Available online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Fluorine Chemistry 125 (2004) 517–525
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Preparation and catalytic applications of partially fluorinated binaphthol ligands

Shahla Yekta, Larissa B. Krasnova, Brian Mariampillai, Christine J. Picard, Gang Chen, Subramanian Pandiaraju, Andrei K. Yudin*

Department of Chemistry, Davenport Research Laboratories, University of Toronto, 80 St. George Street, Toronto, Ont., Canada M5S 3H6

Received 12 October 2003; accepted 17 November 2003

Abstract

New partially fluorinated binaphthols were obtained using a copper-catalyzed oxidative coupling. The corresponding enantiomerically pure compounds were prepared by fractional crystallization of the corresponding bis(menthyl)carbamates. Nucleophilic aromatic substitution using oxygen- and carbon-based nucleophiles resulted in functionalized derivatives without concomitant racemization. The titanium(IV) complexes of these ligands are catalytically active in the asymmetric oxidation of sulfides.

Keywords: Asymmetric catalysis; Coupling; Fluorine; Ligand; Nucleophilic aromatic substitution; BINOL; F_8BINOL; F_4BINOL; Chiral; Sulfoxidation

1. Introduction

Finding the right balance between the steric and electronic demands of a chiral ligand is essential in order to optimize a given catalytic system. Electron deficiency or Lewis acidity of the metal center is one of the fundamental properties explored in many asymmetric transformations. In terms of ligand symmetry, C_2 symmetrical ligands possessing axial chirality have found wide utility in asymmetric catalysis [1]. BINOL (**1**) and its derivatives have generated particular interest because their versatile backbones can be modified, thereby affecting the reaction environment by influencing the metal center [2]. The strategic placement of substituents within the binaphthol framework has been shown to provide improved catalysts. For instance, incorporation of halogens at the 6,6′-positions of BINOL increases enantioselectivity of the ene reaction by increasing the Lewis acidity of the corresponding titanium catalysts [3]. While the BINOL–Ti complex promoted the reaction in 93% yield and 69% enantioselectivity, the 6,6′-Br_2BINOL/Ti catalyst gave the product in 89% e.e. and high yield was maintained. Substituents at the 3,3′-positions are mainly responsible for controlling the steric requirements around the metal coordinated to the binaphthol ligand [2]. For example, the yield and enantioselectivity of the Diels–Alder reaction between methyl propiolate and cyclopentadiene are greatly enhanced when triaryl silyl substituents are used at the 3,3′-positions of the aluminum–binaphthol catalyst [4].

Our explorations in the field of binaphthyl catalysis led us to consider partially fluorinated species. This interest was driven by the known stability of the C–F bond towards oxidation [5], propensity of fluoroaromatics to engage in stabilizing stacking interactions with other aromatic rings [6], and rich nucleophilic aromatic substitution chemistry of fluoroaromatic compounds [7]. We recently, published the synthesis and catalytic applications of polyfluorinated BINOL ligands such as F_8BINOL (**3**), an electronic isostere of BINOL [8]. In terms of catalytic applications, we explored the sulfoxidation [9] as well as the glyoxylate-ene reaction [10]. It was found that the (*R*)-F_8BINOL–Ti system catalyzed the sulfoxidation reaction with higher enantioselectivity (89% in CH_2Cl_2) than the (*R*)-BINOL–Ti system (7% in CH_2Cl_2 and 22% in CCl_4) at 0.05 M concentration. Highly enantioselective ‘‘pseudo-meso’’ aggregates were obtained by combining one of the enantiomers of BINOL with its fluorinated counterpart, F_8BINOL, and were applied in the enantioselective glyoxylate-ene reaction. The reaction between ethyl glyoxylate and α-methyl styrene in the presence of 10 mol% (*S*)-F_8BINOL/Ti(O^iPr)$_4$ (2:1 ratio) afforded the corresponding ene-product in 53% yield and 92% e.e. The catalyst produced from (*R*)-F_8BINOL/(*S*)-BINOL/Ti(O^iPr)$_4$ mixture (1:1:1 ratio) gave the product of the reaction between ethyl glyoxylate and α-methyl styrene

* Corresponding author. Tel.: +1-416-946-5042; fax: +1-416-978-8775.
E-mail address: ayudin@chem.utoronto.ca (A.K. Yudin).

0022-1139/$ – see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2003.11.024

with excellent enantioselectivity (99%). A significant yield improvement was also observed in the mixed case compared to either **1** or **3** alone.

We were additionally intrigued by facile and regioselective nucleophilic aromatic substitution at the 6- and 7-positions of the partially fluorinated rings of F_8BINOL [11]. Interested in using this tool, we proceeded to modify the binaphthol scaffold by placing a variety of substituents at these positions. Unfortunately, separation of the 6,6′- and 7,7′-substituted regioisomers proved to be tedious. Our interest further progressed towards F_4BINOL (**2**) where only one of the naphthyl rings is fluorinated, minimizing the number of sites for possible nucleophilic fluorine displacement. Herein, we report the synthesis of F_4BINOL and its application in the asymmetric sulfoxidation reaction.

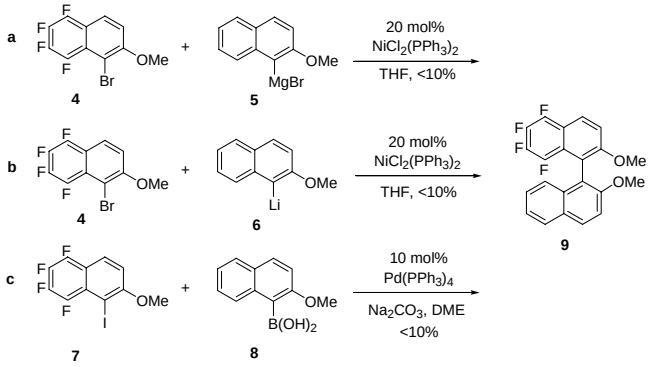
2. Results and discussion

2.1. Synthesis of F_4BINOL

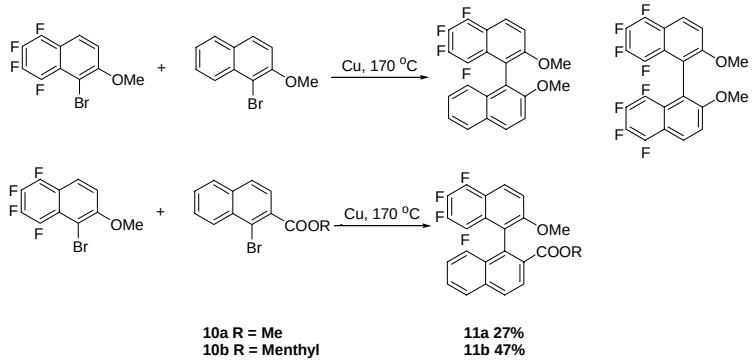
2.1.1. Oxidative and reductive coupling methods

