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Copper-Catalyzed Asymmetric Ring Opening of Oxabicyclic Alkenes with Grignard Reagents

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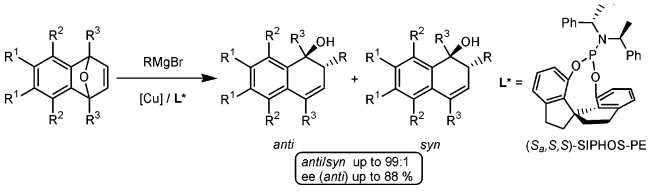

Simple Grignard reagents were applied in copper-catalyzed asymmetric ring-opening reactions of oxabenzonorbornadiene derivatives using spiro phosphoramidite ligands. Excellent *anti*-stereoselectivities and good enantioselectivities were achieved.

Transition-metal-catalyzed desymmetrization of meso oxabicyclic alkenes with a nucleophile, namely asymmetric ring opening (ARO), is an efficient strategy through which the cyclic compounds with multiple stereocenters could be constructed in one operation.[1] By using an organometallic reagent as nucleophile in this reaction a new C−C bond is formed simultaneously. Lautens and co-workers[2] have demonstrated that the alkylzinc reagents can serve as efficient nucleophiles in ARO reaction. Excellent *syn*-stereoselectivities and enantioselectivities were archived in the addition of alkylzinc to oxabicyclic alkenes catalyzed by chiral palladium complexes of BINAP[2] and other chiral ligands.[3] Recently, Pineschi and Feringa reported a copper-catalyzed addition of alkylzinc reagents to oxabicyclic alkenes by using monophosphorus ligand, and high *anti*-stereoselectivity and enantioselectivity were obtained.[4] Besides the alkylzinc, organoboron[5] and organoaluminum reagents[6] were also applied in the asymmetric ring-opening reaction of oxabicyclic alkenes to give the alkylated products in high selectivities. However, the Grignard reagent, the most readily available organometallic reagent, has been scarcely utilized in the ARO reaction.[7] The sole example was reported by Waymouth in the addition of ethylmagnesium bromide to 2,4-dimethyl-3-benzyloxy-8-oxabicyclo-6-octene catalyzed by chiral zirconium complex in a low yield (27%) and a low enantioselectivity (48% ee).[6] The reason for the rare application of Grignard reagent in this important reaction might be attributed to the complex mechanism of the ARO reaction with this hard nucleophile. In this paper, we describe the copper-catalyzed asymmetric ring opening of oxabenzonorbornadienes with Grignard reagents in good enantioselectivity and excellent *anti*-stereoselectivity.

Recently, we have developed new types of monodentate chiral spiro phosphites, phosphonites, and phosphoramidites and demonstrated they are highly efficient ligands in asymmetric rhodium-catalyzed hydrogenation,[8] copper-catalyzed 1,4-addition of dialkylzinc reagents to enones,[9] and other asymmetric reactions.[10,11] In the investigation on the copper-catalyzed ARO reaction of oxabicyclic alkenes with Grignard reagents, we found that the spiro phosphoramidite SIPHOS-PE was a choice of ligand which provided the alkylated ring-opening products in good enantioselectivity and excellent *anti*-stereoselectivity (Scheme 1).

The reaction was initially tested with 7-oxabenzonorbornadiene (**1**). When the compound **1** in toluene was treated with 2.0 equiv of ethylmagnesium bromide[12] in the presence of 3 mol % of copper catalyst, generated from $Cu(OTf)_2$ and (S_a,*S*,*S*)-SIPHOS-PE, at −20 °C for 15 h, the ring-opening product **2a** was given in 85% yield in

(1) (a) Lautens, M. *Synlett* **1993**, 177. (b) Chiu, P.; Lautens, M. *Top. Curr. Chem*. **1997**, *190*, 1. (c) Lautens, M.; Fagnou, K.; Hiebert, S. *Acc. Chem. Res*. **2003**, *36*, 48. (d) Pineschi, M. *New. J. Chem.* **2004**, *28,* 657.

