 137.4, 132.8, 132.0, 131.3, 129.5, 128.1, 127.6, 126.3, 125.0, 124.9, 123.5, 119.2, 67.9, 67.8, 52.5, 49.6, 18.1. MS (ESI): calcd *m*/*z* for $C_{21}H_{24}N_2O$ ($M^+$) 320.19, found: 321.16 $[M + H]^+$. Anal. Calcd for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.74. Found: C, 78.49; H, 7.82; N, 8.69.

*(1S,2S)-2-[4-(4-Fluoro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2i**). Prepared according to general procedure. **2i** was obtained as a white solid (101 mg, 91%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.34 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 45% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 26.9 min (major) and 29.4 min (minor). m.p.: 167–168 °C; $[\alpha]_D^{25}$ = +133.2° (*c* = 48.2 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3592 (br), 3214 (w), 2978 (s), 2934 (s), 2872 (s), 2806 (s), 1627 (w), 1489 (s), 1445 (s), 1415 (s), 1298 (s), 1067 (s), 1044 (s), 935 (m), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 7.2 Hz), 7.29–7.25 (2H, m), 7.09 (1H, d, *J* = 7.2 Hz), 7.00–6.96 (2H, m), 6.91–6.87 (2H, m), 6.57 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 6.13 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.93 (1H, d, *J* = 11.6 Hz), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.8 Hz), 3.27 (1H, br), 3.18–3.13 (4H, m), 3.00–2.95 (2H, m), 2.75–2.71 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 158.7, 156.3, 148.1, 137.2, 131.9, 129.7, 128.1, 127.7, 126.4, 125.0, 125.0, 118.2, 115.9, 67.9, 67.6, 51.0, 49.1. MS (ESI): calcd *m*/*z* for $C_{20}H_{21}FN_2O$ ($M^+$) 324.16, found: 325.15 $[M + H]^+$. Anal. Calcd for $C_{20}H_{21}FN_2O$: C, 74.05; H, 6.53; N, 8.64. Found: C, 74.19; H, 6.74; N, 8.66.

*(1S,2S)-2-[4-(4-Methoxy-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2j**). Prepared according to general procedure. **2j** was obtained as a white solid (99 mg, 85%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.23 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 54% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL / min; Retention times in 10% 2-propanol in hexanes were 32.5 min (major) and 36.4 min (minor). m.p.: 178–179 °C; $[\alpha]_D^{25}$ = +102.5° (*c* = 59.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3566 (br), 3219 (w), 2978 (s), 2934 (s), 2862 (s), 2805 (s), 1491 (s), 1445 (s), 1416 (m), 1383 (s), 1351 (s), 1297 (m),

1077 (s), 1044 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.2 Hz), 7.31–7.23 (2H, m), 7.10 (1H, d, *J* = 8.4 Hz), 6.95–6.84 (4H, m), 6.57 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.15 (1H, dd, *J* = 2.0 Hz, *J* = 2.4 Hz), 4.93 (1H, *J* = 11.6 Hz), 3.73 (3H, s), 3.51 (1H, dt, *J* = 11.6 Hz, *J* = 2.4 Hz), 3.32 (1H, br), 3.19–3.08 (4H, m), 3.01–2.97 (2H, m), 2.76–2.71 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 154.2, 145.8, 137.3, 132.0, 129.6, 128.1, 127.7, 126.5, 125.0, 124.7, 118.6, 114.7, 68.0, 67.7, 55.8, 51.5, 49.3. MS (ESI): calcd *m*/*z* for $C_{21}H_{24}N_2O_2$ ($M^+$) 336.18, found: 337.10 $[M + H]^+$. Anal. Calcd for $C_{21}H_{24}N_2O_2$: C, 74.97; H, 7.19; N, 8.33. Found: C, 74.77; H, 7.40; N, 8.25.

*(1S,2S)-2-[4-(2,5-Dimethyl-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2k**). Prepared according to general procedure. **2k** was obtained as a white solid (119 mg, 98%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.32 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 36% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 13.8 min (major) and 14.3 min (minor). m.p.: 128–130 °C; $[\alpha]_D^{25}$ = +100.0° (*c* = 44.7 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3509 (br), 3216 (w), 2977 (s), 2934 (s), 2862 (s), 2806 (s), 1490 (s), 1445 (s), 1415 (s), 1383 (s), 1351 (s), 1298 (m), 1127 (s), 1077 (s), 1044 (m), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.52 (1H, d, *J* = 7.2 Hz), 7.21–7.13 (2H, m), 6.98 (2H, t, *J* = 6.8 Hz), 6.73 (2H, t, *J* = 11.6 Hz, *J* = 7.6 Hz), 6.47 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 6.10 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.84 (1H, 12.0), 3.42 (1H, dt, *J* = 12.0 Hz, *J* = 2.4 Hz), 3.37 (1H, br), 2.90–2.82 (6H, m), 2.64–2.58 (2H, m), 2.23 (3H, s), 2.19 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.4, 137.3, 136.3, 132.0, 131.1, 129.4, 129.4, 128.0, 127.5, 126.3, 125.0, 124.8, 124.0, 119.9, 67.9, 67.7, 52.4, 49.3, 21.4, 17.7. MS (ESI): calcd *m*/*z* for $C_{22}H_{26}N_2O$ ($M^+$) 334.20, found: 335.23 $[M + H]^+$. Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 78.83; H, 8.12; N, 8.32.