Initial attempts at making F_4BINOL involved direct coupling methods (for selected examples on Ullman and oxidative coupling see [12,13]). The coupling of Grignard or lithium derivatives **5** and **6** with **4** afforded the desired product **9** in less than 10% yield (Scheme 1a and b). Monitoring the reaction with ^{19}F NMR showed substitutions at the 5-, 6-, 7-, and 8-positions. All attempts at making the Grignard reagent from **4** failed. The Suzuki coupling between the iodo compound **7** and boronic acid **8** gave the product in less than 10% yield presumably due to the sensitivity of the Suzuki coupling to steric bulk around the incipient C–C bond (Scheme 2c) [14].

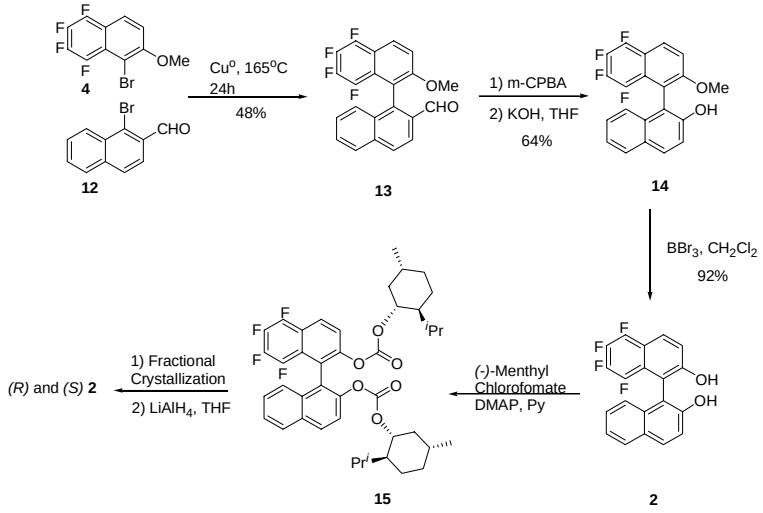
The Ullmann coupling similar to what had been tried in the synthesis of **3** gave **9** in only 5% yield [8]. The major product was the protected F_8BINOL derivative, obtained in 85% yield (Scheme 2). Since the Ullmann coupling reaction is in favor of electron-poor substrates, naphthoic esters **10a** and **10b** were used. The yield of the reaction was improved to 27 and 47% with **11a** and **11b**, respectively. In the case of **11b**, a 1:1 mixture of diastereomers was obtained and they were separated through fractional crystallization. Since the carboxylic acids from which **10a** and **10b** were prepared are not readily available, we attempted the synthesis using readily available aldehyde **12** (Scheme 2). Compound **12** was prepared from commercially available 1-bromo-2-methylnaphthalene in two steps according to literature procedure [15]. The aldehyde **13** was then oxidized through a Baeyer–Villiger reaction with *m*CPBA followed by hydrolysis of the corresponding ester to obtain alcohol **14** in 64% yield (two steps). Demethylation with BBr_3 afforded racemic F_4BINOL in 92% yield and 28% overall yield. Enantiomer resolution was accomplished using a procedure



Scheme 1.



Scheme 2.

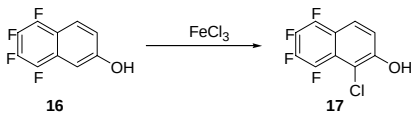


Scheme 3.

similar to that for F_8BINOL through the bis(carbonate) diastereomers **15** prepared from (−)-menthyl chloroformate in pyridine with a catalytic amount of dimethyl aminopyridine (Scheme 3). Fractional crystallization of **15** from 5:1 methanol/isopropanol resulted in the diastereomer separation. Subsequent reduction using $LiAlH_4$ in THF afforded enantiomerically pure **2** (Scheme 3).

Unlike the Ullmann coupling, oxidative coupling methods are known to favor the formation of electron-rich aromatics. Since only one of the naphthyl moieties in **3** is fluorinated, we opted to try the oxidative coupling between **16** and 2-naphthol. Oxidative coupling of 2-naphthols can be promoted by several metal catalysts such as complexes of ruthenium [16], titanium [17], vanadium [18], manganese [19], copper [20], and iron [21]. Unfortunately, the widely used $FeCl_3$-catalyzed reaction cannot be used in our case because the fluorinated 2-naphthol **16** reacts with $FeCl_3$ to give chlorinated product **17** (Scheme 4) [9].

We were nonetheless able to obtain the product in moderate yields using Cu(OH)Cl·TMEDA as the catalyst (Scheme 5) [13b]. Temperature played a key role in influencing product ratios. Since 2-naphthol has a lower oxidation potential (1.54 V versus Ag/AgCl) than the corresponding 5,6,7,8-tetrafluoronaphthol (1.84 V versus Ag/AgCl), it undergoes oxidative coupling at lower temperature (40 °C). Heating the reaction mixture containing the two starting materials (1:1 ratio) to 70 °C resulted only in BINOL with quantitative yield. Only upon increasing the temperature to 125 °C, formation of F_4BINOL was observed. The amount of catalyst used was also essential in achieving the desired conversions. Thus, the use of 10 mol% of the copper catalyst resulted in highest yields of F_4BINOL whereas 25 mol% facilitated the formation of BINOL. The best reaction conditions were obtained using 1 eq. of 2-naphthol, 0.7 eq. of 5,6,7,8-tetrafluoronaphthol and 10 mol% of Cu(OH)Cl·TMEDA at 140 °C for 24 h which afforded F_4BINOL in 40% yield. The main by-product was BINOL, obtained in 50% yield and F_8BINOL, obtained in less than 10% yield.

