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Iridium-Catalyzed Asymmetric Ring Opening of Azabicyclic Alkenes by Amines

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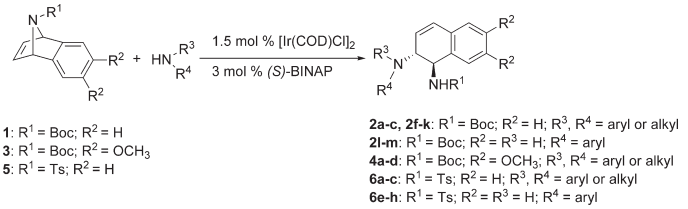

The enantioselective ring-opening reactions of azabicyclic alkenes with primary and secondary aromatic amine nucleophiles are reported using an iridium catalyst generated in situ from 1.5 mol % of $[Ir(COD)Cl]_2$ and 3 mol % of (*S*)-BINAP. The reaction affords the corresponding *trans*-1,2-diamine derivatives in moderate to good yields with moderate to high enantioselectivities (up to 97% ee). The *trans*-configuration of the 1,2-diamino product **2g** was confirmed by X-ray crystallography.

Introduction

Ring-opening reactions of oxa- and azabicyclic olefins are exceedingly important methods of great utility in synthetic chemistry. Recently, this area has been paid increasing attention and extensively investigated.[1] Many parameters have been examined for these reactions, including a variety of metal catalysts such as Rh,[2] Pd,[3] Cu,[4] and Ni[5] etc., and nucleophiles such as dialkylzincs,[2a,6] organoboronic acids,[7] alkynes,[8] organic halides,[9] amines,[10] Grignard reagents,[11] methanol,[12] and others.[13] Iridium-catalyzed allylic substitution is an efficient protocol for the construction of both carbon−carbon bonds and carbon−heteroatom bonds providing a feasible way to generate multifunctional chiral building blocks.[14,15] Ring-opening reaction of azabenzonorbornadienes

(1) For reviews, see: Rayabarapu, D. K.; Cheng, C. H. *Acc. Chem. Res.* **2007**, *40*, 971–983.
(2) (a) Lautens, M.; Hiebert, S.; Renaud, J. L. *Org. Lett.* **2000**, *2*, 1971–1973. (b) Cho, Y. H.; Tseng, N. W.; Senboku, H.; Lautens, M. *Synthesis* **2008**, *15*, 2467–2475.
(3) (a) Chen, C. L.; Martin, S. F. *J. Org. Chem.* **2006**, *71*, 4810–4817. (b) Cabrera, S.; Gomez, A. R.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 3944–3947.
(4) (a) Arrayas, R. G.; Cabrera, S.; Carretero, J. C. *Synthesis* **2006**, *7*, 1205–1219. (b) Arrayas, R. G.; Cabrera, S.; Carretero, J. C. *Org. Lett.* **2005**, *7*, 219–221.
(5) (a) Feng, C. C.; Nandi, M.; Sambaiah, T.; Cheng, C. H. *J. Org. Chem.* **1999**, *64*, 3538–3543. (b) Li, L. P.; Rayabarapu, D. K.; Nandi, M.; Cheng, C. H. *Org. Lett.* **2003**, *5*, 1621–1624.
(6) (a) Cabrera, S.; Alonso, L.; Arrayas, R.; Familiar, O.; Carretero, J. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 1513–1514. (b) Ogura, T.; Yoshida, K.; Yanagisawa, A.; Imamoto, T. *Org. Lett.* **2009**, *11*, 2245–2248.
(7) Lautens, M.; Dockendorff, C. *Org. Lett.* **2003**, *5*, 3695–3698.
(8) Nishimura, T.; Tsurumaki, E.; Kawamoto, T.; Guo, X. X.; Hayashi, T. *Org. Lett.* **2008**, *10*, 4057–4060.
(9) Hen, C. L.; Martin, S. F. *J. Org. Chem.* **2006**, *71*, 4810–4817.
(10) Cho, Y. H.; Zunic, V.; Senboku, H.; Olsen, M.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 6837–6846.
(11) Cabrera, S.; Arrayas, R. G.; Alonso, I.; Carretero, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 17938–17947.
(12) Webster, R.; Biong, C.; Lautens, M. *J. Am. Chem. Soc.* **2009**, *131*, 444–445.
(13) (a) John, J.; Anas, S.; Sajisha, V. S.; Viji, S.; Radhakrishnan, K. V. *Tetrahedron Lett.* **2007**, *48*, 7225–7227. (b) Wu, M. S.; Rayabarapu, D. K.; Cheng, C. H. *J. Org. Chem.* **2004**, *69*, 8407–8412.
(14) For reviews, see: (a) Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164–15165. (b) Alexakis, A.; Hajjaji, S. E.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (c) Yamashita, Y.; Gopalarathnam, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 7508–7509. (d) Kanayama, T.; Yoshida, K.; Miyabe, H.; Kimachi, T.; Takemoto, Y. *J. Org. Chem.* **2003**, *68*, 6197–6201. (e) Weix, D. J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 7720–7721. (f) Nomura, N.; Komiyama, S.; Kasugai, H.; Saba, M. *J. Am. Chem. Soc.* **2008**, *130*, 812–814. (g) Alexakis, A.; Hajjaji, S. E.; Polet, D.; Rathgeb, X. *Org. Lett.* **2007**, *9*, 3393–3395. (h) Polet, D.; Alexakis, A. *Org. Lett.* **2005**, *7*, 1621–1624. (i) Kanayama, T.; Yoshida, K.; Miyabe, H.; Kimachi, T.; Takemoto, Y. *J. Org. Chem.* **2003**, *68*, 6197–6201. (j) Woodward, S. *Angew. Chem., Int. Ed.* **2005**, *42*, 5560–5562. (k) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829–2844.

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represents a type of allylic substitution reaction in which the reaction proceeds under relatively mild conditions, leading to a variety of 1,2-diamino compounds in both high yields and excellent enantioselectivities. Lautens and co-workers[16] have extensively investigated Rh-catalyzed asymmetric ring-opening reactions of azabenzonorbornadienes with amines (up to 99% ee) and successfully employed them in the preparation of new chiral ligands[17] and analgesic compounds.[18] Recently, we have reported Rh-[19] and Ir-catalyzed[20] asymmetric ring-opening reactions of *N*-Boc-azabenzonorbornadiene with N-substituted piperazine nucleophiles in high yields and high enantioselectivities. Our interest in generating carbon−nitrogen bonds has prompted us to expand the scope of the reaction to include primary aromatic amine as well as cyclic and acyclic secondary amine-induced ring openings of azabicyclic alkenes for an efficient access to *trans*-1,2-diamine moieties with high regio-, diastereo-, and enantioselectivities. These methods offer potentially useful synthetic routes to *trans*-1,2-diamines which are the scaffolds for chiral ligands[21] and valuable intermediates for total synthesis of bioactive compounds.[22]

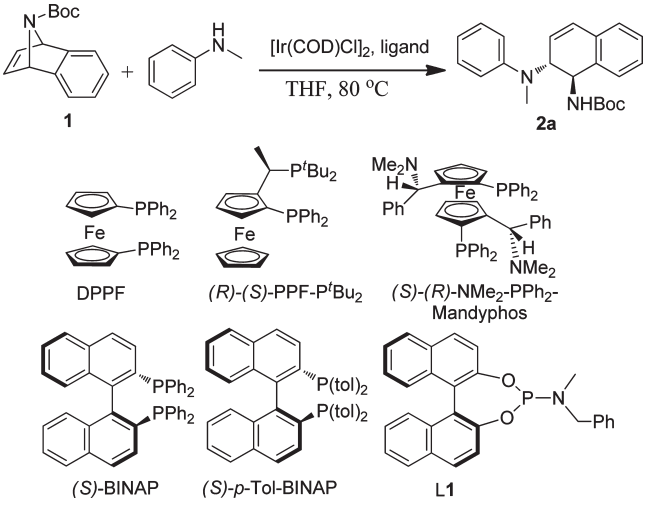
In this paper, we report the full details of the catalytic asymmetric ring-opening reactions of N-substituted azabenzonorbornadienes **1**, **3**, and **5** with a wide variety of amines in the presence of iridium catalysts. The reaction affords the corresponding *trans*-1,2-diamine derivatives in moderate to good yields with moderate to excellent enantioselectivities (up to 97% ee).

Results and Discussion

The substrates **1**, **3**, and **5** were prepared according to the literature procedures.[20a,7,16b] An achiral ligand 1,1′-bis(diphenylphosphino)ferrocene (DPPF) was first chosen to validate the catalytic activity of the iridium complex in the ring-opening reactions of *N*-Boc-azabenzonorbornadiene with *N*-methylaniline. In the presence of 1 mol % of $[Ir(COD)Cl]_2$ and 2 mol % of DPPF, the desired ring-opening product was obtained in a 71% yield (Table 1, entry 1). The yield was increased to 86% when 1.5 mol % of $[Ir(COD)Cl]_2$ and 3 mol % of DPPF were employed (Table 1, entry 2). However, further increase of the catalyst loading did not improve the yield (Table 1, entry 3). Several chiral ligands such as (*R*)-(*S*)-PPF-P^{t}Bu$_2$, (*S*)-(*R*)-NMe$_2$-PPh$_2$-Mandyphos, (*S*)-BINAP, (*S*)-*p*-Tol-BINAP, and **L1** were then examined. From Table 1, we can see that (*S*)-BINAP gave the best yield and enantioselectivity when the molar ratio of (*S*)-BINAP to iridium was 2:1 (Table 1, entry 6). While the molar ratio of (*S*)-BINAP to iridium changed to 1:1 or 3:1, the ring-opening reaction gave a lower yield and enantioselectivity (Table 1, entries 9 and 10). Other ligands such as (*R*)-(*S*)-PPF-P^{t}Bu$_2$, (*S*)-(*R*)-NMe$_2$-PPh$_2$-Mandyphos, (*S*)-*p*-Tol-BINAP, and **L1** gave either unsatisfactory results (Table 1, entries 4 and 7) or no reaction (Table 1, entries 5 and 8).