*(1S,2S)-2-[4-(2,5-Difluoro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2l**). Prepared according to general procedure. **2l** was obtained as a white solid (115 mg, 97%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The absolute stereochemistry was determined by X-ray crystallography. $R_f$ = 0.14 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 43% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 20.2 min (major) and 23.2 min (minor). m.p.: 122–124 °C; $[\alpha]_D^{25}$ = +150.7° (*c* = 26.8 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3507 (br), 3203 (w), 2988 (s), 2943 (s), 2872 (s), 1509 (s), 1445 (s), 1383 (s), 1297 (m), 1131 (s), 935 (s), 846 (s), 793 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 7.2 Hz), 7.31–7.23 (2H, m), 7.09 (1H, d, *J* = 6.0 Hz), 6.95–6.78 (3H, m), 6.57 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.16 (1H, dd, *J* = 2.8 Hz, *J* = 2.8 Hz), 4.93 (1H, 11.6), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.8 Hz), 3.31 (1H, br), 3.13–2.96 (4H, m), 2.96–2.92 (2H, m), 2.75–2.70 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 159.4, 157.0, 154.6, 137.2, 136.9, 131.9, 129.6, 128.1, 127.7, 126.4, 125.0, 119.7, 111.0, 110.8, 105.2, 104.7, 67.9, 67.7, 51.7, 49.2. MS (ESI): calcd *m*/*z* for $C_{20}H_{20}F_2N_2O$ ($M^+$) 342.15, found: 343.20 $[M + H]^+$. Anal. Calcd for $C_{20}H_{20}F_2N_2O$: C, 70.16; H, 5.89; N, 8.18. Found: C, 70.19; H, 5.94; N, 8.26.

*(1S,2S)-2-[4-(2,3-Dimethyl-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2m**). Prepared according to general procedure. **2m** was obtained as a white solid (102 mg, 88%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.29 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 47% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 13.5 min (major) and 14.4 min (minor). m.p.: 163–164 °C; $[\alpha]_D^{25}$ = +82.7° (*c* = 99.7 mg, $CHCl_3$); IR (thin film, $cm^{-1}$); 3590 (br), 3228 (w), 2974 (s), 2934 (s), 2873 (s), 2806 (s), 1490 (s), 1445 (s), 1415 (m), 1383 (s), 1351 (s), 1297 (m), 1133 (s), 1077 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.2 Hz), 7.27–7.23 (2H, m), 7.08 (2H, t, *J* = 7.2 Hz), 6.91 (2H, dd, *J* = 4.8 Hz, *J* = 4.4 Hz), 6.55 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 6.19 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.92 (1H, *J* = 14.6 Hz), 3.50 (1H, dt, *J* = 11.6 Hz, *J* = 2.8 Hz), 3.41 (1H, br), 2.97–2.88 (6H, m), 2.69 (2H, t, *J* = 2.4 Hz), 2.27 (3H, s), 2.24 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.7, 138.3, 137.5, 132.1, 131.5, 129.6, 128.2, 127.7, 126.5, 126.2, 125.4, 125.2, 125.0, 116.9, 68.0, 67.8, 53.0, 49.7, 21.0, 14.3. MS (ESI): calcd *m*/*z* for $C_{22}H_{26}N_2O$ ($M^+$) 334.20, found: 335.28 $[M + H]^+$. Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 78.84; H, 8.17; N, 8.27.

*(1S,2S)-2-[4-(1-Hydroxy1,2-dihydro-naphthalen-2-yl-piperazin-1-yl]–benzo-nitrile* (**2n**). Prepared according to general procedure. **2n** was obtained as a white solid (109 mg, 95%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 54% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 43.6 min (major) and 53.4 min (minor). m.p.: 126–127 °C; $[\alpha]_D^{25}$ = +111.4° (*c* = 64.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$); 3692 (br), 3210 (w), 2934 (s), 2874 (s), 2805 (s), 2272 (w), 1627 (w), 1597 (w), 1491 (s), 1445 (s), 1383 (s), 1298 (s), 1118 (s), 1077 (s), 935 (s), 846 (s), 795 (m); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.61–7.57 (2H, m), 7.51 (1H, td, *J* = 7.6 Hz, *J* = 1.6 Hz), 7.31–7.23 (2H, m), 7.10 (1H, d, *J* = 5.6 Hz), 7.05–7.02 (2H, m), 6.58 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.18 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 6.15 (1H, dd, *J* = 2.0 Hz, *J* = 2.4 Hz), 4.94 (1H, *J* = 11.2 Hz), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.4 Hz), 3.33–3.23 (4H, m), 3.07–3.01 (2H, m), 2.82–2.76 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 155.8, 137.1, 134.5, 134.0, 132.5, 131.9, 128.1, 127.7, 126.4, 124.9, 122.1, 118.6, 106.3, 67.9, 67.7, 52.3, 49.2. MS (ESI): calcd *m*/*z* for $C_{21}H_{21}N_3O$ ($M^+$) 331.17, found: 332.22 $[M + H]^+$. Anal. Calcd for $C_{21}H_{21}N_3O$: C, 76.11; H, 6.39; N, 12.68. Found: C, 76.01; H, 6.69; N, 12.51.

*(1S,2S)-2-[4-(3,4-Dimethyl-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2o**). Prepared according to general procedure. **2o** was obtained as a white solid (111 mg, 96%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 58% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 22.6 min (minor) and 23.8 min (major). m.p.: 125–126 °C; $[\alpha]_D^{25}$ = +109.7° (*c* = 59.5 mg, $CHCl_3$); IR (thin film, $cm^{-1}$); 3512 (br), 3211 (w), 2974 (s), 2806 (s), 1615 (s), 1490 (s), 1445 (s), 1416 (s), 1383 (m), 1298 (s), 1142 (s), 1044 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 7.2 Hz), 7.31–7.23 (2H, m), 7.07 (1H, d, *J* = 7.2 Hz), 7.04 (1H, d, *J* = 7.2 Hz), 6.78 (1H, d, *J* = 2.4 Hz), 6.71 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.56 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 6.15 (1H, dd, *J* = 2.0 Hz, *J* = 2.4 Hz), 4.93 (1H, 12.0), 3.53 (1H, dt, *J* = 11.6 Hz, *J* = 2.8 Hz), 3.37 (1H, br), 3.24–3.14 (4H, m), 3.01–2.96 (2H, m), 2.75–2.70 (2H, m), 2.25 (3H, s), 2.20 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.8, 137.3, 137.2, 131.9, 130.4, 129.6, 128.5, 128.1, 127.6, 126.4, 124.9, 124.7, 118.5, 114.2, 67.9, 67.7, 50.6, 49.2, 20.4, 19.0. MS (ESI): calcd *m*/*z* for $C_{22}H_{26}N_2O$ ($M^+$) 334.20, found: 335.28 $[M + H]^+$. Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 78.72; H, 8.31; N, 8.48.