(2) (a) Lautens, M.; Renaud, J.-L.; Hiebert, S. *J. Am. Chem. Soc.* **2000**, *122*, 1804. (b) Lautens, M.; Hiebert, S.; Renaud, J.-L. *Org. Lett.* **2000**, *2,* 1971. (c) Lautens, M.; Hiebert, S.; Renaud, J.-L. *J. Am. Chem. Soc.* **2001**, *123*, 6834. (d) Lautens, M.; Hiebert, S. *J. Am. Chem. Soc.* **2004**, *126*, 1439.

(3) (a) Priego, J.; Mancheno, O. G.; Cabrera, S. C.; Arrayas, R. G.; Llamas, T.; Carretero, J. C. *Chem. Commun.* **2002**, 2512. (b) Li, M.; Yan, X.-X.; Hong W.; Zhu, X.-Z.; Cao, B.-X.; Sun, J.; Hou, X.-L. *Org. Lett.* **2004**, *6*, 2833. (c) Cabrera, S.; Arrayas, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2004**, *43,* 3944.

(4) Bertozzi, F.; Pineschi, M.; Macchia, F.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2002**, *4*, 2703.

(5) (a) Lautens M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, *4*, 1311. (b) Lautens M.; Dockendorff, C. *Org. Lett.* **2003**, *5*, 3695.

(6) Millward, D. B.; Sammis, G.; Waymouth, R. M. *J. Org. Chem.* **2000**, *65*, 3902.

(7) For nonenantioselective transition-metal-catalyzed ring-opening reaction of oxabicyclic alkenes with Grignard reagents, see: (a) Lautens, M.; Ma, S. *J. Org. Chem.* **1996**, *61*, 7246. (b) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **2000**, *122*, 978. (c) Arrayas, R. G.; Cabrera, S.; Carretero, J. C. *Org. Lett.* **2003**, *5*, 1333. (d) Nakamura, M.; Matsuo, K.; Inoue, T.; Nakamura, E. *Org. Lett.* **2003**, *5*, 1373.

(8) (a) Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou. Q.-L. *Chem. Commun.* **2002**, 480. (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348. (c) Fu, Y.; Guo, X.-X.; Zhu, S.-F.; Hu, A.-G.; Xie, J.-H.; Zhou, Q.-L. *J. Org. Chem.* **2004**, *69,* 4648. (d) Fu, Y.; Hou, G.-H.; Xie, J.-H.; Xing, L.; Wang, L.-X.; Zhou, Q.-L. *J. Org. Chem.* **2004**, *69*, 8157.

(9) Zhou, H.; Wang, W.-H.; Fu, Y.; Xie, J.-H.; Shi, W.-J.; Wang, L.-X.; Zhou, Q.-L. *J. Org. Chem.* **2003**, *68*, 1582.

(10) (a) Shi, W.-J.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2003,** *14*, 3867. (b) Guo, X.-X.; Xie, J.-H.; Hou, G.-H.; Shi, W.-J.; Wang, L.-X.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2004**, *15*, 2231.

(11) For the examples of other chiral spiro ligands applied in asymmetric catalysis, see: (a) Chan, A. C. S.; Hu, W.-H.; Pai, C.-C.; Lau, C.-P.; Jiang, Y.-Z.; Mi, A.-Q.; Yan, M.; Sun, J.; Lou, R.-L.; Deng, J.-G. *J. Am. Chem. Soc*. **1997**, *119*, 9570. (b) Arai, M. A.; Kuraishi, M.; Arai, T.; Sasai, J. *J. Am. Chem. Soc*. **2001**, *123*, 2907. (c) Xie, J.-H.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Fan, B.-M.; Duan, H.-F.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2003**, *125,* 4404. (d) Wu, S.-L.; Zhang, W.-C.; Zhang, Z.-G.; Zhang, X.-M. *Org. Lett.* **2004**, *6*, 3565.

(12) The Grignard reagents used in this paper are as ether solutions. The ether concentration in the reaction solution is around 10% in volume, which is important for keeping the reaction homogeneous. Reducing the ether concentration led to a precipitation of Grignard reagents and resulted in a lower yield and lower selectivity.