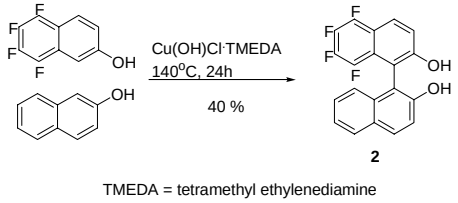


Scheme 4.

2.1.2. Other cross-coupling methods

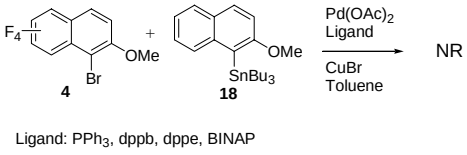
Another attempt at making F_4BINOL using the cross-coupling methods was the Stille coupling [22]. We envisioned that a cross-reaction may occur with the more nucleophilic aryl stannane. Compound **18** was prepared via addition of *n*-butyllithium at low temperature to generate the lithiated intermediate **6** which was trapped by slow addition of tributylstannyl chloride. However, the Stille coupling with **4** in the presence of palladium acetate and a variety of phosphine ligands resulted in no reaction (Scheme 6). This is most likely due to the fact that similar to Suzuki coupling, the Stille reaction is limited to relatively sterically unencumbered substrates.

Fortuitously, recent work by Motherwell and co-workers [23] has shown that tethering the two rings with a sulfonate linkage followed by a radical-induced 1,5-*ipso* substitution works best for sterically hindered biaryls. The process involves intramolecular free radical *ipso* substitution via a spirocyclic intermediate capable of re-aromatization

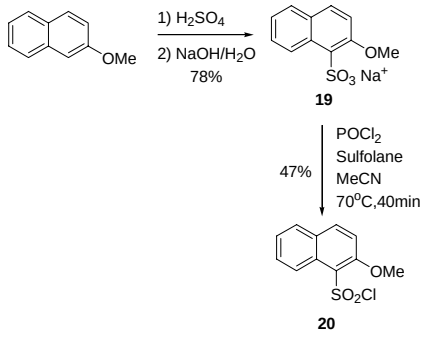


TMEDA = tetramethyl ethylenediamine

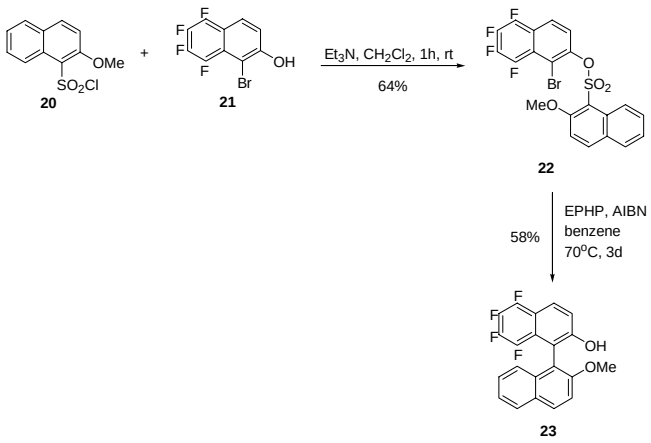
Scheme 5.



Scheme 6.



Scheme 7.



Scheme 8.

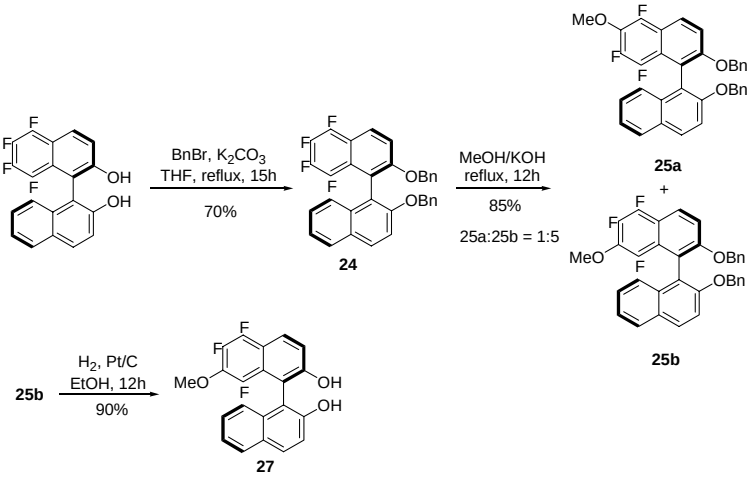
through loss of sulfur dioxide. The presence of bulky groups avoids the direct addition pathway. We therefore, decided that a logical solution to this challenge may be addition of one such linker prior to the coupling step.

The next step involved preparation of the sodium sulfonate salt **19** from 2-methoxynaphthalene by treatment with concentrated sulfuric acid at 80 °C for 10 min. Precipitation of the product with aqueous sodium hydroxide yielded the desired compound in 78% yield. The derivative **19** reacted with phosphorous oxychloride to generate the corresponding sulfonyl chloride **20** (Scheme 7). Coupling of alcohol **21**, prepared by demethylation of **4** with boron tribromide [8], with **20** in the presence of triethylamine gave the desired intermediate for the radical cross-coupling reaction (Scheme 8). The cross-coupling was carried out in the presence of 1-ethylpiperidine hypophosphite (EPHP) and AIBN in benzene at 70 °C for 2 days and gave the product in 65% conversion and 58% yield [24,25]. Demethylation of **23** resulted in racemic F_4BINOL.

2.1.3. Nucleophilic aromatic substitution

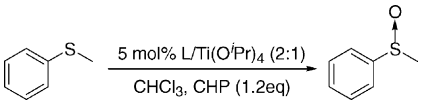
Nucleophilic aromatic substitution on F_4BINOL proceeded similar to our previous reports with F_8BINOL [11]. Initially, F_4BINOL was protected as the benzyl ether **24** using benzyl bromide and K_2CO_3. Nucleophilic aromatic substitution occurred at both the 6- and 7-positions of the fluorinated ring by using potassium methoxide (Scheme 9). Deprotection of **25b** using a catalytic amount of Pt/C (10 mol%) in the presence of H_2 afforded ligand **27** in 90% yield.