In order to obtain better yields and higher enantioselectivities for the asymmetric ring-opening reaction of azabenzonorbornadiene with amine nucleopiles, a number of parameters including solvents, temperature, and additives have therefore been investigated. It was found that solvents played a significant role in improving both reactivity and enantioselectivity. The optimal solvent turned out to be tetrahydrofuran (THF). Iridium-catalyzed asymmetric

TABLE 1. Ligand Optimization for Iridium-Catalyzed Asymmetric Ring-Opening of *N*-Boc-Azabenzonorbornadiene 1 with *N*-Methylaniline[a]



entry	$[Ir(COD)Cl]_2$	ligand	yield[b] (%)	ee[c] (%)
1	1.0 mol %	2 mol % DPPF	71	0
2	1.5 mol %	3 mol % DPPF	86	0
3	2.0 mol %	4 mol % DPPF	83	0
4	1.5 mol %	3 mol % (*R*)-(*S*)-PPF-P^{t}Bu$_2$	10	20
5	1.5 mol %	3 mol % (*S*)-(*R*)-NMe$_2$-PPh$_2$-Mandyphos	nr	
6	1.5 mol %	3 mol % (*S*)-BINAP	56	84
7	1.5 mol %	3 mol % (*S*)-*p*-Tol-BINAP	10	70
8	1.5 mol %	3 mol % **L1**	nr	
9	1.5 mol %	1.5 mol % (*S*)-BINAP	6	43
10	1.5 mol %	4.5 mol % (*S*)-BINAP	30	62

[a]The reaction was carried out with **1** (0.21 mmol) and 3.0 equiv of *N*-methylaniline (0.63 mmol) in THF (2.0 mL) at 80 °C (oil bath temperature). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a Chiralcel AD-H column.

(15) For selected recent examples on iridium-catalyzed allylations, see: (a) Raskatov, J. A.; Spiess, S.; Gnamm, C.; Broedner, K.; Rominger, F.; Helmchen, G. *Chem.—Eur. J.* **2010**, *16*, 6601–6615. (b) Spiess, S.; Raskatov, J. A.; Gnamm, C.; Broedner, K.; Helmchen, G. *Chem.—Eur. J.* **2009**, *15*, 11087–11090. (c) Spiess, S.; Welter, C.; Franck, G.; Taquet, J.-P.; Helmchen, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7652–7655. (d) Helmchen, G.; Dahnz, A.; Duebon, P.; Schelwies, M.; Weihofen, R. *Chem. Commun.* **2007**, 675–691.

(16) (a) Cho, Y. H.; Fayol, A.; Lautens, M. *Tetrahedron: Asymmetry* **2006**, *17*, 416–427. (b) Lautens, M.; Fagnou, K.; Zunic, V. *Org. Lett.* **2002**, *4*, 3465–3468. (c) McManus, A. H.; Fleming, M. J.; Lautens, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 433–436.

(17) (a) Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580–2627. (b) Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282–2316. (c) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552–560. (d) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422. (e) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327–9343. (f) Trost, B. M.; Bunt, R. C.; Lemoine, R. C.; Calkins, T. L. *J. Am. Chem. Soc.* **2000**, *122*, 5968–5976.

(18) (a) Szmuszkovicz, J.; VonVoigtlander, P. F.; Kane, M. P. *J. Med. Chem.* **1981**, *24*, 1230–1236. (b) Cowan, A.; Gmerek, D. E. *Trends Pharmacol. Sci.* **1986**, *7*, 69–72. (c) Millan, M. J. *Trends Pharmacol. Sci.* **1990**, *11*, 70–76.

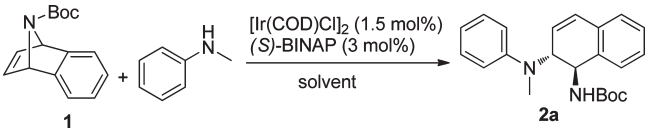
(19) (a) Xie, L.; Yang, D. Q.; Zhao, S. Q.; Wang, H.; Liang, L. H.; Luo, R. S. *Chin. Chem. Lett.* **2007**, *18*, 127–129. (b) Liu, E. C.; Yang, D. Q.; Han, Y. F.; Dong, J. X. *Chin. Chem. Lett.* **2006**, *17*, 717–719.

(20) (a) Yang, D. Q.; Long, Y. H.; Wang, H.; Zhang, Z. M. *Org. Lett.* **2008**, *10*, 4723–4726. (b) Long, Y.-H.; Zhao, S.-Q.; Zeng, H.-P.; Yang, D.-Q. *Catal. Lett.* **2010**, *138*, 124–133. (c) Long, Y.-H.; Yang, D.-Q.; Zeng, H.-P.; Xie, L.; Wu, L.-H; Mo, H.-H.; Zuo, X.-J. *Chin. J. Chem.* **2010**, *28*, 235–242.

(21) (a) Fache, F.; Schulz, E.; Tommasino, M. L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159–2232. (b) Jacobsen, E. N.; Zhang, W.; Muci, A. R.; Ecker, J. R.; Deng, L. *J. Am. Chem. Soc.* **1991**, *113*, 7063–7064. (c) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801–2803.

(22) (a) Alexander van Vliet, L.; Tepper, P. G.; Dijkstra, D.; Damsma, G.; Wikstrom, H.; Pugsley, T. A.; Akunne, H. C.; Heffner, T. G.; Glase, S. A.; Wise, L. D. *J. Med. Chem.* **1996**, *39*, 4233–4237. (b) Degnan, A. P.; Meyers, A. I. *J. Org. Chem.* **2000**, *65*, 3503–3512. (c) Marquet, A. *Pure Appl. Chem.* **1993**, *65*, 1249–1252. (d) Hettinger, T. P.; Craig, L. C. *Biochemistry* **1970**, *9*, 1224–1232. (e) Umezawa, H.; Maeda, K.; Takeuchi, T.; Okami, Y. *J. Antibiot. Ser. A* **1996**, *19*, 200–209.

TABLE 2. Condition Screening for Iridium-Catalyzed Asymmetric Ring-Opening Reaction of *N*-Boc-Azabenzonorbornadiene 1 with *N*-Methylaniline[a]



1 2a

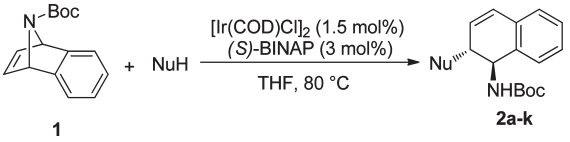
entry	solvent	additive	time (h)	yield[b] (%)	*ee*[c] (%)
1	CH_3CN		48	79	56
2	toluene		48	19	43
3	CH_2Cl_2		48	21	87
4	dioxane		48	39	61
5	THP		48	68	64
6	THF		48	56	84
7	THF[d]		48	trace	
8	THF[e]		48	52	78
9	THF	NH_4I	48	12.5	60
10	THF	NH_4Br	48	trace	
11	THF	Bu_4NI	48	78	62
12	THF	Et_3NHCl	48	13	80

[a]The reaction was carried out with **1** (0.21 mmol) and 3.0 equiv of *N*-methylaniline (0.63 mmol) in solvent (2.0 mL) at 80 °C (oil bath temperature) in the presence of $[Ir(COD)Cl]_2$ (1.5 mol %) and (*S*)-BINAP (3 mol %). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a Chiralcel AD-H column. [d]Oil bath temperature is 60 °C. [e]Oil bath temperature is 100 °C.

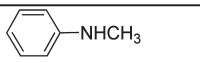
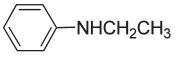
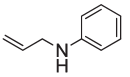
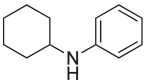
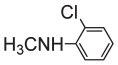
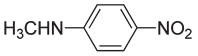
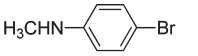
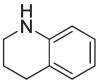
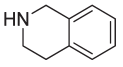
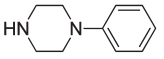
ring-opening reaction of *N*-Boc-azabenzonorbornadiene **1** with *N*-methylaniline afforded the corresponding product **2a** in a 56% yield and 84% ee in THF (Table 2, entry 6). The same reaction afforded the expected product **2a** in a 79% yield and 56% ee in CH_3CN (Table 2, entry 1). In CH_2Cl_2, the desired product **2a** was obtained only in a low yield (21%) though with a high enantioselectivity (87% ee) (Table 2, entry 3). In addition, both modest yields and enantioselectivities were obtained when other solvents such as toluene, dioxane, and THP were employed (Table 2, entries 2, 4, and 5). Temperature also plays a crucial role in this ring-opening reaction. Although a 56% yield and an 84% ee were obtained at 80 °C (Table 2, entry 6), only a trace amount of ring-opening product was obtained at 60 °C after 48 h (Table 2, entry 7). On the other hand, the reaction afforded the desired product in a lower yield and enantioselectivity when the temperature was increased to 100 °C (Table 2, entry 8). The role of ammonium halide additives was also explored. It turned out they were not necessary in this reaction (Table 2, entries 9−12).