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SCHEME 1

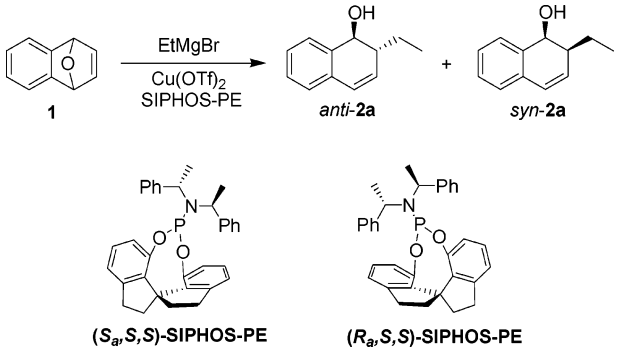


TABLE 1. Asymmetric Ring Opening of Compound 1 with EtMgBr[a]

entry	solvent	*T* (°C)	time (h)	yield[b] (%)	*anti*/*syn*[c]	ee[d,e] (%)
1	toluene	−20	15	85	97:3	56
2	toluene	−40	48	31	95:5	44
3	toluene	0	12	67	94:6	54
4	ether	−20	15	70	97:3	7[f]
5	THF	−20	40	33	92:8	0
6	DME	−20	40	13	93:7	0

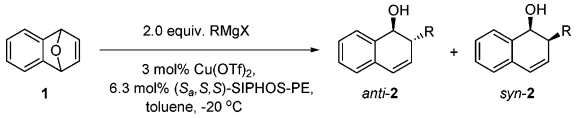
[a] Reaction conditions: 3 mol % of $Cu(OTf)_2$, 6.3 mol % of (S_a,*S*,*S*)-SIPHOS-PE, 2.0 equiv of EtMgBr, 4 mL of solvent. [b] Isolated yield. [c] Determined by HPLC. [d] ee of *anti*-adduct determined by HPLC. [e] The absolute configuration of *anti*-**2a** was (1*S*,2*R*), ref 4. [f] The configuration was (1*R*,2*S*).

97:3 *anti*/*syn* ratio and 56% ee for the *anti*-isomer (Table 1, entry 1),[13] while using the ligand (R_a,*S*,*S*)-SIPHOS-PE, which has mismatched chiralities, under the same conditions led to a slightly lower enantioselectivity (82% yield, 94/6 *anti*/*syn*, 49% ee).[14] The absolute configurations of products obtained from both (S_a,*S*,*S*)-SIPHOS-PE and (R_a,*S*,*S*)-SIPHOS-PE are (1*S*,2*R*), implying that the configuration of product was determined by the chirality of the amino moiety of the ligand. As the reaction temperature dropped to −40 °C, the decreases in the yield and enantioselectivity of desired ARO product were observed (entry 2). In the coordinating solvents, especially in THF and 1,2-dimethoxyethane (DME), the racemic product was given.[15] Other copper resources, such as CuCl, $[Cu(OTf)]_2 \cdot C_6H_6$, $CuBr \cdot Me_2S$, and CuCN, were also examined, and similar enantioselectivities were obtained.

To extend the range of Grignard reagents used in copper-catalyzed ARO reaction, different alkylmagnesium halides were studied in the ring opening reaction of **1**. The data, summarized in Table 2, showed that the reaction is sensitive to the type of used Grignard reagent. The EtMgCl and EtMgI displayed lower enantioselectivities (11% ee and 43% ee, respectively), indicating that the halogen anion of Grignard reagent played a critical role in the control of enantioselectivity. The size of the alkyl group in the Grignard reagent also significantly influenced the enantioselectivity of the reaction. For instance, in the reaction of **1** with MeMgBr, which has a smaller alkyl group, the alkylated ring-opening product was obtained in 99:1 *anti*/*syn* selectivity with good enantioselectivity (79% ee), although the yield of desired product was low, while in the reaction of **1** with *n*-BuMgBr, which has a larger alkyl group, the enantioselectivity decreased to 33% ee. When the Grignard reagent changed to a more sterically hindered *i*-BuMgBr, the ring-opening product became racemic. There was no reaction when the aromatic Grignard reagent PhMgBr was used.