Alkyllithium species have also been used as nucleophiles to modify the 7-position of the fluorinated ring system. In this case, the reaction occurs by using unprotected F_4BINOL at −78 °C mixed with three equivalents of the organolithium reagent (Scheme 10). Lower reaction yields observed compared with alkoxides could be a result of the longer reaction times required at low temperatures.

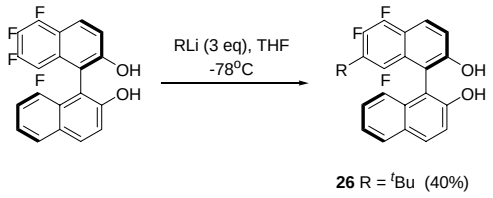


Scheme 9.

Table 1
Titanium-catalyzed oxidation of sulfides to sulfoxides



Entry	Ligand	Time (h)	Temperature (°C)	Yield (%)	e.e. (%)
1	(*R*)-BINOL	42	0	69	3
2	(*R*)-F$_8$BINOL	4.5	0	77	75
3	(*R*)-F$_4$BINOL	2	0	78	80
4	(*R*)-F$_4$BINOL	2	RT	46	75
5	(*R*)-F$_4$BINOL	18	−20	46	84
6	(*R*)-**27**	3	0	49	28
7	(*R*)-**26**	2	0	32	27



Scheme 10.

2.1.4. *F$_4$BINOL in catalysis: sulfoxidation reaction*

We previously, reported the asymmetric oxidation of sulfides to sulfoxides using F$_8$BINOL and its 7,7′-substituted derivatives [2,9]. Our initial results indicated that fluorine substitution is responsible for improved enantioselectivity where minimum amount of sulfone by-product is formed. An inverse sense of chiral induction is observed using our fluorinated ligands. Kinetic studies showed that the reaction catalyzed by **3**/Ti(IV) is five times faster than that catalyzed by **1**/Ti(IV). Optimized reaction conditions were used to compare our new ligands, F$_4$BINOL as well as its 7-substituted derivatives **26** and **27**, with previous examples. F$_4$BINOL gives the same sense of chiral induction as F$_8$BINOL. The yields and enantioselectivities obtained are also similar to those obtained with F$_8$BINOL was used as ligand (Table 1, entries 2–5).

Lowering the reaction temperature resulted in increased enantioselectivity, however, the yield decreased (entries 3–5). The best conditions were obtained at 0 °C where the product was obtained in 78% yield with 80% enantioselectivity. Whereas addition of water (2 eq.) increased the enantioselectivity of the reaction using F$_8$BINOL, no change was observed when F$_4$BINOL was used as the ligand.

When the reaction was catalyzed by F$_8$BINOL, the sulfone by-product was produced in greater amount than the reaction catalyzed using BINOL [9]. Surprisingly, no sulfone by-product was observed when F$_4$BINOL was used as the ligand. The presence of electron-withdrawing fluorine atoms on F$_8$BINOL makes the F$_8$BINOL/Ti catalyst more Lewis acidic than the corresponding BINOL/Ti catalyst. The overoxidation of sulfoxides to sulfone can, therefore, be attributed to the higher reactivity of F$_8$BINOL/Ti catalyst. The average pKa of F$_4$BINOL is 9.8, just between that of F$_8$BINOL (10.3) and BINOL (9.3) [26]. Based on Lewis acidity, one would, therefore, expect its reactivity to be also somewhere between the F$_8$BINOL and BINOL. When ligands (*R*)-**26** and (*R*)-**27** are used, both the yield and enantioselectivity of the reaction are dramatically decreased (entries 6 and 7).

3. Conclusion

In summary, new partially fluorinated binaphthols have been synthesized using oxidative coupling. We have shown that different substituents can be placed on the fluorinated naphthyl ring, allowing easy access to a variety of different ligands. When the substitution is performed on enantiomerically pure starting materials, no change in enantioselectivity is observed. The catalytic applications of F$_4$BINOL in sulfoxidation show that the ligand produces no sulfone by-product and gives the product with moderate enantioselectivity.

3.1. General considerations

All commercial reagents were used as such without purification. Wherever necessary, solvents were dried as per the standard procedures. Melting points were taken using a capillary melting point apparatus. Unless otherwise stated, all ^{1}H NMR measurements were carried out at 400 MHz and ^{13}C NMR at 100 MHz using TMS as internal standard. ^{19}F NMR measurements were carried out at 300 MHz using CFCl$_3$ as internal standard. Column chromatographic purifications were performed using silica gel with 230–400 mesh size. Compounds **4** and **16** were prepared according to literature procedures [8]. Characterization for compound **20** was verified according to literature [27].

3.1.1. *2-Methoxy-naphthalene-1-sodium sulfonate (**19**)*

Concentrated sulfuric acid (35 ml) was added to 2-methoxynaphthalene (48 g, 300 mmol) at room temperature. The white solid immediately turned red. The mixture was heated to 80 °C for 30 min until all the solid melted and the starting

material disappeared on TLC. A solution of 5% NaOH was slowly added until the solution was basic. The white precipitate was filtered and dried in vacuo overnight (65.6 g, 80%). Decomposes at >250 °C ^{1}H NMR (400 MHz, D_2O) δ 8.16 ppm(1H, s), 7.86 (2H, t, $J = 8.69$), 7.68 (1H, dd, $J = 8.69$), 7.29 (1H, d, $J = 2.38$), 7.18 (1H, dd, $J = 9.06$), 3.84 (3H, s); ^{13}C NMR (100 MHz, D_2O) δ 158.3, 137.4, 135.4, 130.5, 127.9, 127.4, 125.4, 122.5, 119.4, 106.3, 55.7. MS-EI *m/z* found 237.