*(1S,2S)-2-[4-p-Tolyl-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2p**). Prepared according to general procedure. **2p** was obtained as a white solid (94 mg, 85%) by flash chromatography (ethyl acetate: petroleum ether = 1:3 , *v*/*v*). $R_f$ = 0.28 on silica gel (ethyl acetate: petroleum ether = 1:3, *v*/*v*). The *ee* was determined to be 27% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 23.0 min (major) and 23.6 min (minor). m.p.: 193–194 °C; $[\alpha]_D^{25}$ = +108.9° (*c* = 57.1 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3422 (br), 3022 (w), 2918 (w), 2833 (m), 1649 (s), 1515 (s), 1499 (s), 1382 (s), 1241 (s), 1140 (s), 1046 (s), 781 (s), 746 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 6.8 Hz), 7.31–7.23 (2H, m), 7.09 (3H, d, *J* = 7.2 Hz), 6.86 (2H, d, *J* = 7.2 Hz), 6.57 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.15 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.94 (1H, d, *J* = 11.6 Hz), 3.52 (1H, dt, *J* = 11.2 Hz, *J* = 2.8 Hz), 3.36 (1H, br), 3.24–3.14 (4H, m), 3.01–2.96 (2H, m), 2.75–2.70 (2H, m), 2.29 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.4, 137.2, 131.9, 129.9, 129.7, 129.6, 128.1, 127.6, 126.4, 124.9, 124.6, 116.8, 67.9, 67.7, 50.6, 49.2, 20.6. MS (ESI): calcd *m*/*z* for $C_{21}H_{24}N_2O$ ($M^+$) 320.19, found: 321.25 $[M + H]^+$. Anal. Calcd for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.74. Found: C, 78.52; H, 7.81; N, 8.66.

*(1S,2S)-2-(4-Benzo[1,3] dioxol-5-yl-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2q**). Prepared according to general procedure. **2q** was obtained as a white solid (108 mg, 86%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.27 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 57% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 20.5 min (minor) and 25.5 min (major). m.p.: 112–113 °C; $[\alpha]_D^{25}$ = +81.8° (*c* = 99.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3514 (br),

3211 (w), 2925 (s), 2868 (s), 1627 (w), 1488 (s), 1446 (s), 1415 (s), 1298 (s), 1044 (s), 935 (s), 846 (s), 795 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 6.8 Hz), 7.29–7.25 (2H, m), 7.09 (1H, d, *J* = 8.4 Hz), 6.89 (1H, s), 6.78 (2H, s), 6.55 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 6.45 (1H, dd, *J* = 2.0, *J* = 2.4 Hz), 5.97 (2H, s), 4.90 (1H, d, *J* = 11.2 Hz), 3.49–3.46 (4H, m), 2.89–2.84 (2H, m), 2.63–2.53 (6H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 147.8, 146.8, 137.3, 132.0, 132.0, 129.3, 128.0, 127.6, 126.3, 125.0, 124.8, 122.5, 109.7, 108.1, 67.9, 67.5, 62.9, 53.6, 49.0. MS (ESI): calcd *m*/*z* for $C_{22}H_{24}N_2O_3$ ($M^+$) 364.18. Found 365.26 $[M + H]^+$. Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.50; H, 6.64; N, 7.69. Found: C, 72.29; H, 6.44; N, 7.76.

*(1S,2S)-2-[4-(2,4-Dimethyl-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2r**). Prepared according to general procedure. **2r** was obtained as a white solid (103 mg, 89%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.26 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 59% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 13.1 min (major) and 14.7 min (minor). m.p.: 113–114 °C; $[\alpha]_D^{25}$ = +67.6° (*c* = 65.1 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3589 (br), 3209 (w), 2990 (s), 2806 (s), 2778 (s), 1627 (w), 1491 (s), 1445 (s), 1415 (s), 1383 (s), 1298 (m), 1141 (s), 1076 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.62 (1H, d, *J* = 7.6 Hz), 7.31–7.23 (2H, m), 7.09 (1H, d, *J* = 7.2 Hz, *J* = 2.4 Hz), 7.02–6.95 (3H, m), 6.57 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.21 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.94 (1H, d, *J* = 11.6 Hz), 3.51 (1H, dt, *J* = 12 Hz, *J* = 2.4 Hz), 3.38 (1H, s), 2.99–2.90 (6H, m), 3.72–2.69 (2H, m), 2.31 (6H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.2, 137.4, 132.8, 132.6, 132.0, 132.0, 129.4, 128.0, 127.6, 127.2, 126.3, 125.1, 124.9, 119.1, 67.9, 67.7, 52.6, 49.6, 20.9, 17.9. MS (ESI): calcd *m*/*z* for $C_{22}H_{26}N_2O$ ($M^+$) 334.20, found: 335.25 $[M + H]^+$. Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 79.03; H, 8.13; N, 8.27.