Besides the 7-oxabenzonorbornadiene (**1**), a variety of oxabenzonorbornadiene derivatives were investigated in the copper-catalyzed ARO reaction with different Grignard reagents (Table 3). As illustrated in the Table 3, most of the reactions produced the corresponding alcohols in good yields and excellent *anti*-stereoselectivities. The enantioselectivities are moderate to good, and the highest ee values were achieved in the reactions of substrates

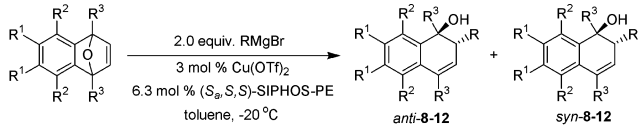
TABLE 2. Asymmetric Ring Opening of Compound 1 with Various Grignard Reagents



entry	RMgX	product	time (h)	yield[a] (%)	*anti*/*syn*[b]	ee[c] (%)
1	EtMgBr	**2a**	15	85	97:3	56
2	EtMgCl	**2a**	18	60	88:12	11
3	EtMgI	**2a**	14	86	97:3	46
4	MeMgBr	**2b**	36	23	99:1	79
5	*n*-BuMgBr	**2c**	24	60	99:1	31
6	*i*-BuMgBr	**2d**	18	63	95:5	0

[a] Isolated yield of adducts. [b] Determined by HPLC. [c] ee of *anti*-adduct was determined by HPLC.

TABLE 3. Asymmetric Ring Opening of Oxabenzonorbornadiene with Grignard Reagent



3: R^1 = Me, R^2 = H, R^3 = H
4: R^1 = H, R^2 = Me, R^3 = H
5: R^1 = H, R^2 = H, R^3 = Me
6: R^1 = H, R^2 = OMe, R^3 = H
7: R^1 = H, R^2 = OMe, R^3 = Me

entry	substrate	R	time (h)	product	yield[a] (%)	*anti*/*syn*[b]	ee[c] (%)
1	**1**	Et (**a**)	15	**2a**	85	97:3	56
2	**3**	Et (**a**)	15	**8a**	89	95:5	42
3	**4**	Et (**a**)	15	**9a**	60	99:1	65
4	**5**	Et (**a**)	12	**10a**	87	99:1	88
5	**5**	Me (**b**)	8	**10b**	85	99:1	43
6	**5**	*n*-Bu(**c**)	12	**10c**	81	99:1	65
7	**6**	Et (**a**)	18	**11a**	66	94:6	72
8	**6**	*n*-Bu(**c**)	24	**11c**	81	99:1	70
9	**7**	Et (**a**)	9	**12a**	90	99:1	87
10	**7**	Me (**b**)	40	**12b**	54	99:1	55
11	**7**	*n*-Bu(**c**)	15	**12c**	80	99:1	70

[a] Isolated yield of adducts. [b] Determined by HPLC. [c] ee of *anti*-adduct was determined by HPLC.

(13) The minor *syn*-adducts obtained in all reactions throughout this work were racemic. The side product 1,2-dihydronaphthalen-1-ol (<2%) was detected.

(14) For comparison, we tested all chiral monophosphorus ligands which are available in our laboratory and found that only Feringa's ligands (S_a,*R*,*R*)-Monophos-PE and (S_a,*S*,*S*)-Monophos-PE gave comparable enantioselectivities. They produced the alkylated ring-opening product **2a** in 51% yield in 93:7 *anti*/*syn* ratio with 51% ee and 38% yield in 98:2 *anti*/*syn* ratio with 47% ee, respectively.

(15) The 7-oxabenzonorbornadienes could not be completely converted in the coordinating solvents.

bearing methyl groups at the 1,4-position with ethylmagnesium bromide (88% ee in entry 4 and 87% ee in entry 9).

In conclusion, we have demonstrated a copper-catalyzed asymmetric ring-opening reaction of oxabenzonorbonenediene derivatives with Grignard reagents using spiro phosphoramidite ligands in excellent *anti*-stereoselectivity and good enantioselectivity. We have so far been unable to discuss the detailed reaction mechanism, which may involve a (π-allyl)-copper or a (σ-allylic)-copper intermediate.[4,7c] The investigation on the scope of this reaction and its mechanism is in progress in our laboratory.