3.1.2. 2-Methoxy-naphthalene-1-sulfonyl chloride (**20**)

To a solution of **19** (65 g, 239 mmol) in equal amounts of tetramethylene sulfone (150 ml) and acetonitrile (150 ml) was added phosphorous oxychloride (41 ml, 441 mmol) dropwise on ice. The reaction was warmed to room temperature, and then heated to 70 °C for 2 h. The mixture was cooled to 4 °C in an ice bath. Water was added dropwise keeping the temperature at 4 °C until all excess $POCl_3$ was quenched. The resulting mixture was extracted with dichloromethane and purified by flash column chromatography (8:2 hexanes:ethyl acetate) to afford a yellow powder (36 g, 48%). Mp: 65 °C; ^{1}H NMR ($CDCl_3$) δ 8.50 ppm (1H, s), 7.89–7.96 (m, 3H), 7.31 (dd, $J = 2.4$ Hz, $J = 9.0$ Hz, 1H), 7.21 (d, $J = 2.56$ Hz, 1H), 3.97 (3H, s); ^{13}C NMR ($CDCl_3$) δ 161.43, 139.02, 138.10, 131.65, 129.04, 128.79, 127.18, 122.36, 121.66, 106.26, 55.86.

3.1.3. Bromo-2-hydroxy-5,6,7,8-tetrafluoronaphthalene (**21**)

To a solution of **4** (927 mg, 3 mmol) in dichloromethane (15 ml) was added BBr_3 (2.25 g, 9 mmol) at room temperature under nitrogen atmosphere. The reaction was stirred for 15 h at room temperature, then cooled to 0 °C and quenched by slow addition of water. The aqueous layer was separated and the organic layer was washed with water (15 ml) twice, dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude solid was purified by flash column chromatography on silica gel. Elution with hexanes/ethyl acetate (8:2) afforded the product as white solid (97%). ^{1}H NMR ($CDCl_3$) δ 7.97 (d, $J = 9.16$, 1H), 7.35 (d, $J = 9.16$, 1H), 6.41(s, 1H); ^{19}F NMR (300 MHz, $CDCl_3$): δ −145.4, −148.5, −155.8, −161.3; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 143.4, 141.7, 140.85, 139.2, 137.6, 135.1, 122, 118.7, 99.2. HREI-MS, *m/z*: Calcd for $C_{10}H_3OF_4$ 293.9303; found 293.9313.

3.1.4. 2-Methoxy-naphthalene-1-sulfonic acid 1-bromo-5,6,7,8-tetrafluoro-naphthalen-2-yl ester (**22**)

To a solution of **20** (14 g, 52 mmol) and **21** (13 g, 52 mmol) in dichloromethane (200 ml) at 0 °C was added triethylamine (8.7 ml, 62.7 mmol) dropwise. The reaction was warmed to room temperature and stirred for 24 h. Water was added and the organic layer was separated. The aqueous layer was extracted with dichloromethane (100 ml). The combined organic layers were washed with dilute HCl, dried over Na_2SO_4 and concentrated in vacuo. Flash column chromatography with hexanes/ethyl acetate (9:1) resulted in product as a light yellow solid (20 g, 76%).Mp: 173 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 8.47(s, 1H), 8.01 (dd, $J = 8.8$ Hz, $J = 1.83$ Hz 1H), 7.46 (d, $J = 9.2$, 1H), 7.34(d, $J = 8.6$ Hz, 1H), 7.28 (d, $J = 9.3$ Hz), 7.17 (d, $J = 8.0$ Hz, 1H), 6.94 (dd, $J = 8.8$ Hz, $J = 2.6$ Hz, 1H), 6.66(d, $J = 2.4$, 1H), 3.23(s, 3H); ^{19}F NMR (300 MHz, C_6D_6) δ −140.4 (t, $J = 16.8$ Hz), −148.18 (t $J = 19.8$ Hz), −155.2 (t, $J = 19.8$ Hz), −157.5 (t, $J = 22.9$ Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 160.8, 147.2, 144.1, 140.3, 138.7, 137.7, 136.7, 134.1, 131.2, 130.7, 130.2, 128, 7, 128.2, 127.4, 124.3, 124.1, 121.1, 116.8, 106.1, 55.7. HREI-MS, *m/z*: Calcd for $C_{21}H_{11}O_4F_4SBr$ 513.9497; found 513.9498.

3.1.5. 5,6,7,8-Tetrafluoro-2′-methoxyl-[1,1′]binaphthalenyl-2-ol (**23**)

A solution of **22** and EPHP in benzene (0.5 ml) was refluxed for 1 h. AIBN (45 mg, 0.27 mmol) was added in two portions over 30 min and the reaction was refluxed for additional 3 h, then cooled to room temperature. Water (2 ml) and ether (2 ml) were added. The organic layer was separated and the aqueous layer was extracted with ether (1 ml) twice. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification by flash column chromatography on silica gel with hexanes/ethyl acetate (8:2) afforded the product as a yellow solid (54 mg, 38%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, $J = 8.8$ Hz, 1H), 7.91(d, $J = 8.4$ Hz, 1H), 7.78(d, $J = 10$ Hz, 2H), 7.39 (t, $J = 9.2$ Hz, 2H), 7.25(m, 2H), 3.99(s, 3H). ^{19}F NMR (300 MHz, $CDCl_3$) δ −142.4 (t, $J = 15.3$ Hz), −150.4 (t, $J = 18.3$ Hz), −158.46(t, $J = 18.3$ Hz), −163.3 (t, $J = 19.8$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 158.4, 152.8, 137.0, 134.5, 134.4, 129.5, 128.9, 128.8, 128.76, 128.7, 128.3, 128.2, 128.0, 127.8, 121.8, 119.8, 119.6, 118.9, 105.8, 55.4. MS-EI, *m/z* found 372.