On the basis of these studies, the asymmetric ring opening of **1** with a variety of *N*-alkylanilines and aliphatic amines was explored under the optimal reaction conditions: 1.5 mol % of $[Ir(COD)Cl]_2$ and 3 mol % of (*S*)-BINAP in THF at 80 °C. In general, *N*-alkylanilines reacted with **1** to give the corresponding products in higher yields and enantioselectivities (Table 3, entries 1−8) than substituted aliphatic amines (Table 3, entries 9−11). The substituent on the aniline nitrogen has a significant impact on both the chemical yield and enantioselectivity (Table 3, entries 1−4). Due to the steric bulkiness of the cyclohexyl group, the ring-opening reaction by *N*-cyclohexylaniline did not afford any desired product (Table 3, entry 4). A similar result was observed when 2-chloro-*N*-methylaniline was used as the nucleophile in the ring opening (Table 3, entry 5). The yields decreased in the case of 4-nitro- or 4-bromo-*N*-methylaniline nucleophiles, presumably due to the effect of the electron-withdrawing substitutents (Table 3, entries 6 and 7).

TABLE 3. Iridium-Catalyzed Asymmetric Ring-Opening of 1 with Secondary Amine Nucleophiles[a]



1 2a-k

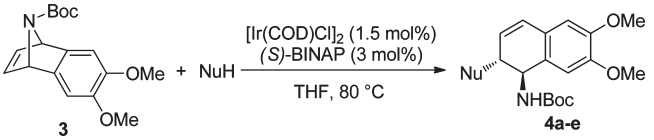
entry	NuH	time (h)	product	yield[b] (%)	ee[c] (%)
1		48	**2a**	56	84
2		48	**2b**	45	76
3		48	**2c**	28	69
4		60	**2d**	--	--
5		48	**2e**	--	--
6		48	**2f**	25	61
7		48	**2g**	29	65
8		24	**2h**	65	75
9[d]		48	**2i**	29	64
10[d]		48	**2j**	12	19
11		24	**2k**	40	37

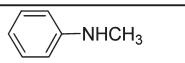
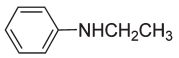
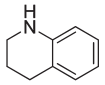
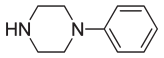
[a]The reaction was carried out with **1** (0.21 mmol) and 3.0 equiv of amine (0.63 mmol) in THF (2 mL) at 80 °C (oil bath temperature) in the presence of $[Ir(COD)Cl]_2$ (1.5 mol %) and (*S*)-BINAP (3 mol %). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a chiral stationary column (Chiralcel AD-H column for **2a**, **2b**, **2c, 2f**, and **2g**; Chiralcel OD-H column for **2h**, **2i**, **2j**, and **2k**). [d]The reaction solvent is THP at 100 °C (oil bath temperature).

In order to extend the scope of this reaction to other substrates, we then examined the ring opening of 6,7-dimethoxy-*N*-Boc-azabenzonorbornadiene (**3**) by amines. An obvious increase in terms of enantioselectivity was observed when *N*-methylaniline instead of *N*-ethylaniline was used as the nucleophile (Table 4, entries 1 and 2). Only moderate enantioselectivities were obtained when secondary aliphatic amines such as 1,2,3,4-tetrahydroquinoline and 1-phenylpiperazine were employed (Table 4, entries 3 and 4). No ring-opening product of substrate **3** was observed when piperidine was used as the nucleophile (Table 4, entry 5).

The asymmetric ring-opening reactions of *N*-Ts-azabenzonorbornadiene **5** with secondary amines were also investigated. It was known that these ring-opening reactions afforded the products in high yield (90%) but low enantioselectivity (10% ee) in the presence of a rhodium catalyst

TABLE 4. Iridium-Catalyzed Asymmetric Ring Opening of 3 with Secondary Amine Nucleophiles[a]



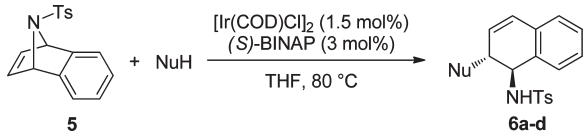
entry	NuH	time (h)	product	yield[b] (%)	*ee*[c] (%)
1		36	**4a**	55	83
2		48	**4b**	45	53
3		48	**4c**	58	44
4[d]		60	**4d**	32	59
5[d]		48	**4e**	--	--

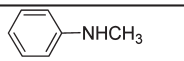
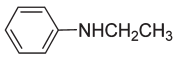
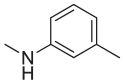
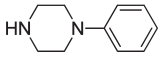
[a]The reaction was carried out with **3** (0.20 mmol) and 3.0 equiv of amine (0.60 mmol) in THF (2 mL) at 80 °C (oil bath temperature) in the presence of $[Ir(COD)Cl]_2$ (1.5 mol %) and (*S*)-BINAP (3 mol %). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a chiral stationary column (Chiralcel AD-H column for **4a**; Chiralcel OD-H column for **4b**, **4c** and **4d**). [d]The reaction solvent is THP at 100 °C (oil bath temperature).

system.[10] To our delight, the ring opening of **5** with *N*-methylaniline afforded the corresponding product **6a** not only in a high yield (92%) but also in a higher enantioselectivity (70% *ee*) in the presence of 1.5 mol % of $[Ir(COD)Cl]_2$ and 3 mol % of (*S*)-BINAP (Table 5, entry 1). The enantioselectivity is even better when *N*-ethylaniline is used as the nucleophile compared to *N*-methylaniline though with a slightly lower yield (Table 5, entry 2). The best results of 88% yield and 86% ee were obtained when 3-methyl-*N*-methylaniline was used as the nucleophile (Table 5, entry 3). However, the reaction with an aliphatic amine nucleophile, *N*-phenylpiperazine, did not afford any ring-opening product (Table 5, entry 4).

Both aniline and 1-aminonaphthalene proved to be efficient nucleophiles in the rhodiun-catalyzed asymmetric ring-opening reaction of azabicyclic alkenes.[10] This encouraged us to screen primary aromatic amine nucleophiles, as well. The results summarized in Table 6 show that the nature of the substituent group on the nitrogen in the azabicyclic alkene substrate plays a significant role in the enantioselectivity of the products. For example, the ee value of the products decreased when a Boc group was present in substrate **1**, while the presence of a Ts group in substrate **5** enhanced the ee value (Table 6, entries 2 and 3). It was observed that both the substituted groups on nitrogen of the azabicyclic alkenes and the electronic effect of nucleophiles were found to have remarkable impacts on the enantioselectivity of the ring-opening reaction. Nucleophiles with electron-rich functional groups on the benzene ring such as 2,4-dimethoxyaniline and 4-propylaniline gave moderate yields with excellent enantioselectivities (up to 97% ee) (Table 6, entries 4 and 5). On the other hand, when a slightly electron-withdrawing Br group was present on the aniline benzene ring, both chemical yield and enantioselectivity decreased dramatically (Table 6, entry 6).

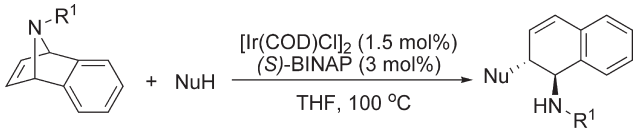
TABLE 5. Iridium-Catalyzed Asymmetric Ring-Opening of 5 with Secondary Amine Nucleophiles[a]



entry	NuH	time (h)	product	yield[b] (%)	ee[c] (%)
1		36	**6a**	92	70
2		48	**6b**	79	80
3		48	**6c**	88	86
4		48	**6d**	nr	--

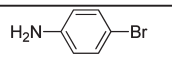
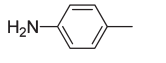
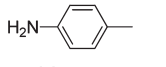
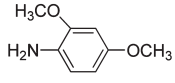
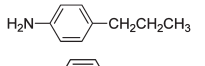
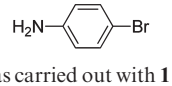
[a]The reaction was carried out with **5** (0.20 mmol) and 3.0 equiv of amine (0.60 mmol) in THF (2.0 mL) at 80 °C (oil bath temperature) in the presence of $[Ir(COD)Cl]_2$ (1.5 mol %) and (*S*)-BINAP (3 mol %). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a chiral stationary column (Chiralcel AD-H column for **6c**; Chiralcel OD-H column for **6a** and **6b**).

TABLE 6. Iridium-Catalyzed Asymmetric Ring-Opening of Azabicyclic Alkenes with Primary Aromatic Amine Nucleophiles[a]



1: R^1 = Boc
5: R^1 = Ts

2l-m
6e-h

entry	substrate	NuH	time (h)	product	yield[b] (%)	*ee*[c] (%)
1	**1**		24	**2l**	79	83
2	**1**		24	**2m**	58	86
3	**5**		14	**6e**	96	94
4	**5**		22	**6f**	58	97
5	**5**		23	**6g**	72	94
6	**5**		10	**6h**	22	22

[a]The reaction was carried out with **1** or **5** (0.20 mmol) and 3.0 equiv of amine (0.60 mmol) in THF (2.0 mL) at 100 °C (oil bath temperature) in the presence of $[Ir(COD)Cl]_2$ (1.5 mol %) and (*S*)-BINAP (3 mol %). [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC with a chiral stationary column (Chiralcel AD-H column for **2l**, **6f**, **6g**, and **6h**; Chiralcel OD-H column for **2m** and **6e**).