*(1S,2S)-2-[4-m-Tolyl-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2s**). Prepared according to general procedure. **2s** was obtained as a white solid (100 mg, 90%) by flash chromatography (ethyl acetate: petroleum ether = 1:4, *v*/*v*). $R_f$ = 0.26 on silica gel (ethyl acetate: petroleum ether = 1:4, *v*/*v*). The *ee* was determined to be 59% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 22.2 min (minor) and 22.7 min (major). m.p.: 94–96 °C; $[\alpha]_D^{25}$ = +107.4° (*c* = 46.2 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3507 (br), 3158 (w), 2978 (s), 2934 (s), 2861 (s), 2806 (m), 1491 (s), 1445 (s), 1416 (s), 1383 (s), 1351 (s), 1298 (m), 1154 (s), 1077 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.69 (1H, d, *J* = 7.2 Hz), 7.36 (2H, td, *J* = 2.4 Hz, *J* = 7.2 Hz), 7.27 (1H, t, *J* = 7.6 Hz), 7.19 (1H, d, *J* = 7.2 Hz), 6.84 (3H, dd, *J* = 4.8 Hz, *J* = 7.6 Hz), 6.66 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.23 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 5.03 (1H, d, *J* = 11.6 Hz), 3.62 (1H, dt, *J* = 11.6 Hz, *J* = 2.0 Hz), 3.43 (1H, br), 3.36–3.27 (4H, m), 3.09–3.04 (2H, m), 2.83–2.78 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.5, 139.0, 137.2, 131.9, 129.7, 129.1, 128.1, 127.6, 126.4, 124.6, 121.0, 117.3, 113.6, 67.9, 67.7, 50.1, 49.2, 21.9. MS (ESI): calcd *m*/*z* for $C_{21}H_{24}N_2O$ ($M^+$) 320.19, found: 321.25 $[M + H]^+$. Anal. Calcd for $C_{21}H_{24}N_2O$: C, 78.71; H, 7.55; N, 8.74. Found: C, 78.69; H, 7.94; N, 8.56.

*(1S,2S)-2-(4-Phenethyl-cyclohexyl)-1,2-dihydro-naphthalen-1-ol* (**2t**). Prepared according to general procedure. **2t** was obtained as a white solid (90 mg, 78%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 50% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 10.1 min (major) and 11.4 min (minor). m.p.: 112–113 °C; $[\alpha]_D^{25}$ = +87.9° (*c* = 36.5 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3519 (br), 3089 (w), 2978 (s), 2934 (s), 2863 (s), 2805 (s), 1490 (s), 1445 (s), 1415 (s), 1383 (s), 1351 (s), 1297 (m), 1076 (s), 1044 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.2 Hz), 7.34–7.21 (7H, m), 7.09 (1H, d, *J* = 1.2 Hz), 6.56 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.15 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.91 (1H, d, *J* = 11.6 Hz), 3.48 (2H, ddd, *J* = 2.4 Hz, *J* = 2.4 Hz, *J* = 6.8 Hz), 2.85–2.96 (4H, m), 2.65 (8H, dd, *J* = 4.8 Hz, *J* = 6.4 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 140.5, 137.4, 132.1, 129.5, 128.9, 128.8, 128.7, 128.6, 128.1, 127.6, 126.3, 125.1, 67.7, 67.6, 60.7, 53.9, 49.1, 33.9. MS (ESI): calcd *m*/*z* for $C_{22}H_{26}N_2O$ ($M^+$) 334.20, found: 335.18 $[M + H]^+$. Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.00; H, 7.84; N, 8.38. Found: C, 79.89; H, 8.05; N, 8.26.

*(1S,2S)-4-(1-Hydroxy-1,2-dihydro-naphthalen-2-yl)-piperazine-1-carboxy-lic acid ethyl ester* (**2u**). Prepared according to general procedure. **2u** was obtained as a white solid (89 mg, 85%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.17 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 51% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 16.0 min (minor) and 21.7 min (major). m.p.: 147–148 °C; $[\alpha]_D^{25}$ = +93.2° (*c* = 65.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3517 (br), 3087 (w), 2977 (s), 2934 (s), 2867 (s), 2806 (s), 1710 (m), 1490 (s), 1445 (s), 1415 (m), 1383 (s), 1351 (s), 1298 (m), 1077 (s), 1044 (m), 935 (m), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.57 (1H, d, *J* = 7.6 Hz), 7.31–7.23 (2H, m), 7.09 (1H, d, *J* = 6.8 Hz), 6.56 (1H, dd, *J* = 2.0 Hz, *J* = 2.0 Hz), 6.03 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 4.90 (1H, d, *J* = 10.8 Hz), 4.16 (2H, dd, *J* = 14.4 Hz, *J* = 6.8 Hz), 3.56–3.47 (5H, m), 3.38 (1H, br), 2.74 (2H, t, *J* = 6.8 Hz), 2.54 (2H, t, *J* = 6.0 Hz), 1.29 (3H, t, *J* = 7.2 Hz); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 155.5, 137.0, 131.8, 129.5, 128.0, 127.6, 126.3, 125.2, 124.5, 67.8, 67.6, 61.4, 48.9, 44.2, 14.7. MS (ESI): calcd *m*/*z* for $C_{17}H_{22}N_2O_3$ ($M^+$) 302.16, found: 303.08 $[M + H]^+$. Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.26. Found: C, 67.39; H, 7.68; N, 9.15.

*(1S,2S)-2-[4-(3-Trifluoromethyl-phenyl)-piperazin-1-yl]-1,2-dihydro–naphthalen-1-ol* (**2v**). Prepared according to general procedure. **2v** was obtained as a white solid (107 mg, 83%) by flash chromatography (ethyl acetate: petroleum ether = 1:3, *v*/*v*). $R_f$ = 0.26 on silica gel (ethyl acetate: petroleum ether = 1:3, *v*/*v*). The *ee* was determined to be 54% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 2% 2-propanol in hexanes were 35.2 min (minor) and 36.3 min (major). m.p.: 120–121 °C; $[\alpha]_D^{25}$ = +87.6° (*c* = 46.8 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3517 (br), 3092 (w), 2978 (s), 2869 (s) 1628 (w), 1491 (m), 1444 (s), 1383 (s), 1351 (s), 1297 (m), 1133 (s), 1077 (s), 934 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.59 (1H, d, *J* = 7.2 Hz), 7.34 (1H, t, *J* = 8.0 Hz), 7.29–7.23 (2H, m), 7.13–7.06 (4H, m), 6.57 (1H, d, *J* = 10.0 Hz), 6.11 (1H, dd, *J* = 2.0 Hz, *J* = 2.0 Hz), 4.94 (1H, d, *J* = 12.0 Hz), 3.53 (1H, dd, *J* = 2.4 Hz, *J* = 2.0 Hz), 3.30–3.22 (5H, m), 2.97 (2H, dd, *J* = 3.2 Hz, *J* = 5.2 Hz), 2.72 (2H, t, *J* = 11.2 Hz); $^{13}$C-NMR(100 MHz, $CDCl_3$) δ 151.5, 137.1, 131.9, 129.8, 129.7, 128.2, 127.8, 126.5, 125.1, 124.7, 119.1, 116.2, 116.2, 112.5, 112.5, 68.0, 67.6, 49.5, 49.0. MS (ESI): calcd *m*/*z* for $C_{21}H_{21}F_3N_2O$ ($M^+$) 374.16, found: 375.12 $[M + H]^+$. Anal. Calcd for $C_{21}H_{21}F_3N_2O$: C, 67.37; H, 5.65; N, 7.48. Found: C, 67.16; H, 5.89; N, 7.36.