Experimental Section

General Procedure for the Copper/Spiro-phosphoramidite-Catalyzed Asymmetric Ring-Opening of Oxabicyclic Alkenes. A solution of $Cu(OTf)_2$ (4 mg, 0.011 mmol) and (S_a,*S*,*S*)-SIPHOS-PE (11.8 mg, 0.023 mmol) in anhydrous toluene (3 mL) was stirred at room temperature for 50 min. This colorless solution was cooled to −20 °C, and a solution of corresponding oxabenzonorbornadiene (0.375 mmol) in toluene (1 mL) was added. After the mixture was stirred for 5 min, Grignard reagent (0.75 mmol) was added by a syringe pump in 2 h and stirred at −20 °C until the reaction was complete. The reaction was quenched by addition of 1 M aqueous NH_4Cl (4 mL). The mixture was extracted with ether, dried over $MgSO_4$, filtered, and concentrated to give a crude product which was subjected to column chromatography.

(1*S*,2*R*)-(−)-2-Ethyl-1,2-dihydronaphth-1-ol (2a):[4] colorless oil; 85% yield; 56% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min; t_R = 27.4 min (major) and 33.3 min.

(1*S*,2*R*)-(−)-2-Methyl-1,2-dihydronaphth-1-ol (2b):[4] colorless oil; 23% yield; 79% ee, chiral HPLC Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 23.6 min (major) and 25.9 min.

(1*S*,2*R*)-(−)-2-*n*-Butyl-1,2-dihydronaphth-1-ol (2c):[4] colorless oil; 60% yield; 31% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R =19.3 min (major) and 24.1 min.

(1*S*,2*R*)-(−)-2-Isobutyl-1,2-dihydronaphth-1-ol (2d):[7c] colorless oil; 63% yield; 0% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 28.6 and 32.8 min.

(1*S*,2*R*)-(−)-2-Ethyl-6,7-dimethyl-1,2-dihydronaphth-1-ol (8a):[7c] colorless oil; 89% yield; 42% ee, chiral HPLC Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 37.9 and 66.5 min (major).

(1*S*,2*R*)-(−)-2-Ethyl-5,8-dimethyl-1,2-dihydronaphth-1-ol (9a):[4] colorless oil; 60% yield; 65% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 16.8 min (major) and 20.2 min.

(1*S*,2*R*)-(−)-2-Ethyl-1,4-dimethyl-1,2-dihydronaphth-1-ol (10a):[4] colorless oil; 87% yield; 88% ee, chiral HPLC Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 12.2 min (major) and 17.7 min.

(1*S*,2*R*)-(−)-1,2,4-Trimethyl-1,2-dihydronaphth-1-ol (10b): colorless oil; 85% yield; $[\alpha]^{20}_D$ = −21.2 (*c* 1.0, CH_2Cl_2); 43% ee, chiral HPLC Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 17.8 min (major) and 28.7 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 6.9 and 3.0 Hz, 1H), 7.30−7.23 (m, 3H), 5.62 (s, 1H), 2.64−2.53 (m, 1H), 2.06 (s, 3H), 1.77 (s, 1H), 1.31 (s, 3H), 1.11 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.2, 133.9, 131.0, 130.3, 127.7, 127.3, 123.4, 123.2, 74.6, 41.5, 22.1, 18.9, 14.0; EI MS *m/z* 188.2 (M^+). Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.50; H, 8.47.

(1*S*,2*R*)-(−)-2-*n*-Butyl-1,4-dimethyl-1,2-dihydronaphth-1-ol (10c): colorless oil; 81% yield; $[\alpha]^{20}_D$ = −59.8 (*c* 1.0, CH_2Cl_2); 65% ee, chiral HPLC Chiralpak AD-H column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R =14.4 min (major) and 24.0 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63−7.58 (m, 1H), 7.31−7.21 (m, 3H), 5.73 (dd, *J* = 3.0 and 1.5 Hz, 1H), 2.37−2.32 (m, 1H), 2.07 (t, *J* = 1.8 Hz, 3H), 1.79−1.72 (m, 1H), 1.45−1.27 (m, 6H), 1.30 (s, 3H), 0.92 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 134.0, 131.4, 128.4, 127.7, 127.2, 123.2, 123.1, 74.7, 46.7, 29.9, 27.9, 22.9, 22.5, 19.1, 14.0; EI MS *m/z* 230.1 (M^+). Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.35; H, 9.78.