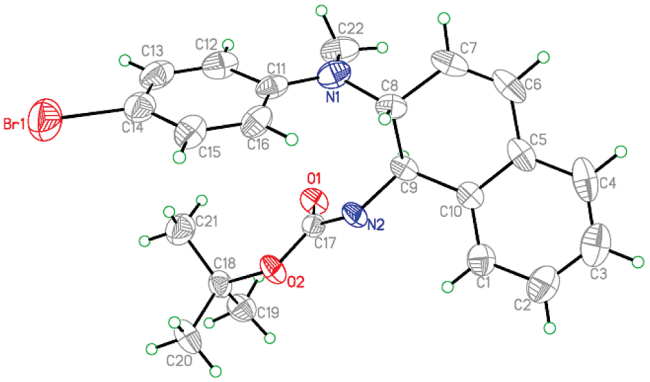
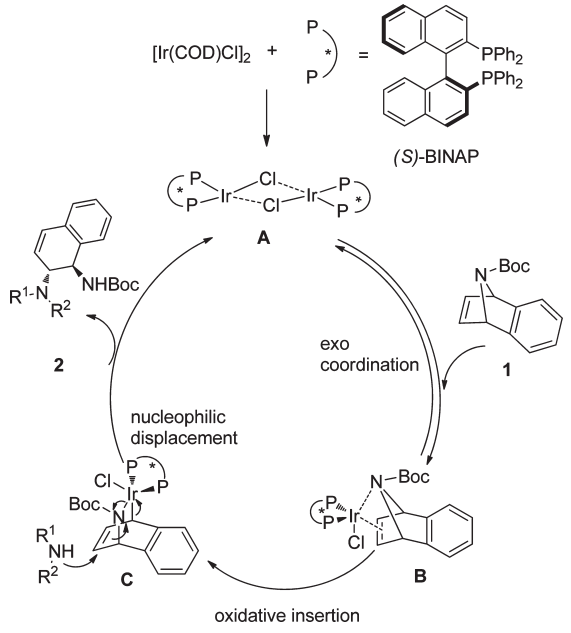


FIGURE 1. ORTEP plot for **2g**.

SCHEME 1. Working Hypothesis for the Asymmetric Ring Opening of *N*-Boc-Azabenzonorbornadiene 1 with a Secondary Amine Nucleophile



The absolute configuration of ring-opened product **2g** was demonstrated by X-ray crystallography. The single crystal was obtained by solvent evaporation from a solution consisting of dichloromethane, petroleum ether, and ethyl acetate. Its configuration was assigned as (1*R*,2*R*) and confirmed as 1,2-*trans*-configuration, as shown in Figure 1. It is obvious that the reaction favors the formation of *trans*-1,2-diamino products.

On the basis of our studies, a working hypothesis is shown in Scheme 1. First, the chiral dimeric iridium complex **A** is formed. The nitrogen atom and the double bond of *N*-Boc-azabenzonorbornadiene **1** are then reversibly coordinated to the iridium center of the catalyst to give the intermediate **B**. In this step, the intermediate **B** containing a larger Boc group is less stable than the counterpart containing a relatively smaller Ts group. Insertion of the iridium into the C−N bond of **B** forms **C**. Nucleophilic attack of **C** by an amine nucleophile occurs in an S_N2' displacement of the iridium catalyst with an inversion of configuration. Electron-rich amine nucleophiles are beneficial for the nucleophilic attack. The *trans*-1,2-diamino product **2** is subsequently released and the iridium complex **A** is regenerated.

Conclusions

We have developed an asymmetric ring-opening reaction of N-subsitituted azabicyclic alkenes by a number of primary and secondary amine nucleophiles in the presence of $[Ir(COD)Cl]_2$/(*S*)-BINAP catalyst. It provides an efficient and practical access to the optically active 1,2-diamine derivatives in moderate to good yields and enantioselectivities under mild conditions. Our results further reveal that the nature of the chiral ligand has a significant impact on this ring-opening reaction. The new method is significant in terms of the low cost for the ligands and facile manipulation compared to literature precedents. An investigation on the biological and pharmaceutical activities of the products is in progress. Studies on further expansion of the scope and synthetic utility of this Ir-catalyzed reaction are also being pursued in our laboratory.

Experimental Section

General. THF, THP, dioxane, and toluene were distilled from sodium benzophenone ketyl immediately prior to use. CH_3CN and CH_2Cl_2 were distilled from calcium hydride. Azabenzonorbornadienes **1**,[20a] **3**,[7] **5**,[16b] and $[Ir(COD)Cl]_2$[20a] were prepared according to the reported procedures. All flasks were flame-dried under a stream of nitrogen and cooled to room temperature before use. Solvents and solutions were transferred with syringes and cannulae using standard inert atmosphere techniques. All ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $CDCl_3$ as a solvent. The chemical shifts of all ^1H and ^{13}C NMR spectra are referenced to the residual signal of $CDCl_3$ (δ 7.27 ppm for the ^1H NMR spectra and δ 77.23 ppm for the ^{13}C NMR spectra). Spectral features are tabulated in the following order: chemical shift (δ, ppm); multiplicity (s-singlet, d-doublet, t-triplet, q-quadruplet, m-complex multiplet, br-broad); coupling constants (*J*, Hz); number of protons. IR spectra were obtained using a KBr pellet or using a neat film on a NaCl plate. MS spectra were recorded using ESI. The melting points are uncorrected.

General Procedure (I) for the Asymmetric Ring-Opening Reactions of *N*-Boc-Azabenzonorbornadiene 1 with Secondary Amine Nucleophiles. A 5 mL round-bottom flask fitted with a reflux condenser was flame-dried under a stream of nitrogen and cooled to room temperature. $[Ir(COD)Cl]_2$ (2.1 mg, 1.5 mol %) and (*S*)-BINAP (3.9 mg, 3 mol %) were added, followed by the addition of anhydrous THF (2.0 mL). After the mixture was stirred for 10 min at room temperature, *N*-Boc-azabenzonorbornadiene **1** (50 mg, 0.21 mmol) was added and the temperature of the oil bath was increased to 80 °C. On the first sign of reflux, nucleophile (3−5 equiv to **1**) was added. The reaction was stirred at 80 °C until completion as monitored by thin layer chromatography. After the reaction mixture was cooled to room temperature, the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (200−300 mesh) to give the desired product.

(1*R*,2*R*)-[2-(Methylphenylamino)-1,2-dihydronaphthalen-1-yl]-carbamic acid *tert*-butyl ester (2a). Following the general procedure (I), **2a** was obtained as a white solid (40.2 mg, 56%): R_f = 0.24 on silica gel (ethyl acetate/petroleum ether = 1:20, v/v); mp 160−161 °C; ee was determined to be 84% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 11.4 min (minor) and 12.5 min (major); $[\alpha]^{20}_D$ = −31.8 (*c* = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3380(s), 3063(w), 2976(w), 2819(w), 1688(s), 1575 (s), 1525(m), 1406(m), 1178(s), 1050(w), 745(m); ^1H NMR (400 MHz, $CDCl_3$)

δ 7.34 (d, J = 6.4 Hz, 1H), 7.21 (t, J = 7.6 Hz, 3H), 7.10 (d, J = 5.2 Hz, 1H), 6.85 (d, J = 7.6 Hz, 2H), 6.72 (t, J = 6.0 Hz, 1H), 6.61 (d, J = 5.2 Hz, 1H), 5.93 (d, J = 9.6 Hz, 1H), 5.20 (t, J = 10.0 Hz, 1H), 4.79 (d, J = 10.0 Hz, 1H), 4.51 (d, J = 9.2 Hz, 1H), 2.83 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 150.1, 135.8, 130.0, 129.1, 128.0, 127.9, 126.6, 125.8, 121.0, 117.1, 114.8, 113.6, 79.5, 60.7, 52.4, 33.0, 28.3; MS (ESI) calcd m/z for $C_{22}H_{26}N_2O_2$ (M^+) 350.20, found 351.03 $(M + H)^+$. Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.69; H, 7.20; N, 8.23.

(1*R*,2*R*)- [2-(Ethylphenylamino)-1,2-dihydronaphthalen-1-yl]-carbamic acid *tert*-butyl ester (2b). Following the general procedure (I), **2b** was obtained as a white solid (34.4 mg, 45%): R_f = 0.19 on silica gel (ethyl acetate/petroleum ether = 1:25, v/v); mp 128−129 °C; ee was determined to be 76% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 95/5, 0.5 mL/min, λ = 254 nm); retention times were 14.4 min (minor) and 21.3 min (major); $[\alpha]^{20}_D$ = −56.5 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3355(w), 3248(w), 2975 (w), 2927(w), 1696(s), 1596(s), 1505(s), 1365(m), 1249(w), 1116(s), 987(m), 781(w), 745(m), 642(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 6.8 Hz, 1H), 7.26 (t, J = 8. 0 Hz, 3H), 7.13 (d, J = 6.4 Hz, 1H), 6.91 (d, J = 8.4 Hz, 2H), 6.75 (t, J = 7.2 Hz, 1H), 6.65 (dd, J = 11.6 Hz, 8.0 Hz, 1H), 6.00 (dd, J = 12.0 Hz, 6.8 Hz, 1H), 5.20 (t, J = 9.2 Hz, 1H), 4.74 (d, J = 8.4 Hz, 1H), 4.63 (d, J = 8.8 Hz, 1H), 3.32 (q, 2H), 1.43 (s, 9H), 1.11 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 148.3, 135.5, 132.6, 130.2, 129.2, 128.8, 128.1, 128.0, 126.8, 125.9, 121.7, 116.9, 114.7, 79.6, 61.0, 33.2, 28.3, 13.9; MS (ESI) calcd m/z for $C_{23}H_{28}N_2O_2$ (M^+) 364.22, found 364.97. Anal. Calcd for $C_{23}H_{28}N_2O_2$: C, 75.79; H, 7.74; N, 7.69. Found: C, 75.69; H, 7.71; N, 7.92.