3.1.6. 5,6,7,8-Tetrafluoro-[1,1′]binaphthalenyl-2,2′-diol (**2**)

To a mixture of **23** (7 mg, 0.3 mmol) in dichloromethane (1 ml) was added boron tribromide (15 mg, 0.6 mmol) at room temperature. The reaction was stirred for 15 h at room temperature and then cooled to 0 °C and quenched by slow addition of water. The aqueous layer was separated and the organic layer was washed with water (1 ml) twice, dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford an orange solid. Purification with flash column chromatography with hexanes/ethyl acetate (7:3) resulted in pure F_4BINOL (7 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (s, 1H), 5.35 (s, 1H), 7.09 (d, $J = 7.8$ Hz, 1H), 7.30–7.40 (m, 3H), 7.48 (d, $J = 9$ Hz, 1H), 7.88 (d, $J = 7.8$ Hz, 1H), 7.96 (d, $J = 8.7$ Hz, 1H), 8.20 (d, $J = 7.8$ Hz, 1H). ^{19}F NMR (280 MHz, $CDCl_3$) δ −147.63, −149.59, −156.91, −162.25. HRMS (EI) *m/z* calcd for $[C_{20}H_{10}O_2F_4]$ 358.0617 found 358.1617.

3.2. Oxidative coupling method

A 250 ml round-bottom flask containing a mixture of **16** (1 g, 4.97 mmol), 2-naphthol (500 mg, 3.48 mmol), and Cu(OH)Cl·TMEDA (107 mg, 0.5 mmol) was placed in an oven at 130 °C for 24 h, then cooled to room temperature. Ether (25 ml) was added and the mixture was washed with water (50 ml) three times, dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting brown oil was purified by flash column chromatography with gradient elution from 100% hexanes to a 7:3 mixture of hexanes/ethyl acetate to afford F_4BINOL as a light yellow solid (270 mg, 47%).

3.2.1. Bis[(−)-menthl]5,6,7,8-tetrafluoro-1,1′-binaphthyl-2.2′-biscarbonate (*15*)

To a solution of **2** (1.0 g, 3 mmol) in dichloromethane (100 ml), pyridine (4 ml), (−)-menthyl chloroformate (2.2 g, 10 mmol), and 4-(dimethylamino)pyridine (10 mg) were added in sequence. The mixture was allowed to stir at room temperature for 2 h. A solution of 2 M aqueous hydrochloric acid (50 ml) was added. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 100 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuo to give a mixture of two diastereomers as brown oil. This mixture was purified by silica gel flash column chromatography (hexane/EtOAc 20:1) to afford a mixture of the two diastereomers (1.6 g, 80%). Recrystallization in methanol/2-propanol (5:1) afforded (*R*)-F_4BINOL-(−)-menthyl carbonate as white crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (d, $J = 7.2$ Hz, 3H), 0.38 (d, $J = 6.9$ Hz, 3H), 0.53 (d, $J = 6.9$ Hz, 3H), 0.67 (d, $J = 6.9$ Hz, 3H), 0.75–1.90 (m, 24H), 4.15–4.35 (m, 2H), 7.23 (t, $J = 8.24$ Hz, 1H), 7.32 (td, $J = 6.9$ Hz, $J = 0.9$ Hz, 1H), 7.43–7.48 (m 2H), 7.61 (d, $J = 9.3$ Hz, 1H), 7.90 (d, $J = 8.1$ Hz, 1H), 7.97 (d, $J = 8.7$ Hz, 1H), 8.24 (d, $J = 9.6$ Hz, 1H). ^{19}F NMR (280 MHz, $CDCl_3$) δ −141.13, −149.66, −156.38, −158.89.

3.2.2. (R)-5,6,7,8-Tetrafluoro-[1,1′]binaphthalenyl-2,2′-diol (*2*)

To **15** (single diastereomer, 0.7 g, 1 mmol) in freshly distilled THF (20 ml) was added lithium aluminum hydride portion wise at 0 °C. The mixture was stirred at that temperature for 2 h. A solution of 5% aqueous HCl was added and the product was extracted with diethyl ether (3 × 20 ml). The combined extracts were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The product was purified by flash column chromatography (gradient from 100% hexanes to 30% EtOAc in hexanes) to give (*R*)-F_4BINOL ($[a]_{21}^{D} = 59°$, $c = 1.64$, THF) as an off-white powder (350 mg, 95%). Enantiomeric excess determination was performed using chiral HPLC analysis (CHIRALPAK AD column, Daicel co., Japan, 1 ml/min, hexanes : ^{i}PrOH 9:1, λ_{max} 230 nm) $R_t = 16.51$ min, (*R*)-isomer, $R_t = 17.54$ min, (*S*)-isomer >99% e.e.

3.2.3. 2,2′-bis-benzyloxy-5,6,7,8-Tetrafluoro-[1,1′]-binaphthalenyl (*24*)

To a mixture of **2** (100 mg, 0.28 mmol) and benzyl bromide (0.34 ml, 2.8 mmol) in THF (10 ml) was added potassium carbonate (0.31 g, 2.25 mmol). The mixture was refluxed for 24 h at which point TLC analysis showed complete consumption of the starting material. A solution of 5% aqueous HCl was added and the product extracted with diethyl ether (3 × 5 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuo. Purification by flash column chromatography (hexane/EtOAc 8:2) afforded the product as a yellow solid (105 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93 (s, 2H), 5.00 (s, 2H), 6.70–7.40 (m, 15H), 7.80 (t, $J = 9$ Hz, 2H), 8.05 (d, $J = 8.4$ Hz, 1H). ^{19}F NMR (300 MHz, $CDCl_3$) δ −144.4 (t, $J = 16.8$ Hz), −150.3 (t, $J = 15.3$ Hz), −158.0 (t, $J = 18.3$ Hz), −162.7 (t, $J = 19.8$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 153.4, 137.4, 136.6, 133.7, 129.3, 129.2, 128.2, 128.1, 128.0, 127.5, 127.4, 126.6, 126.5, 126.4, 124.5, 123.6, 121.6, 121.0, 120.9, 120.6, 117.7, 117.6, 116.7, 116.0, 115.8, 115.3, 115.2, 71.1, 70.9.