*(1S,2S)-2-[4-(4-Trifluoromethyl-phenyl)-piperazin-1-yl]-1,2-dihydro-naphth-alen-1-ol* (**2w**). Prepared according to general procedure. **2w** was obtained as a white solid (98 mg, 76%) by flash chromatography (ethyl acetate: petroleum ether = 1:3, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:3, *v*/*v*). The *ee* was determined to be 56% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 13.7 min (major) and 15.5 min (minor). m.p.: 215–216 °C; $[\alpha]_D^{25}$ = +102.8° (*c* = 52.7 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3591 (br), 3210 (w), 2978 (s), 2873 (s), 2805 (s) 1617 (w), 1490 (s), 1445 (s), 1416 (s), 1389 (s), 1297 (s), 1131 (s), 1077 (s), 935 (s), 845 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.51 (1H, d, *J* = 7.2 Hz), 7.42 (2H, d, *J* = 8.8 Hz), 7.18 (2H, m), 7.02 (1H, d, *J* = 7.2 Hz), 6.86 (2H, d, *J* = 8.8 Hz), 6.50 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 6.03 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 4.86 (1H, d, *J* = 11.2 Hz), 3.47 (1H, d, *J* = 11.2 Hz), 3.30–3.20 (5H, m), 2.93–2.88 (2H, m), 2.68–2.63 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 153.5, 137.1, 131.9, 129.9, 128.3, 127.8, 126.7, 126.7, 126.7, 126.6, 126.5, 125.1, 124.2, 114.9, 68.1, 67.8, 49.0, 48.9. MS (ESI): calcd *m*/*z* for $C_{21}H_{21}F_3N_2O$ ($M^+$) 374.16, found: 375.25 $[M + H]^+$. Anal. Calcd for $C_{21}H_{21}F_3N_2O$: C, 67.37; H, 5.65; N, 7.48. Found: C, 67.13; H, 5.86; N, 7.36.

*(1S,2S)-2-[4-(4-Chloro-phenyl)-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**2x**). Prepared according to general procedure. **2x** was obtained as a white solid (97 mg, 82%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.3 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 39% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 15.2 min (major) and 16.9 min (minor). m.p.: 203–204 °C; $[\alpha]_D^{25}$ = +100.1° (*c* = 65.1 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3585 (br), 3212 (w), 2978 (s), 2935 (s), 2806 (s) 1634 (w), 1490 (s), 1445 (s), 1415 (s), 1351 (s), 1298 (s), 1134 (s),

1076 (s), 935 (s), 845 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1H, *J* = 7.2 Hz), 7.30–7.22 (m, 4H), 7.1 (d, 1H, *J* = 7.2 Hz), 6.86 (d, 2H, *J* = 8.8 Hz), 6.58 (dd, 1H, *J* = 2.0 Hz, *J* = 2.4 Hz), 6.13 (dd, 1H, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.94 (d, 1H, *J* = 11.6 Hz), 3.54 (d, 1H, *J* = 11.6 Hz), 3.24–3.19 (m, 5H), 3.00–2.96 (m, 2H), 2.76–2.71 (m, 2H); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 150.1, 137.2, 131.9, 129.8, 129.2, 128.2, 127.8, 126.5, 125.1, 125.0, 124.4, 117.6, 68.0, 67.7, 50.0, 49.1. MS (ESI): calcd *m*/*z* for $C_{20}H_{21}ClN_2O$ ($M^+$) 340.13, found: 341.20 $[M + H]^+$. Anal. Calcd for $C_{20}H_{21}ClN_2O$: C, 70.48; H, 6.21; N, 8.22. Found: C, 70.29; H, 6.44; N, 8.16.

*(1S,2S)-2-[4-(1-Hydroxy-6,7-dimethoxy-1,2-dihydro-naphthalen-2-yl)-piper-azin-1-yl]-benzonitrile* (**3a**). Prepared according to general procedure. **3a** was obtained as a white solid (74 mg, 77%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.16 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 37% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 73.4 min (major) and 86.0 min (minor). m.p.: 192–193 °C; $[\alpha]_D^{25}$ = +65.5° (*c* = 37.8 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3512 (br), 3018 (w), 2927 (s), 2809 (s), 2271 (w), 1635 (w), 1490 (s), 1445 (s), 1351 (s), 1297 (s), 1135 (s), 1078 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.57 (1H, dd, *J* = 1.2 Hz, *J* = 1.2 Hz), 7.48 (1H, t, *J* = 7.2 Hz), 7.13 (1H, s), 7.03–6.99 (2H, m), 6.45 (1H, s), 6.47 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.07 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.86 (1H, d, *J* = 11.2 Hz), 3.93 (3H, s), 3.87 (3H, s), 3.45 (1H, d, *J* = 7.2 Hz), 3.28–3.22 (4H, m), 3.15 (1H, br), 2.99–2.98 (2H, m), 2.78–2.77 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 155.7, 148.8, 148.2, 134.5, 134.0, 130.0, 129.1, 124.8, 122.1, 118.8, 110.2, 108.8, 106.2, 68.0, 67.8, 56.2, 56.2, 52.2, 49.2. MS (ESI): calcd *m*/*z* for $C_{23}H_{25}N_3O_3$ ($M^+$) 391.19, found: 392.10 $[M + H]^+$. Anal. Calcd for $C_{23}H_{25}N_3O_3$: C, 70.57; H, 6.44; N, 10.73. Found: C, 70.46; H, 6.67; N, 10.55.