(1*R*,2*R*)-[2-(Allylphenylamino)-1,2-dihydronaphthalen-1-yl]-carbamic acid *tert*-butyl ester (2c). Following the general procedure (I), **2c** was obtained as a white solid (22.2 mg, 28%): R_f = 0.19 on silica gel (ethyl acetate/petroleum ether = 1:25, v/v); mp 111−113 °C; ee was determined to be 69% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 95/5, 0.5 mL/min, λ = 254 nm); retention times were 14.7 min (minor) and 18.9 min (major); $[\alpha]^{20}_D$ = −56.1 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3356(w), 2975(m), 2927(m), 1709(s), 1597(m), 1503(m), 1456(w), 1367(s), 1332(s), 1252(s), 1168(s), 1074(m), 858(w), 782(w), 747(m), 694(w), 542(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 7.2 Hz, 1H), 7.27−7.18 (m, 3H), 7.11 (d, J = 6.4 Hz, 1H), 6.88 (d, J = 7.6 Hz, 2H), 6.72 (t, J = 7.0 Hz, 1H), 6.61 (d, J = 9.6 Hz, 1H), 5.98 (d, J = 9.2 Hz, 1H), 5.78−5.73 (m, 1H), 5.16 (d, J = 8.4 Hz, 1H), 5.12 (d, J = 6.0 Hz, 1H), 5.07 (d, J = 10.0 Hz, 1H), 4.81 (d, J = 6.4 Hz, 1H), 4.58 (d, J = 6.8 Hz, 1H), 3.84 (s, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 148.4, 135.7, 135.4, 132.5, 130.0, 129.0, 128.7, 128.1, 128.0, 126.7, 124.8, 117.1, 115.7, 114.2, 79.5, 59.7, 52.3, 29.7, 28.3; MS (ESI) calcd m/z for $C_{24}H_{28}N_2O_2$ (M^+) 376.22, found 399.24 $(M + Na)^+$. Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.69; H, 7.80; N, 7.23.

(1*R*,2*R*)-{2-[Methyl-(4-nitrophenyl)amino]-1,2-dihydronaphthalen-1-yl}carbamic acid *tert*-butyl ester (2f). Following the general procedure (I), **2f** was obtained as a yellow solid (20.7 mg, 25%): R_f = 0.39 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 151−152 °C; ee was determined to be 61% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 30.4 min (minor) and 36.5 min (major); $[\alpha]^{20}_D$ = −124.3 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3353(m), 3065(w), 2976(w), 2920(w), 1686(s), 1595(s), 1510(s), 1392(m), 1366(w), 1316(s), 1166(m), 1104(m), 1008(w), 938(w), 825(w), 784(m), 751(m), 616(w), 562(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 2H), 7.34 (d, J = 7.2 Hz, 1H), 7.29−7.22 (m, 1H), 7.13 (d, J = 6.8 Hz, 1H), 6.81 (d, J = 7.6 Hz, 2H), 6.67 (d, J = 9.6 Hz, 1H), 5.85 (d, J = 10.0 Hz, 1H), 5.17 (t, J = 9.6 Hz, 1H), 4.97 (d, J = 9.2 Hz, 1H), 4.62 (d, J=9.2 Hz, 1H), 2.95 (s, 3H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 154.4, 137.3, 134.3, 132.3, 131.0, 128.5, 128.4, 127.3, 127.1, 126.3, 126.0, 111.2, 79.9, 60.5, 52.3, 33.8, 28.2; MS (ESI) calcd m/z for $C_{22}H_{25}N_3O_4$ (M^+) 395.18, found 418.24 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{25}N_3O_4$: C, 66.82; H, 6.37; N, 10.63. Found: C, 66.69; H, 6.20; N, 10.33.

(1*R*,2*R*)-{2-[(4-Bromophenyl)methylamino]-1,2-dihydronaphthalen-1-yl}carbamic acid *tert*-butyl ester (2g). Following the general procedure (I), **2g** was obtained as a white solid (25.6 mg, 29%): R_f = 0.16 on silica gel (ethyl acetate/petroleum ether = 1:25, v/v); mp 179−181 °C; ee was determined to be 65% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 10.6 min (minor) and 11.6 min (major)l $[\alpha]^{20}_D$ = −78.3 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3374(m), 3043(m), 2963(m), 2920(w), 1682(s), 1520 (s), 1495(s), 1366(m), 1108(m), 783(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.21 (m, 4H), 7.11 (d, J = 6.0 Hz 1H), 6.73 (d, J = 8.8 Hz, 2H), 6.61 (dd, J = 12.0 Hz, 7.6 Hz, 1H), 5.87 (dd, J = 12.4 Hz, 6.8 Hz, 1H), 5.16 (t, J = 9.6 Hz, 1H), 4.67 (d, J = 9.6 Hz, 1H), 4.52 (d, J = 8.8 Hz, 1H), 2.78 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 149.0, 135.4, 132.6, 131.7, 130.2, 129.0, 128.1, 128.0, 126.8, 125.9, 115.1, 108.8, 79.6, 60.8, 52.2, 33.2, 28.2; MS (ESI) calcd m/z for $C_{22}H_{25}BrN_2O_2$ (M^+) 428.11, found 429.03 $(M + H)^+$. Anal. Calcd for $C_{22}H_{25}BrN_2O_2$: C, 61.54; H, 5.87; N, 6.52. Found: C, 61.23; H, 5.62; N, 6.86.

(1*R*,2*R*)-[2-(3,4-Dihydro-2*H*-quinolin-1-yl)-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (2h). Following the general procedure (I), **2h** was obtained as a white solid (51.4 mg, 65%): R_f = 0.25 on silica gel (ethyl acetate/petroleum ether = 1:25, v/v); mp 120−121 °C; ee was determined to be 75% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 9.5 min (major) and 12.8 min (minor); $[\alpha]^{20}_D$ = −56.4 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3372(s), 2927(w), 1688(w), 2898(m), 1600(w), 1499(m), 1365(w), 1301(w), 1250(w), 1169(m), 1048(w), 783(w), 742(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 6.4 Hz, 1H), 7.24−7.21 (m, 1H), 7.10 (d, J = 6.8 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 7.2 Hz, 1H), 6.78 (d, J = 8.0 Hz, 1H), 6.63−6.56 (m, 2H), 5.91 (d, J = 9.6 Hz, 1H), 5.28 (t, J = 9.8 Hz, 1H), 4.80 (d, J = 9.6 Hz, 1H), 4.62 (s, 1H), 3.22 (s, 2H), 2.72 (t, J = 6.4 Hz, 2H), 1.94−1.80 (m, 2H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 145.4, 136.0, 132.8, 130.1, 129.5, 128.0, 127.8, 126.9, 126.6, 126.3, 125.9, 123.6, 116.1, 111.2, 79.5, 58.3, 51.7, 43.5, 28.3, 28.2, 22.3; MS (ESI) calcd m/z for $C_{24}H_{28}N_2O_2$ (M^+) 376.22, found 399.33 $(M + Na)^+$; Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.31; H, 7.18; N, 7.63.

(1*R*,2*R*)-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (2i). Following the general procedure (I), **2i** was obtained as colorless oil (22.9 mg, 29%): R_f = 0.37 on silica gel (ethyl acetate/petroleum ether = 1:6, v/v); ee was determined to be 64% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 10.2 min (major) and 12.5 min (minor); $[\alpha]^{20}_D$ = −84.5 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3346(m), 3065(m), 2976 (m), 2926(m), 2803(w), 1707(s), 1496(s), 1453(m), 1365(m), 1248(m), 1167(s), 1093(w), 1044(w), 1022(w), 934(w), 780(w), 741(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 7.2 Hz, 1H), 7.28−7.21 (m, 1H), 7.12 (d, J = 6.8 Hz, 1H), 7.05 (d, J = 7.2 Hz, 3H), 6.94 (d, J = 6.8 Hz, 1H), 6.68 (d, J = 9.6 Hz,1H), 6.30 (dd, J = 12.8 Hz, 5.2 Hz, 1H), 5.10 (br s, 1H), 4.65 (dd, J = 10.0 Hz, 2.0 Hz, 1H), 3.90 (d, J=14.8 Hz, 1H), 3.73 (d, J = 15.2 Hz, 1H), 3.60 (t, J = 4.8 Hz, 1H), 2.87−2.80 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 135.3, 135.2, 134.5, 132.4, 129.7, 128.7, 128.3, 128.1, 127.7, 126.8, 126.6, 125.8, 125.8, 125.4, 79.5, 63.5, 51.4, 48.5, 46.6, 29.9, 28.4; MS (ESI) calcd m/z for $C_{24}H_{28}N_2O_2$ (M^+) 376.22, found 399.03 $(M + Na)^+$. Anal. Calcd for $C_{24}H_{28}N_2O_2$: C, 76.56; H, 7.50; N, 7.44. Found: C, 76.69; H, 7.20; N, 7.63.