3.2.4. 2,2′-bis-benzyloxy-5,6,8-Trifluoro-7-methoxy-[1,1′]-binaphthalenyl (*25b*)

A solution of **24** (25 mg, 0.05 mmol) and potassium hydroxide (26 mg, 0.5 mmol) in methanol (2 ml) was refluxed for 10 h under N_2 atmosphere. The mixture was cooled to room temperature and diluted with ether (2 ml). A 5% solution of hydrochloric acid was added and the organic layer was separated. The aqueous layer was extracted with ether twice. The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash column chromatography (hexanes/EtOAc 8:2) to afford the product as a white solid (23 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, $J = 9.3$ Hz, 1H), 7.74–7.80 (m, 3H), 7.68 (s, 1H), 7.52 (m, 3H), 7.31–7.45 (m, 6H), 7.21–7.27 (m, 3H), 7.18–7.20 (m, 3H), 5.24 (s, 2H), 5.08 (s, 2H), 4.09 (s, 3H for 6-substituted product), 3.92 (s, 3H for 7-substituted product). ^{19}F NMR (300 MHz, $CDCl_3$) δ −132.6 (d, $J = 16.8$ Hz), −152.5 (t, $J = 25.2$ Hz), −157.0 (d, $J = 18.3$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 154.7, 137.0, 136.7, 133.5, 132.6, 129.6, 128.8, 128.6, 128.5, 128.4, 128.35, 128.3, 128.25, 128.24, 128.20, 128.0, 127.8, 127.7, 127.6, 127.5, 126.8, 125.8, 121.2, 119.1, 119.0, 116.4, 107.2, 71.5, 70.1, 62.3.

3.2.5. 7-tert-butyl-5,6,8-Trifluoro-[1,1′]-binaphthalenyl-2,2′-diol (*26*)

To a solution of **2** (50 mg, 0.14 mmol) in dry Et_2O (2 ml) was added *t*-BuLi (1.7 M in pentane, 0.42 mmol) at −78 °C. The reaction was stirred at −78 °C for 2 h, then warmed to room temperature and stirred overnight. Water (5 ml) was added to quench the reaction. The organic layer was separated and washed with a solution of 5% aqueous hydrochloric acid (5 ml), dried over Na_2SO_4 and concentrated in vacuo. The brown oil obtained was purified using flash

column chromatography (hexanes/EtOAc 7:3) to afford the product as white powder (22 mg, 40%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, $J = 11$ Hz, 1H), 7.90 (m, 2H), 7.35 (m, 4H), 7.15 (m, 1H), 5.2 (b, 2H), 1.34 (s, 9H). ^{19}F NMR (300 MHz, $CDCl_3$) δ −116.5 (d, $J = 6.0$ Hz), −139.23 (d, $J = 14.7$ Hz), −153.4 (t, $J = 14.7$ Hz). MS-EI, *m/z* found 396.

*3.2.6. 5,6,8-Trifluoro-7-methoxy-[1,1′]-binaphthalenyl-2,2′-diol (**28**)*

A solution of **25** (20 mg, 0.036 mmol) in EtOH (1 ml) was stirred under argon for 5 min. Pd/C (10 mg, 10%) was added and the reaction was stirred under H_2 atmosphere at room temperature for 12 h, then filtered through a pad of silica gel and concentrated. The crude product was purified using flash column chromatography (7:3 hexane/EtOAc) to afford the product as white powder (12 mg, 90%). ^{1}H NMR (400 MHz, $CD_3CN/CDCl_3$) δ 7.95 (d, $J = 9.2$ Hz, 1H), 7.69–7.77 (m, 3H), 7.51 (s, 2H), 7.26–7.33 (m, 2H), 7.21 (s, 1H), 7.12 (dd, $J = 2.5$ Hz, $J = 8.8$ Hz, 1H), 4.04 (s, 3H for 6-substituted product), 3.87 (s, 3H for 7-substituted product). ^{19}F NMR (300 MHz, $CD_3CN/CDCl_3$) δ −135.0 (d, $J = 14.5$ Hz), −153.1 (t, $J = 16.0$ Hz), −159.6 (d, $J = 19.1$ Hz).

3.2.7. General procedure for the oxidation of methyl p-tolyl sulfide

To a mixture of (*R*)-F_4BINOL (0.025 mmol, 0.0978 M solution in chloroform) and $Ti(OiPr)_4$ (0.0125 mmol, 0.669 M solution in chloroform) in 0.5 ml of chloroform was added water (4.5 μl, 0.25 mmol). The mixture was stirred under N_2 atmosphere for 30 min then cooled to 0 °C for 15 min. Methyl *p*-tolyl sulfide (33 μl, 0.25 mmol) and cumyl hydroperoxide (55.5 μl, 0.3 mmol) were added at an interval of 15 min. The reaction was stirred for 16 h and loaded onto a short silica gel pad. The product was obtained as a white solid from elution by EtOAc/hexanes (1:1) followed by pure ethyl acetate (78%). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK AS column, Daicel co., Japan, 1 ml/min, hexane : ^{i}PrOH = 7 : 3, λ_{max} 230 nm) $R_t = 16.51$ (*R*)-isomer, $R_t = 17.54$ min (*S*)-isomer (80% e.e.).

Acknowledgements

We thank NSERC, Canada Foundation for Innovation, ORDCF, and University of Toronto for financial support. Andrei Yudin is a Cottrell Scholar of Research Corporation.