*(1S,2S)-2-[4-(4-Fluoro-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-dihydro-Naphthalen-1-ol* (**3b**). Prepared according to general procedure. **3b** was obtained as a white solid (69 mg, 73%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 49% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 40.5 min (major) and 42.9 min (minor). m.p.: 200–201 °C; $[\alpha]_D^{25}$ = +79.1° (*c* = 41.2 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3516 (br), 3022 (w), 2972 (s), 2935 (s), 2806 (s), 1635 (w), 1490 (s), 1445 (s), 1351 (s), 1298 (s), 1135 (s), 1078 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.15 (1H, s), 6.97 (2H, d, *J* = 8.4 Hz), 6.91–6.87 (2H, m), 6.66 (1H, s), 6.49 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.03 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 4.87 (1H, d, *J* = 11.2 Hz), 3.94 (3H, s), 3.88 (3H, s), 3.49 (1H, dt, *J* = 11.2 Hz, *J* = 2.4 Hz), 3.25 (1H, br), 3.18–3.13 (4H, m), 2.96–2.94 (2H, m), 2.74–2.73 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 158.7, 156.3, 148.9, 148.3, 148.1, 130.0, 129.2, 124.8, 122.5, 118.2, 115.8, 115.6, 110.3, 108.9, 67.9, 67.8, 56.3, 56.3, 51.0, 49.2. MS (ESI): calcd *m*/*z* for $C_{22}H_{25}FN_2O_3$ ($M^+$) 384.18, found: 385.07 $[M + H]^+$. Anal. Calcd for $C_{22}H_{25}FN_2O_3$: C, 68.73; H, 6.55; N, 7.29. Found: C, 68.56; H, 6.78; N, 7.19.

*(1S,2S)-2-[4-(2-Fluoro-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-dihydro-naphthalen-1-ol* (**3c**). Prepared according to general procedure. **3c** was obtained as a white solid (74 mg, 79%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.29 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 38% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL/min; Retention times in 10% 2-propanol in hexanes were 55.6 min (minor) and 60.3 min (major). m.p.: 160–161 °C; $[\alpha]_D^{25}$ = 70.9° (*c* = 35.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3507 (br), 3188 (w), 2968 (s), 2890 (s), 2811 (s), 1610 (w), 1458 (s), 1379 (s), 1281 (s), 1183 (s), 1099 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.14 (1H, s), 7.06–6.93 (4H, m), 6.65 (1H, s), 6.47 (1H, dd, *J* = 2.4 Hz, *J* = 2.0 Hz), 6.05 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.86 (1H, d, *J* = 11.6 Hz), 3.93 (3H, s), 3.87 (3H, s), 3.46 (1H, d, *J* = 11.2 Hz), 3.22 (1H, br), 3.15–3.11 (4H, m), 2.98–2.95 (2H, m), 2.76–2.72 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 148.8, 148.2, 130.0, 129.1, 124.8, 124.6, 122.7, 119.1, 119.1, 116.4, 116.2, 110.1, 108.8, 67.9, 67.8, 56.2, 56.2, 51.2, 51.2, 49.2. MS (ESI): calcd *m*/*z* for $C_{22}H_{25}FN_2O_3$ ($M^+$) 384.18, found: 385.10 $[M + H]^+$. Anal. Calcd for $C_{22}H_{25}FN_2O_3$: C, 68.73; H, 6.55; N, 7.29. Found: C, 68.62; H, 6.73; N, 7.18.

*(1S,2S)-6,7-Dimethoxy-2-(4-(4-methoxy-phenyl)-piperazin-1-yl]-1,2-dihydro–naphthalene-1-ol* (**3d**). Prepared according to general procedure. **3d** was obtained as a white solid (60 mg, 62%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 59% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 0.5 mL / min; Retention times in 5% 2-propanol in hexanes were 92.2 min (major) and 110.1 min (minor). m.p.: 174–175 °C; $[\alpha]_D^{25}$ = +77.4° (*c* = 26.5 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3696 (br), 3036 (w), 2924 (s), 2877 (s), 1682 (s), 1512 (s), 1452 (s), 1383 (w), 1244 (s), 1111 (s), 1013 (s), 935 (w), 815 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.15 (1H, s), 6.92 (2H, d, *J* = 2.0 Hz), 6.85 (2H, d, *J* = 2.0 Hz), 6.66 (1H, s), 6.48 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 6.05 (1H, dd, *J* = 2.4 Hz, *J* = 2.8 Hz), 4.86 (1H, d, *J* = 11.2 Hz), 3.94 (3H, s), 3.88 (3H, s), 3.77 (3H, s), 3.48 (1H, dt, *J* = 11.2 Hz, *J* = 2.4 Hz), 3.25 (1H, br), 3.15–3.10 (4H, m), 2.98–2.93 (2H, m), 2.75–2.70 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 154.2, 148.9, 148.3, 145.9, 130.1, 129.1, 124.8, 122.8, 118.6, 114.7, 110.3, 108.9, 68.0, 67.9, 56.3, 56.3, 51.5, 49.3. MS (ESI): calcd *m*/*z* for $C_{23}H_{28}N_2O_4$ ($M^+$) 396.20, found: 397.14 [M + H] $^+$. Anal. Calcd for $C_{23}H_{28}N_2O_4$: C, 69.67; H, 7.12; N, 7.07. Found: C, 74.89; H, 7.44; N, 8.56.