(1*R*,2*R*)-(2-Piperidin-1-yl-1,2-dihydronaphthalen-1-yl)carbamic acid *tert*-butyl ester (2j). Following the general procedure (I), **2j** was obtained as a white solid (8.3 mg, 12%): R_f = 0.31 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 115−118 °C; ee was determined to be 19% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 7.4 min (major) and 7.7 min (minor); $[\alpha]^{20}_D$ = −44.9 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3353(m), 2930 (s), 2854(w), 1714(s), 1494 (s), 1366(w), 1305(w), 1248(m), 1172(s), 745(m), 1119(w), 1045(w), 861(w), 779(w), 745(w), 613(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.13 (m, 2H), 7.02−6.99 (m, 1H), 6.56 (dd, J = 10.8 Hz, 8.8 Hz, 1H), 5.92 (dd, J = 14.4 Hz, 4.8 Hz, 1H), 4.96 (br s, 1H), 4.53 (br s, 1H), 3.32−3.29 (m, 1H), 2.57−2.49 (m, 2H), 2.39−2.34 (m, 2H),1.45−1.41 (m, 4H), 1.38 (s, 9H), 1.33−1.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 135.6, 132.4, 129.2, 128.1, 127.9, 127.7, 126.6, 126.1, 64.7, 49.9, 48.0, 29.7, 28.4, 26.4, 24.5; MS (ESI) calcd m/z for $C_{20}H_{28}N_2O_2$ (M^+) 328.22, found 329.24 $(M + H)^+$; Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.14; H, 8.59; N, 8.53. Found: C, 73.49; H, 8.30; N, 8.23.

(1*R*,2*R*)-[2-(4-Phenylpiperazin-1-yl)-1,2-dihydronaphthalen-1-yl]-carbamic acid *tert*-butyl ester (2k). Following the general procedure (I), **2k** was obtained as a white solid (35.2 mg, 40%): R_f = 0.36 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 164−165 °C; ee was determined to be 37% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 13.7 min (major) and 15.0 min (minor); $[\alpha]^{20}_D$ = −80.2 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3333(s), 3036(w), 2963(m), 2824(m), 1679(s), 1601(m), 1497(m), 1368(m), 1231(m), 1173(s), 758(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, J = 7.6 Hz, 1H), 7.27−7.20 (m, 3H), 7.11−7.09 (m, 1H), 6.86 (d, J = 8.0 Hz, 2H), 6.82 (t, J = 7.2 Hz, 1H), 6.67 (d, J = 10.0 Hz, 1H), 6.01 (dd, J = 7.2 Hz, 4.8 Hz, 1H), 5.06 (br s, 1H), 4.62 (br d, J = 6.8 Hz, 1H), 3.48 (t, J = 4.4 Hz, 1H), 3.11 (t, J = 4.8 Hz, 4H), 2.83−2.77 (m, 2H), 2.71−2.68 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 151.6, 135.5, 132.6, 129.9, 129.2, 128.5, 128.3, 128.0, 126.9, 125.6, 119.7, 116.3, 79.7, 64.1, 49.8, 48.9, 29.7, 28.4; MS (ESI) calcd m/z for $C_{25}H_{31}N_3O_2$ (M^+) 405.24, found 406.12 $(M + H)^+$. Anal. Calcd for $C_{25}H_{31}N_3O_2$: C, 74.04; H, 7.70; N, 10.36. Found: C, 74.09; H, 8.00; N, 10.47.

(1*R*,2*R*)-[2-(4-Bromophenylamino)-1,2-dihydronaphthalen-1-yl]-carbamic acid *tert*-butyl ester (2l). Following the general procedure (I), **2l** was obtained as a white solid (65.6 mg, 79%): R_f = 0.31 on silica gel (ethyl acetate/petroleum ether = 1:8, v/v); mp 93−95 °C; ee was determined to be 83% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 16.6 min (major) and 31.2 min (minor); $[\alpha]^{20}_D$ = −132.1 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3398(w), 2976(w), 1702(s), 1593(m), 1496(s), 1453(w), 1367(w), 1319(w), 1248(m), 1168(s), 814(m), 782(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.19 (m, 4H), 7.12 (d, J = 7.2 Hz, 1H), 6.58 (q, J = 7.2 Hz, 3H), 6.03 (q, J = 5.2 Hz, 1H), 4.97 (t, J = 6.8 Hz, 1H), 4.68 (d, J = 8.4 Hz, 1H), 4.21 (s 1H), 3.85 (s, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 145.8, 133.6, 132.3, 132.1, 128.9, 128.6, 128.4, 128.1, 127.8, 127.0, 114,8, 109.1, 80.0, 53.4, 52.1, 28.4; MS (ESI) calcd m/z for $C_{21}H_{23}BrN_2O_2$ (M^+) 415.32, found 416.94 $(M + H)^+$. Anal. Calcd for $C_{21}H_{23}BrN_2O_2$: C, 60.73; H, 5.58; N, 6.74. Found: C, 60.42; H, 5.72; N, 6.32.

(1*R*,2*R*)-[2-(*p*-Toluidino)-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (2m). Following the general procedure (I), **2m** was obtained as a white solid (40.6 mg, 58%): R_f = 0.38 on silica gel (ethyl acetate/petroleum ether = 1:8, v/v); mp 80−82 °C; ee was determined to be 86% using HPLC analysis on a Chiralcel OD column (hexane/2-propanol=90/10, 0.5 mL/min, λ=254 nm); retention times were 10.1 min (major) and 12.3 min (minor); $[\alpha]^{20}_D$ = −24.5 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3386(w), 2976(w), 1706(s), 1616(w), 1519(s), 1366(w), 1299(w), 1245(w), 1166(s), 808(m), 782(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.23 (m, 2H), 7.16 (d, J = 7.2 Hz, 1H), 7.04 (d, J = 7.6 Hz, 2H), 6.67 (d, J = 7.6 Hz, 2H), 6.57 (d, J = 9.2 Hz, 1H), 6.11 (dd, J = 4.4 Hz, 5.2 Hz, 1H), 5.08 (t, J = 7.2 Hz, 1H), 4.87 (d, J = 8.8 Hz, 1H), 4.27 (s, 1H), 3.75 (s, 1H), 2.29 (s, 3H), 1.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 145.8, 133.6, 132.3, 132.1, 128.9, 128.6, 128.4, 128.1, 127.8, 127.0, 114.8, 109.1, 80.0, 53.4, 52.1, 28.4; MS (ESI) calcd m/z for $C_{22}H_{26}N_2O_2$ (M^+) 350.45, found 373.27 $(M + Na)^+$. Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.09; H, 7.88; N, 7.47.

General Procedure (II) for the Asymmetric Ring-Opening Reactions of *N*-Boc-6,7-dimethoxy Azabenzonorbornadiene 3 with Secondary Amine Nucleophiles. A 5 mL round-bottom flask fitted with a reflux condenser was flame-dried under a stream of nitrogen and cooled to room temperature. $[Ir(COD)Cl]_2$ (2.0 mg, 1.5 mol %) and (*S*)-BINAP (3.7 mg, 3 mol %) were simultaneously added and followed by the addition of anhydrous THF (2 mL). After the reaction mixture was stirred for 10 min at room temperature, *N*-Boc-6,7-dimethoxy azabenzonorbornadiene **3** (60 mg, 0.20 mmol) was added and the temperature of the oil bath was increased to 80 °C. On the first sign of reflux, nucleophile (3−5 equiv to **3**) was added. The reaction was stirred at 80 °C until completion as monitored by thin layer chromatography. After the reaction mixture was cooled to room temperature, the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (200−300 mesh) to give the desired product.

(1*R*,2*R*)-[6,7-Dimethoxy-2-(methylphenylamino)-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (4a). Following the general procedure (II), **4a** was obtained as a white solid (45.1 mg, 55%): R_f = 0.37 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 137−140 °C; ee was determined to be 83% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm); retention times were 25.2 min (minor) and 28.1 min (major); $[\alpha]^{20}_D$ = −49.3 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3369(m), 3069(w), 2971(m), 2972(m), 1717(s), 1595(m), 1506(s), 1385(m), 1278(m), 1161(m), 1100(m), 944(m), 908(m), 866(m), 742(m), 575(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.21 (m, 1H), 6.89 (d, J = 8.8 Hz, 3H), 6.73 (t, J = 7.2 Hz, 1H), 6.66 (s, 1H), 6.57 (dd, J = 1.6 Hz, 1.2 Hz, 1H), 5.84 (dd, J = 13.6 Hz, 6.0 Hz, 1H), 5.07 (t, J = 8.8 Hz, 1H), 4.71 (d, J = 7.6 Hz, 1H), 4.55 (d, J = 8.4 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.76 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 149.9, 148.6, 148.4, 129.7, 129.1, 128.3, 126.6, 125.4, 124.1, 117.1, 113.7, 110.3, 79.5, 60.2, 56.0, 56.0, 52.0, 33.0, 28.2; MS (ESI) calcd m/z for $C_{24}H_{30}N_2O_4$ (M^+) 410.22, found 433.27 $(M + Na)^+$. Anal. Calcd for $C_{24}H_{30}N_2O_4$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.60; H, 7.60; N, 6.79.