References

[1] H.B. Kagan, in: J.D. Morrison (Ed.), Asymmetric Synthesis, vol. 5, Academic Press, New York, 1985, pp. 1–39.
[2] Y. Chen, S. Yekta, A.K. Yudin, Chem. Rev. 103 (2003) 3155.
[3] (a) K. Mikami, M. Shimizu, Chem. Rev. 92 (1992) 1021–1050;
(b) K. Mikami, M. Terada, T. Nakai, J. Am. Chem. Soc. 112 (1990) 3949–3954;
(c) M. Terada, Y. Motoyama, K. Mikami, Tetrahedron Lett. 35 (1994) 6693–6696;
(d) K. Mikami, Y. Motoyama, M. Terada, Inorg. Chim. Acta 222 (1994) 71–75.
[4] K. Maruoka, A.B. Concepcion, H. Yamamoto, Bull. Chem. Soc. Jpn. 65 (1992) 3501–3503.
[5] M. Aizenberg, D. Milstein, Science 265 (1994) 359–361.
[6] (a) A.P. West, S. Mecozzi, D.A. Dougherty, J. Phys. Org. Chem. 10 (1997) 347–350;
(b) J.H. Williams, Acc. Chem. Res. 26 (1993) 593–598.
[7] J.T. Welch, D. Peters, R. Miethchen, A.Y. Il'chenko, S. Rüdiger, J. Podlech, in: B. Baasner, H. Hagemann, J.C. Tatlow (Eds.), Organo-Fluorine Compounds, 4th ed., vol. E10b/Part 2, Georg Thieme Verlag, Stuttgart, 2000, pp. 293–459.
[8] A.K. Yudin, L.J.P. Martyn, S. Pandiaraju, J. Zheng, A. Lough, Org. Lett. 2 (2000) 41–44.
[9] L.J.P. Martyn, S. Pandiaraju, A.K.J. Yudin, Organomet. Chem. 603 (2000) 98–104.
[10] S. Pandiaraju, G. Chen, A. Lough, A.K. Yudin, J. Am. Chem. Soc. 123 (2001) 3850–3851.
[11] Y. Chen, S. Yekta, L.J.P. Martyn, J. Zheng, A.K. Yudin, Org. Lett. 2 (2000) 3433–3436.
[12] (a) M.S. Newman, J.A. Cella, J. Org. Chem. 39 (1974) 2084–2087;
(b) S. Miyano, M. Tobita, M. Nawa, S. Sato, H. Hashimoto, J. Chem. Soc. Chem. Commun. 24 (1980) 1233–1234;
(c) S. Miyano, M. Tobita, H. Hashimoto, Bull. Chem. Soc. Jpn. 54 (1981) 3522–3526;
(d) R. Hong, R. Hoen, J. Zhang, G.-Q. Lin, Synlett 10 (2001) 1527–1530;
(e) G.-Q. Ling, R. Hong, J. Org. Chem. 66 (2001) 2877–2880.
[13] (a) R. Pummerer, E. Prell, A. Rieche, Chem. Ber. 59 (1926) 2159;
(b) M. Noji, M. Nakajima, K. Koga, Tetrahedron Lett. 35 (1994) 7983–7984;
(c) M. Nakajima, I. Miyoshi, K. Kanayama, S. Hashimota, M. Noji, K. Koga, J. Org. Chem. 64 (1999) 2264–2271;
(d) Z. Xin, C. Da, S. Dong, D. Liu, J. Wei, R. Wang, Tetrahedron: Asymmetry 13 (2002) 1937–1940.
[14] (a) S. Gronowitz, V. Bobosik, K. Lawitz, Chem. Scripta 23 (1984) 120;
(b) S. Gronowitz, A.-B. Honfeldt, Y. Wang, Chem. Scripta 28 (1988) 281;
(c) W.J. Thompson, J. Gaudino, J. Org. Chem. 49 (1984) 5237;
(d) T. Watanabe, N. Miyaura, A. Suzuki, Synlett 3 (1992) 207.
[15] D.M. Hall, E.E. Turner, J. Chem. Soc. 4 (1955) 1242.
[16] T. Hamada, H. Ishida, S. Usui, Y. Watanabe, K. Tsumura, K. Ohkubo, J. Chem. Soc. Chem. Commun. 11 (1993) 909.
[17] J. Doussot, A. Guy, C. Ferroud, Tetrahedron Lett. 41 (2000) 2545.
[18] W.L. Carrick, G.L. Karapinka, G.T. Kwiatkowski, J. Org. Chem. 38 (1969) 2388.
[19] B. Feringa, H. Wynberg, J. Org. Chem. 46 (1981) 2547.
[20] (a) B. Feringa, H. Wynberg, Tetrahedron Lett. 50 (1997) 4447;
(b) J. Brussee, J.L.G. Groenendijk, M. te, A.C.A. Jansen, Tetrahedron 41 (1985) 3313;
(c) M. Smrcina, J. Poláková, Š. Vyskocil, P. Kocovský, J. Org. Chem. 58 (1993) 4534.
[21] (a) F. Toda, K. Tanaka, S. Iwata, J. Org. Chem. 54 (1989) 3007;
(b) K. Ding, Y. Wang, L. Zhang, Y. Wu, Tetrahedron 52 (1996) 1005;
(c) H.-J. Deußen, P. Frederiksen, T. Bjørnholm, K. Bechgaard, Org. Prep. Proced. Int. 28 (1996) 484.
[22] (a) M. Kosugi, K. Fugami, J. Organomet. Chem. 653 (2002) 50–53;
(b) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, Chem. Rev. 102 (2002) 1359–1469;
(c) T. Okujima, S. Ito, N. Morita, Tetrahedron Lett. 43 (2002) 1261–1264;
(d) M.A. Brimble, L.J. Duncalf, Aust. J. Chem. 52 (1999) 19–29;
(e) G.P. Roth, V. Farina, Tetrahedron Lett. 36 (1995) 2191–2194.

[23] (a) M. da Mata, W.B. Motherwell, F. Ujjainwalla, Tetrahedron Lett. (1997) 137.;
(b) M. da Mata, W. Motherwell, F. Ujjainwalla, Tetrahedron Lett. 1 (1997) 141;
(c) E. Bonfand, L. Forslund, W.B. Motherwell, S. Vazquez, Synlett 4 (2000) 475.
[24] (a) T. Laird, S.A. Hermitage, U. Tilstam, Org. Process Res. Dev. 6 (2002) 90;
(b) D.O. Jang, D.H. Cho, C.-M. Chung, Synlett 12 (2001) 1923.
[25] (a) S.R. Graham, J.A. Murphy, D. Coates, Tetrahedron Lett. 40 (1999) 2415;
(b) C.G. Martin, J.A. Murphy, C.R. Smith, Tetrahedron Lett. 41 (2000) 1833.
[26] G. Chen, Synthesis and asymmetric catalysis study of fluorinated BINOL ligands, M.Sc. Thesis, University of Toronto, 2001.
[27] H.J.E. Loewenthal, L. Gottlieb, J. Org. Chem. 57 (1992) 2631.