*(1S,2S)-2-[4-(3,4-Dichloro-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-dihydronaphthalen-1-ol* (**3e**). Prepared according to general procedure. **3e** was obtained as a white solid (50 mg, 47%) by flash chromatography (ethyl acetate: petroleum ether = 2:3, *v*/*v*). $R_f$ = 0.20 on silica gel (ethyl acetate: petroleum ether = 2:3, *v*/*v*). The *ee* was determined to be 16% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 10% 2-propanol in hexanes were 44.9 min (major) and 49.4 min (minor). m.p.: 187–188 °C; $[\alpha]_D^{25}$ = +25.2° (*c* = 11.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3591 (br), 3210 (w), 2973 (s), 2933 (s), 2874 (s), 2806 (s), 1676 (s), 1490 (s), 1445 (s), 1415 (s), 1383 (s), 1297 (m), 1077 (s), 1044 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.28 (1H, dd, *J* = 2.8 Hz, *J* = 2.8 Hz), 7.15 (1H, s), 6.97 (1H, t, *J* = 2.8 Hz), 6.75 (1H, dt, *J* = 8.8 Hz, *J* = 2.7 Hz), 6.66 (1H, d, *J* = 2.4 Hz), 6.50 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 6.01 (1H, dd, *J* = 2.8 Hz, *J* = 2.4 Hz), 4.86 (1H, d, *J* = 11.6 Hz), 3.95 (3H, d, *J* = 2.4 Hz), 3.89 (3H, *J* = 2.4 Hz), 3.49 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 3.24–3.16 (5H, m), 2.95–2.91 (2H, m), 2.73–2.69 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 150.8, 148.9, 148.3, 133.0, 130.6, 129.9, 129.3, 124.7, 122.5, 122.2, 117.5, 115.6, 110.3, 109.0, 68.0, 67.8, 56.2, 56.2, 49.4, 48.9. MS (ESI): calcd *m*/*z* for $C_{22}H_{24}Cl_2N_2O_3$ ($M^+$) 434.12, found: 435.04 $[M + H]^+$. Anal. Calcd for $C_{22}H_{24}Cl_2N_2O_3$: C, 60.70; H, 5.56; N, 6.43. Found: C, 60.57; H, 5.84; N, 6.36.

*(1S,2S)-2-[4-(2-Chloro-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-dihydro-naphthalen-1-ol* (**3f**). Prepared according to general procedure. **3f** was obtained as a white solid (50 mg, 51%) by flash chromatography (ethyl acetate: petroleum ether = 1:1, *v*/*v*). $R_f$ = 0.22 on silica gel (ethyl acetate: petroleum ether = 1:1, *v*/*v*). The *ee* was determined to be 43% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 2% 2-propanol in hexanes were 114.4 min (minor) and 125.3 min (major). m.p.: 140–141 °C; $[\alpha]_D^{25}$ = +75.3° (*c* = 38.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3591 (br), 3211 (w), 2975 (s), 2934 (s), 2875 (s), 2806 (s), 1678 (w), 1490 (s), 1445 (s), 1378 (s), 1297 (m), 1108 (s), 1077 (s), 918 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.49 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 7.39–7.33 (1H, m), 7.27 (1H, s), 7.18 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.95 (1H, t, *J* = 7.2 Hz), 6.77 (1H, s), 6.60 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.21 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.98 (1H, d, *J* = 11.6 Hz), 4.07 (3H, s), 3.99 (3H, s), 3.61 (1H, d, *J* = 11.6 Hz), 3.24 (4H, br), 3.15–2.95 (2H, m), 2.83–2.64 (2H, m); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.4, 148.9, 148.3, 130.9, 130.1, 139.1, 129.0, 127.8, 124.9, 124.0, 122.9, 120.6, 110.3, 108.9, 68.0, 56.3, 56.3, 52.0, 49.4, 29.9. MS (ESI): calcd *m*/*z* for $C_{22}H_{25}ClN_2O_3$ ($M^+$) 400.16, found: 401.12 $[M + H]^+$. Anal. Calcd for $C_{22}H_{25}ClN_2O_3$: C, 65.91; H, 6.29; N, 6.99. Found: C, 65.79; H, 6.48; N, 6.76.

*(1S,2S)-6,7-Dimethoxy-2-(4-o-tolyl-piperazin-1-yl]-1,2-dihydro-naphthalen-1-ol* (**3g**). Prepared according to general procedure. **3g** was obtained as a white solid (71 mg, 76%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.18 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 38% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 2% 2-propanol in hexanes were 79.8 min (minor) and

85.1 min (major). m.p.: 120–121 °C; $[\alpha]_D^{25}$ = +40.1° (*c* = 38.9 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3693 (br), 3218 (w), 2980 (s), 2869 (s), 1681 (w), 1498 (s), 1445 (s), 1381 (s), 1351 (s), 1297 (m), 1142 (s), 935 (s), 846 (s);. $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.21–7.18 (3H, m), 7.06–6.99 (2H, m), 6.67 (1H, s), 6.50 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.12 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.88 (1H, d, *J* = 11.6 Hz), 3.96 (3H, s), 3.89 (3H, s), 3.49 (1H, dt, *J* = 6.8 Hz, *J* = 2.4 Hz), 3.27 (1H, br), 3.02–2.96 (6H, m), 2.75–2.71 (2H, m), 2.34 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.6, 148.8, 148.2, 132.7, 131.3, 130.2, 128.9, 126.8, 124.8, 123.4, 123.0, 119.2, 110.2, 108.8, 68.0, 68.0, 56.3, 56.2, 52.4, 49.7, 18.1. MS (ESI): calcd *m*/*z* for $C_{23}H_{28}N_2O_3$ ($M^+$) 380.21, found: 381.15 $[M + H]^+$. Anal. Calcd for $C_{23}H_{28}N_2O_3$: C, 72.60; H, 7.42; N, 7.36. Found: C, 72.30; H, 7.64; N, 7.18.