(1*R*,2*R*)-[2-(Ethylphenylamino)-6,7-dimethoxy-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (4b). Following the general procedure (II), **4b** was obtained as a white solid (38.2 mg, 45%): R_f = 0.29 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 130−135 °C; ee was determined to be 53% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 98/2, 1.0 mL/min, λ = 254 nm); retention times were 26.2 min (major) and 28.4 min (minor); $[\alpha]^{20}_D$ = −59.7 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3347(w), 3046(w), 2971(w), 29279(w), 1709(s), 1062(m), 1502(s), 1371(w), 1256(s), 1159(s), 1085(m), 988(m), 840(m), 746(m), 688(m), 515(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 7.2 Hz, 2H), 6.86 (s, 1H), 6.72 (t, J = 6.8 Hz, 1H), 6.66 (s, 1H), 6.57 (d, J = 9.6 Hz, 1H), 5.85 (dd, J = 12.8 Hz, 6.0 Hz, 1H), 5.01 (t, J = 8.2 Hz, 1H), 4.60 (br s, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.21 (q, 2H), 1.41 (s, 9H), 1.03 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 149.5, 148.6, 148.5, 130.1, 129.2, 128.3, 126.2, 125.2, 124.1, 116.8, 114.0, 110.8, 80.5, 59.5, 56.0, 56.0, 51.9, 39.9, 28.3, 14.1; MS (ESI) calcd m/z for $C_{25}H_{32}N_2O_4$ (M^+) 424.24, found 447.26 $(M + Na)^+$. Anal. Calcd for $C_{25}H_{32}N_2O_4$: C, 70.73; H, 7.60; N, 6.60. Found: C, 70.93; H, 7.50; N, 6.43.

(1*R*,2*R*)-[2-(3,4-Dihydro-2*H*-quinolin-1-yl)-6,7-dimethoxy-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (4c). Following the general procedure (II), **4c** was obtained as a white solid (50.6 mg, 58%): R_f = 0.3 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 140−145 °C; ee was determined to be 44% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 18.3 min (major) and 25.0 min (minor); $[\alpha]^{20}_D$ = −72.2 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3363(m), 2971(m), 2932(m), 2833(w), 1710(s), 1600(m), 1504(s), 1455(m), 1390(w), 1366(w), 1274(m), 1227(w), 1160(m), 1108(w), 1015(w), 867(w), 742(m), 604(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (d, J = 7.2 Hz, 1H), 6.87 (t, J = 8.6 Hz, 2H), 6.66 (s, 1H), 6.61−6.55 (m, 2H), 5.82 (dd, J = 12.8 Hz, 6.0 Hz, 1H), 5.12 (q, 1H), 4.72 (dd, J = 36.0 Hz, 21.2 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H),3.22−3.17 (m, 1H), 3.07 (s, 1H), 2.72 (t, J = 6.4 Hz, 2H), 1.87−1.78 (m, 2H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 148.5, 148.4, 145.2, 129.8, 129.5, 128.5, 127.0, 126.2, 125.5, 123.7, 116.1, 111.3, 110.3, 110.2, 79.5, 57.9, 56.0, 56.0, 51.4, 43.3, 28.3, 28.2, 22.4; MS (ESI) calcd m/z for $C_{26}H_{32}N_2O_4$ (M^+) 436.24, found 459.35 (M + Na)$^+$. Anal. Calcd for $C_{26}H_{32}N_2O_4$: C, 71.53; H, 7.39; N, 6.42. Found: C, 71.22; H, 7.60; N, 6.49.

(1*R*,2*R*)-[6,7-Dimethoxy-2-(4-phenylpiperazin-1-yl)-1,2-dihydronaphthalen-1-yl]carbamic acid *tert*-butyl ester (4d). Following the general procedure (II), **4d** was obtained as a white solid (29.8 mg, 32%): R_f = 0.29 on silica gel (ethyl acetate/petroleum ether = 1:3, v/v); mp 184−185 °C; ee was determined to be 56% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 19.0 min (minor) and 25.9 min (major); $[\alpha]^{20}_D$ = −37.1 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3347(m), 2928(m), 2826(w), 1702(s), 1599(s), 1501(s), 1446(m), 1309(w), 1232(s), 1164(m), 993(m), 758(m), 593(m), 605(w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.18 (m, 2H), 6.84 (d, J = 8.4 Hz, 3H), 6.80 (t, J = 7.4 Hz, 1H), 6.62 (s, 1H), 6.58 (d, J = 10.0 Hz, 1H), 5.85 (dd, J = 14.4 Hz, 4.4 Hz, 1H), 4.94 (br s, 1H), 4.58 (br s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.41 (s, 1 H), 3.08 (d, J = 4.4 Hz, 4H), 2.79 (t, J = 10.8 Hz, 2H), 2.62 (t, J = 10.4 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 151.4, 148.8, 148.6, 129.3, 129.0, 127.6, 125.1, 122.9, 119.5, 116.0, 111.4, 110.0, 79.5, 63.5, 56.1, 56.0, 49.6, 48.6, 47.9, 28.4; MS (ESI) calcd m/z for $C_{27}H_{35}N_3O_4$ (M^+) 465.26, found 466.18 (M + H)$^+$. Anal. Calcd for $C_{27}H_{35}N_3O_4$: C, 69.65; H, 7.58; N, 9.03. Found: C, 69.99; H, 7.22; N, 9.40.

General Procedure (III) for the Asymmetric Ring-Opening Reactions of *N*-Ts-Azabenzonorbornadiene 5 with Secondary Amine Nucleophiles. A 5 mL round-bottom flask fitted with a reflux condenser was flame-dried under a stream of nitrogen and cooled to room temperature. $[Ir(COD)Cl]_2$ (2.0 mg, 1.5 mol %) and (*S*)-BINAP (3.7 mg, 3 mol %) were simultaneously added and followed by the addition of anhydrous THF (2 mL). After the reaction mixture was stirred for 10 min at room temperature, *N*-Ts-azabenzonorbornadiene **5** (60 mg, 0.20 mmol) was added and the temperature of the oil bath was increased to 100 °C. On the first sign of reflux, nucleophile (3−5 equiv to **5**) was added. The reaction was stirred at 100 °C until completion as monitored by thin layer chromatography. After the reaction mixture was cooled to room temperature, the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (200−300 mesh) to give the desired product.

(1*R*,2*R*)-4-Methyl-*N*-[2-(methylphenylamino)-1,2-dihydronaphthalen-1-yl]-benzenesulfonamide (6a). Following the general procedure (III), **6a** was obtained as a white solid (74.3 mg, 92%): R_f = 0.36 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 130−132 °C; ee was determined to be 70% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 23.0 min (minor) and 29.6 min (major); $[\alpha]^{20}_D$ = −102.6 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3277(m), 3063(w), 2925(w), 1596(s), 1503(s), 1451(w), 1323(s), 1156(s), 1093(m), 1030(w), 919(w), 811(w), 1030(w), 747(m), 663(m), 546(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.0 Hz, 2H), 7.25−7.16 (m, 5H), 7.11 (d, J = 7.6 Hz, 2H), 6.93 (d, J = 7.6 Hz, 1H), 6.75 (t, J = 7.8 Hz, 3H), 6.69 (dd, J = 10.8 Hz, 8.4 Hz, 1H), 5.85 (dd, J = 14.4 Hz, 4.8 Hz, 1H), 4.78 (d, J = 8.0 Hz, 1H), 4.70−4.67 (m, 1H), 4.57 (dd, J = 13.2 Hz, 2.0 Hz, 1H), 2.40 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 143.3, 137.6, 133.8, 132.2, 130.4, 129.6, 129.1, 128.7, 128.4, 127.6, 127.2, 127.0, 126.1, 117.6, 113.9, 59.1, 54.6, 32.4, 21.6; MS (ESI) calcd m/z for $C_{24}H_{24}N_2O_2S$ (M^+) 404.16, found 427.30 (M + Na)$^+$. Anal. Calcd for $C_{24}H_{24}N_2O_2S$: C, 71.26; H, 5.98; N, 6.93. Found: C, 71.29; H, 6.28; N, 6.78.

(1*R*,2*R*)-*N*-[2-(Ethylphenylamino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6b). Following the general procedure (III), **6b** was obtained as a white solid (66.8 mg, 79%): R_f = 0.35 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 134−135 °C; ee was determined to be 80% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 10.6 min (major) and 13.1 min (minor); $[\alpha]^{20}_D$ = −119.8 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3268(m), 3053(w), 2956(w), 2924(m), 1595(s), 1501(s), 1323(m), 1262(m), 1156(s), 1092(w), 914(m), 813(m), 748(m), 663(m), 564(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.4 Hz, 2H), 7.16−7.09 (m, 5H), 7.04 (dd, J = 8.4 Hz, 6.4 Hz, 1H), 6.96 (ddd, J = 16.4 Hz, 14.0 Hz, 1.2 Hz, 1H), 6.70 (d, J = 8.4 Hz, 2H), 6.66 (t, J = 3.6 Hz, 2H), 6.63 (d, J = 1.2 Hz, 1H), 5.88 (dd, J = 14.8 Hz, 4.4 Hz, 1H), 4.73 (d, J = 8.0 Hz, 1H), 4.51−4.49 (m, 1H), 4.46 (dd, J = 11.6 Hz, 4.4 Hz, 1H), 2.85 (q, 2H), 2.33 (s, 3H), 0.71 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 143.3, 137.7, 133.5, 132.2, 130.4, 129.6, 129.2, 128.8, 128.4, 128.2, 127.3, 127.1, 126.1, 116.9, 113.8, 58.2, 54.1, 39.8, 21.6, 14.1; MS (ESI) m/z calcd for $C_{25}H_{26}N_2O_2S$ (M^+) 418.17, found 441.23 (M + Na)$^+$. Anal. Calcd for $C_{25}H_{26}N_2O_2S$: C, 71.74; H, 6.26; N, 6.69. Found: C, 71.51; H, 6.48; N, 6.91.