(1*S*,2*R*)-(−)-2-Ethyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (11a):[8] colorless oil; 66% yield; 72% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, t_R = 15.7 and 30.6 min (major).

(1*S*,2*R*)-(+)-2-*n*-Butyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (11c): colorless oil; 81% yield; $[\alpha]^{20}_D$ = −256.1 (*c* 1.0, CH_2Cl_2); 70% ee, chiral Chiralcel OD column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, t_R = 11.2 and 18.8 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, *J* = 9.9 Hz, 1H), 6.76 (d, *J* = 0.9 Hz, 2H), 6.08 (dd, *J* = 9.9 Hz, 4.2 Hz, 1H), 4.97 (s, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 2.64−2.57 (m, 1H), 2.09 (s, 1H), 1.42−1.17 (m, 6H), 0.86 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 149.5, 130.7, 124.0, 122.3, 119.0, 111.1, 110.3, 65.3, 56.2, 56.1, 41.5, 32.1, 29.5, 22.8, 13.9; EI MS *m/z* 262.1 (M^+). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.75; H, 8.82.

(1*S*,2*R*)-(+)-2-Ethyl-1,4-dimethyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (12a): colorless oil; 90% yield; $[\alpha]^{20}_D$ = +56 (*c* 1.0, CH_2Cl_2); 87% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 5.1 and 7.4 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.75−6.82 (m, 2H), 5.58 (br, 1H), 5.53 (s, 1H), 3.87 (s, 3H), 3.75 (s, 3H), 2.38−2.34 (m, 1H), 2.16 (s, 3H), 1.95−1.88 (m, 1H), 1.25 (m, 5H), 1.02 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.6, 150.6, 134.2, 131.5, 129.9, 125.8, 111.7, 111.5, 76.4, 56.3, 56.2, 46.6, 22.8, 20.3, 12.3; EI MS *m/z* 262.2 (M^+). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.94; H, 7.91.

(1*S*,2*R*)-(+)-1,2,4-Trimethyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (12b): colorless oil; 54% yield; $[\alpha]^{20}_D$ = +35 (*c* 1.0, CH_2Cl_2); 55% ee, chiral HPLC Chiralcel OD column, *n*-hexane/*i*-PrOH = 99:1, 1.0 mL/min, t_R = 14.4 and 31.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (d, *J* = 2.4 Hz, 2H), 5.53 (br, 1H), 5.45 (s, 1H), 3.87 (s, 3H), 3.75 (s, 3H), 2.71−2.68 (m, 1H), 2.13 (s, 3H), 1.26 (s, 3H), 1.14 (d, *J* = 7.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 150.8, 134.2, 132.3, 131.3, 126.0, 111.9, 111.6, 76.6, 56.5, 56.4, 39.2, 23.0, 19.9, 14.0; EI MS *m/z* 248.1 (M^+). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.60; H, 8.27.

(1*S*,2*R*)-(+)-2-*n*-Butyl-1,4-dimethyl-5,8-dimethoxy-1,2-dihydronaphth-1-ol (12c): colorless oil; 80% yield; $[\alpha]^{20}_D$ = +18.6 (*c* 1.0, CH_2Cl_2); 70% ee, chiral Chiralcel OD column, *n*-hexane/*i*-PrOH = 90:10, 1.0 mL/min, t_R = 5.1 and 6.7 min (major); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.81 (d, *J* = 2.7 Hz, 2H), 5.57 (br, 1H), 5.53 (s, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 2.46−2.41 (m, 1H), 2.15 (t, *J* = 2.4 Hz, 3H), 1.88−1.80 (m, 1H), 1.55−1.22 (m, 6H), 1.25 (s, 3H), 0.93 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 151.5, 150.6, 134.2, 130.4, 130.4, 125.9, 111.7, 111.5, 76.4, 56.3, 56.1, 44.5, 30.0, 27.1, 22.9, 22.7, 20.3, 14.1; EI MS *m/z* 290.2 (M^+). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.34; H, 7.82.

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