*(1S,2S)-2-[4-(2,5-Dimethyl-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-di-hydro-naphthalen-1-ol* (**3h**). Prepared according to general procedure. **3h** was obtained as a white solid (83 mg, 86%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.29 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 35% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 2% 2-propanol in hexanes were 63.6 min (minor) and 65.1 min (major). m.p.: 138–139 °C; $[\alpha]_D^{25}$ = +73.2° (*c* = 68.5 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3592 (br), 3211 (w), 2975 (s), 2934 (s), 2863 (s), 2805 (s), 1677 (w), 1490 (s), 1444 (s), 1381 (s), 1297 (m), 1119 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.19 (1H, s), 7.08 (1H, d, *J* = 7.6 Hz), 6.87 (1H, s), 6.83 (1H, d, *J* = 7.6 Hz), 6.67 (1H, s), 6.50 (1H, dd, *J* = 2.0 Hz, *J* = 2.0 Hz), 6.12 (1H, dd, *J* = 2.0 Hz, *J* = 2.0 Hz), 4.89 (1H, d, *J* = 11.6 Hz), 3.96 (3H, s), 3.90 (3H, s), 3.49 (1H, d, *J* = 12.0 Hz), 3.37 (1H, br), 3.04–2.95 (6H, m), 2.72 (2H, t, *J* = 6.8 Hz), 2.33 (3H, s), 2.29 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 151.4, 148.8, 148.2, 136.3, 131.1, 130.2, 129.4, 129.0, 124.8, 124.0, 123.0, 119.9, 110.2, 108.8, 68.0, 67.9, 56.2, 56.2, 52.4, 49.7, 21.3, 17.6. MS (ESI): calcd *m*/*z* for $C_{24}H_{30}N_2O_3$ ($M^+$) 394.23, found: 395.15 $[M + H]^+$. Anal. Calcd for $C_{24}H_{30}N_2O_3$: C, 73.07; H, 7.66; N, 7.10. Found: C, 73.16; H, 7.91; N, 6.95.

*(1S,2S)-2-[4-(3,4-Dimethyl-phenyl)-piperazin-1-yl]-6,7-dimethoxy-1,2-di-hydro-naphthalen-1-ol* (**3i**). Prepared according to general procedure. **3i** was obtained as a white solid (78 mg, 81%) by flash chromatography (ethyl acetate: petroleum ether = 1:2, *v*/*v*). $R_f$ = 0.16 on silica gel (ethyl acetate: petroleum ether = 1:2, *v*/*v*). The *ee* was determined to be 45% using HPLC analysis on a CHIRALCEL AD column, λ = 254 nm. Flow rate = 1.0 mL/min; Retention times in 2% 2-propanol in hexanes were 21.6 min (major) and 22.6 min (minor). m.p.: 145–146 °C; $[\alpha]_D^{25}$ = +95.6° (*c* = 29.3 mg, $CHCl_3$); IR (thin film, $cm^{-1}$) 3695 (br), 3219 (w), 2978 (s), 2936 (s), 2867 (s), 1699 (w), 1490 (w), 1445 (s), 1383 (s), 1351 (s), 1297 (m), 1124 (s), 1077 (s), 935 (s), 846 (s); $^1$H-NMR (400 MHz, $CDCl_3$) δ 7.16 (1H, s), 7.04 (1H, d, *J* = 8.4 Hz), 6.78 (1H, d, *J* = 2.4 Hz), 6.77 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 6.66 (1H, s), 6.48 (1H, dd, *J* = 2.4 Hz, *J* = 2.4 Hz), 4.88 (1H, d, *J* = 6.8 Hz), 3.95 (3H, s), 3.89 (3H, s), 3.48 (1H, dt, *J* = 6.8 Hz, *J* = 2.4 Hz), 3.20 (1H, br), 3.19–3.16 (4H, m), 2.95–2.87 (2H, m), 2.75–2.69 (2H, m), 2.25 (3H, s), 2.21 (3H, s); $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 149.7, 148.7, 148.1, 137.2, 130.3, 130.0, 129.0, 128.4, 124.7, 122.6, 118.4, 114.1, 110.1, 108.8, 67.8, 67.8, 56.2, 56.2, 50.6, 49.2, 20.3, 18.9. MS (ESI): calcd *m*/*z* for $C_{24}H_{30}N_2O_3$ ($M^+$) 394.23, found: 395.15 $[M + H]^+$. Anal. Calcd for $C_{24}H_{30}N_2O_3$: C, 73.07; H, 7.66; N, 7.10. Found: C, 73.30; H, 8.16; N, 6.74.

## 4. Conclusions

In conclusion, we have developed the iridium-catalyzed asymmetric ring-opening of oxabicyclic alkenes with *N*-substituted piperazine nucleophiles. It may provide an efficient and practical access to optically pure *trans*-2-*N*-substituted piperazine 1,2-dihydronaphthalen-1-ols in high yields and moderate enantioselectivities. Catalyst systems consisting of four different kinds of chiral bisphosphine ligands with $[Ir(COD)Cl]_2$ to form complexes as iridium catalysts were investigated, and (*S*)-*p*-Tol-BINAP ligand was found to give high yields and moderate enantioselectivities. Further investigation to expand the scope of the reactions as well as the study of the iridium-catalyzed asymmetric ring-opening reactions of oxabicyclic alkenes with other nucleophiles are in progress in our laboratory.

**Supplementary Materials:** The full characterization data for all compounds **1a**–**1b**, **2a**–**2x** and **3a**–**3i**, including optical rotations, $^{1}$H-NMR and $^{13}$C-NMR, MS, elemental analysis and X-ray structure data for compound **2i** in CIF format, and HPLC conditions and spectra of compounds **2a**, **2c**, **2g**–**2h**, **2i**–**2k**, **2m**–**2o**, **2q**–**2r**, **2u**–**2x** and **3b** are provided in the Supplementary materials at: http://www.mdpi.com/1420-3049/20/12/19748/s1.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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**Sample Availability:** Samples of the compounds **1a–1b, 2a–2x and 3a–3i** are available from the authors.