(1*R*,2*R*)-*N*-[2-(Methyl-*m*-tolylamino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6c). Following the general procedure (III), **6c** was obtained as a white solid (73.6 mg, 88%): R_f = 0.20 on silica gel (ethyl acetate/petroleum ether = 1:6, v/v); mp 120−124 °C; ee was determined to be 86% using HPLC analysis on a Chiralcel AD column (hexane/2-propanol = 90/10, 1.0 mL/min, λ = 254 nm); retention times were 12.2 min (minor) and 14.0 min (major)l $[\alpha]^{20}_D$ = −93.4 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3271(m), 3028(w), 2917(w), 1598(s), 1494(s), 1450(m), 1323(s), 1302(s), 1155(s), 1092(m), 1081(w), 949(w), 782(m), 664(s), 616(w), 564(s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 8.2 Hz, 2H), 7.02 (t, J = 7.8 Hz, 3H), 6.83 (d, J = 6.8 Hz, 1H), 6.60 (d, J = 9.6 Hz, 1H), 6.56 (s, 1H), 6.52 (d, J = 7.6 Hz, 1H), 6.50 (dd, J = 10.8 Hz, 6.0 Hz, 1H), 5.79 (dd, J = 14.4 Hz, 4.8 Hz, 1H), 4.64−4.61 (m, 1H), 4.58−4.49 (m, 2H), 2.37 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 143.2, 138.9, 137.6, 133.8, 132.3, 130.3, 129.5, 129.0, 128.7, 128.3, 127.7, 127.2, 127.0, 126.2, 118.6, 114.7, 111.1, 59.0, 54.6, 32.4, 21.8, 21.5; MS (ESI) calcd m/z for $C_{25}H_{26}N_2O_2S$ (M^+) 418.17, found 441.20 (M + Na)$^+$. Anal. Calcd for $C_{25}H_{26}N_2O_2S$: C, 71.74; H, 6.26; N, 6.69. Found: C, 71.50; H, 6.50; N, 6.91.

(1*R*,2*R*)-*N*-[2-(*p*-Toluidino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6e). Following the general procedure (III), **6e** was obtained as a white solid (77.6 mg, 96%): R_f = 0.25 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 56−58 °C; ee was determined to be 94% using HPLC analysis on a Chiralcel OD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 27.3 min (major) and 34.9 min (minor); $[\alpha]^{20}_D$ = −91.1 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3277(w), 3026(w), 2920(w), 1615(m), 1518(s), 1407(w), 1328(s), 1158(s), 1093(m), 1041(w), 922(w), 811(m),

762(w), 664(m), 565(m), 547(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 2.0 Hz, 6.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 6.8 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 6.60 (d, J = 7.6 Hz, 1H), 6.55 (d, J = 9.6 Hz, 1H), 6.48 (dd, J = 2.0 Hz, 6.4 Hz, 2H), 6.05−6.01 (m, 1H), 5.13 (d, J = 7.6 Hz, 1H), 4.46−4.44 (m, 1H), 4.28 (s, 1H), 3.26 (s, 1H), 2.44 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 134.9, 129.5, 129.3, 127.3, 127.2, 126.6, 126.4, 125.7, 124.8, 124.6, 124.4, 124.2, 110.9, 50.9, 49.8, 19.0, 17.9; MS (ESI) calcd m/z for $C_{24}H_{24}N_2O_2S$ (M^+) 404.52, found 427.38 $(M + Na)^+$. Anal. Calcd for $C_{24}H_{24}N_2O_2S$: C, 71.26; H, 5.98; N, 6.93. Found: C, 71.65; H, 6.35; N, 6.60.

(1*R*,2*R*)-*N*-[2-(2,4-Dimethoxyphenylamino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6f). Following the general procedure (III), **6f** was obtained as a white solid (52.2 mg, 58%): R_f = 0.26 on silica gel (ethyl acetate/petroleum ether = 1:4, v/v); mp 140−142 °C; ee was determined to be 97% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 102.3 min (major) and 116.0 min (minor); $[\alpha]^{20}_D$ = −108.4 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3258(w), 2924 (m), 1596(w), 1514(s), 1453(m), 1416(m), 1497(m), 1289(m), 1205(m), 1156(s), 1093(w), 1032(m), 796(m), 664(m), 566(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.22 (t, J = 6.4 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.00 (t, J = 7.2 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.59 (d, J = 9.6 Hz, 1H), 6.54 (d, J = 7.2 Hz, 1H), 6.46 (dd, J = 2.4 Hz, 6.0 Hz, 1H), 6.38 (d, J = 2.4 Hz, 1H), 6.08 (q, J = 4.0 Hz, 1H), 4.95 (s, 1H), 4.47 (dd, J = 2.4 Hz, 5.2 Hz, 1H), 4.28 (q, J = 2.4 Hz, 1H), 3.78 (s, 3H), 3.63 (s, 3H), 2.45 (s, 3H), 1.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 145.5, 140.9, 134.9, 129.5, 129.2, 127.2, 127.1, 126.7, 126.3, 125.6, 124.8, 124.6, 124.1, 108.6, 101.3, 96.7, 53.2, 52.7, 50.8, 50.2, 19.0; MS (ESI) calcd m/z for $C_{25}H_{26}N_2O_4S$ (M^+) 450.55, found 473.30 $(M + Na)^+$. Anal. Calcd for $C_{25}H_{26}N_2O_4S$: C, 66.64; H, 5.82; N, 6.22. Found: C, 66.34; H, 6.12; N, 6.62.

(1*R*,2*R*)-*N*-[2-(4-Propylphenylamino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6g). Following the general procedure (III), **6g** was obtained as colorless oil (48.4 mg, 56%): R_f = 0.15 on silica gel (ethyl acetate/petroleum ether = 1:6, v/v); ee was determined to be 94% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 40.9 min (major) and 43.9 min (minor); $[\alpha]^{20}_D$ = −116.4 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3394(w), 3276(m), 3037 (w), 2957(m), 2927(m), 2870(w), 1615 (m), 1518(s), 1454(w), 1412(m), 1329(m), 1160(s), 1094(m), 1043(m), 923(w), 796(m), 665(m), 567(m), 548(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.21 (t, J = 7.2 Hz, 1H), 7.09 (d, J = 7.2 Hz, 1H), 7.02−6.96 (m, 3H), 6.57 (t, J = 6.8 Hz, 2H), 6.51 (d, J = 8.0 Hz, 2H), 6.04 (q, J = 4.0 Hz, 1H), 4.91 (t, J = 8.0 Hz, 1H), 4.44 (dd, J = 3.2 Hz, 4.4 Hz, 1H), 4.30 (t, J = 4.8 Hz, 1H), 3.35 (s, 1H), 2.47 (q, J = 8.0 Hz, 4H), 1.64−1.55 (m, 2H), 1.26 (s, 1H), 0.94 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 143.5, 137.5, 132.1, 131.8, 129.8, 129.3, 129.2, 129.0, 128.9, 128.3, 127.4, 127.2, 126.8, 113.3, 53.5, 52.4, 37.2, 24.9, 21.6, 13.9; MS (ESI) calcd m/z for $C_{26}H_{28}N_2O_2S$ (M^+) 432.58, found 455.36 $(M + Na)^+$. Anal. Calcd for $C_{26}H_{28}N_2O_2S$: C, 72.19; H, 6.52; N, 6.48. Found: C, 72.45; H, 6.89; N, 6.87.

(1*R*,2*R*)-*N*-[2-(4-Bromophenylamino)-1,2-dihydronaphthalen-1-yl]-4-methylbenzenesulfonamide (6h). Following the general procedure (III), **6h** was obtained as a white solid (78.8 mg, 84%): R_f = 0.15 on silica gel (ethyl acetate/petroleum ether = 1:6, v/v); mp 165−167 °C; ee was determined to be 22% using HPLC analysis on a Chiralcel AD-H column (hexane/2-propanol = 90/10, 0.5 mL/min, λ = 254 nm); retention times were 67.2 min (major) and 88.5 min (minor); $[\alpha]^{20}_D$ = −51.6 (c = 1.00, $CHCl_3$); IR (KBr, cm^{-1}) 3276(w), 3028(w), 2848(w), 1592(s), 1493(s), 1402(m), 1317(s), 1156(s), 1092(m), 812 (s), 663(m), 571(m), 547(m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.15 (t, J = 8.0 Hz, 2H), 7.10 (d, J = 7.6 Hz, 1H), 7.01 (t, J = 7.2 Hz, 1H), 6.71 (t, J = 7.6 Hz, 1H), 6.59−6.56 (m, 4H), 6.05 (q, J = 4.0 Hz, 1H), 4.87 (d, J = 7.6 Hz, 1H), 4.45 (dd, J = 3.6 Hz, 4.4 Hz, 1H), 4.33 (t, J = 4.0 Hz, 1H), 3.46 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 143.7, 137.3, 132.1, 131.8, 131.7, 129.8, 129.3, 129.2, 129.0, 128.5, 127.3, 126.2, 114.9, 109.4, 53.3, 52.3, 21.6; MS (ESI) calcd m/z for $C_{23}H_{21}BrN_2O_2S$ (M^+) 469.39, found 491.30 $(M + Na)^+$. Anal. Calcd for $C_{23}H_{21}BrN_2O_2S$: C, 58.85; H, 4.51; N, 5.97. Found: C, 58.49; H, 4.90; N, 6.25.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of compounds **2a**−**2m**, **4a**−**4d**, and **6a**−**6h**, and X-ray structure data for compound **2g**. This material is available free of charge via the Internet at http://pubs.acs.org.