Tetrahedron 64 (2008) 11852–11859

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Atroposelective radical aryl migration reactions from sulfur to carbon

Birte Schulte, Roland Fröhlich †, Armido Studer *

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität, Corrensstraße 40, 48149 Münster, Germany

ARTICLE INFO

Article history:
Received 30 May 2008
Accepted 12 August 2008
Available online 20 September 2008

ABSTRACT

The paper describes stereoselective radical aryl migration reactions from sulfur in sulfonates to aryl radicals for the synthesis of axially chiral biaryls. A chirality center in secondary benzylic sulfonates is used to diastereoselectively (atroposelectively) install a stereogenic axis via a 1,5 aryl migration reaction. Atroposelectivity has not been investigated in stereoselective radical chemistry before. Good yields (53–82%) but low selectivities (up to 2 to 1) were obtained.

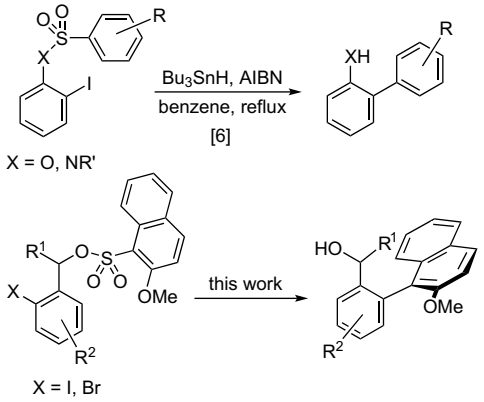
1. Introduction

Functionalized biaryls are often used as ligands in catalytic asymmetric synthesis.[1] Moreover, biaryls occur in many natural products[2] and they are also found as components in new organic materials.[3,4] Biaryls are most often prepared by using transition metals to couple the two arene subunits.[1,5] In addition, radical chemistry has been successfully used for biaryl synthesis. In pioneering studies Motherwell showed that biaryls can be prepared via 1,4 as well as 1,5 aryl migration reactions from sulfur to aryl radicals (Scheme 1).[6–8] Readily available arenesulfonates as well as arenesulfonamides were used as starting materials in these reactions. Radical biaryl synthesis was also achieved via aryl migration from phosphorous to aryl radicals in phosphonates[9] and from silicon to aryl radicals in phenylsilylethers.[10] Importantly, radical aryl migration from sulfur[11] or silicon[12] to secondary alkyl radicals was used for stereoselective C(sp^2)–C(sp^3)-bond formation. To the best of our knowledge radical aryl migration has not been applied to stereoselectively synthesize axially chiral biaryls.[1b,13] We assumed that the chirality center in secondary benzylic sulfonates might be used to diastereoselectively (atroposelectively) install a stereogenic axis via a 1,5 aryl migration reaction (see Scheme 1). Herein we present first results on atroposelective radical aryl migration reactions from sulfur to aryl radicals.

2. Results and discussion

Radical precursors **8**–**13** were readily prepared in good yields (60–82%) from the corresponding secondary benzylic alcohols **1**–**6** and sulfonyl chloride **7** in CH_2Cl_2 by using NEt_3 in combination with $NMe_3 \cdot HCl$ as bases.[14,15] The syntheses of **1**–**6** are described in (Scheme 2) Section 3.

Radical aryl migrations were best conducted by slow addition (syringe pump, 7 h) of a benzene solution of Bu_3SnH (1.5 equiv) and V-40 (1,1′-azobis(cyclohexane-1-carbonitrile), 1.0 equiv) to a solution of the arenesulfonate (**8**–**13**) in refluxing benzene (0.03 M) to afford the corresponding aryl transfer products **14**–**18** in 53–84% yield (Scheme 3, Table 1). Aryl transfer reaction with **8** under these conditions gave the desired biaryls **14a** and **14b** in good yields with moderate selectivity (**14a**: 30%, **14b**: 54%). By using AIBN (α,α′-azobisisobutyrodinitrile) as an initiator the aryl transfer products were isolated in a slightly lower combined yield with the same selectivity (**14a**: 24%, **14b**: 43%). We also ran the reaction at rt by using Et_3B/O_2 as an initiator under otherwise identical conditions. However, selectivity was not improved (**14a**/**14b**=1:1.8) and a slightly lower combined yield was obtained (50%). Importantly, the two diastereoisomers were readily separated by flash chromatography (SiO_2). The relative configuration of **14a** and **14b** was



Scheme 1. Radical aryl migration for the preparation of biaryls.

* Corresponding author. Tel.: +49 (0)251 8333291; fax: +49 (0)251 8336523.
E-mail address: studer@uni-muenster.de (A. Studer).
† X-ray structure analysis.

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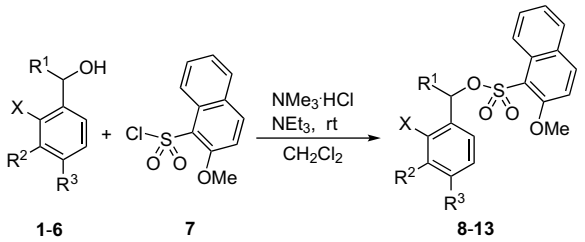
doi:10.1016/j.tet.2008.08.111

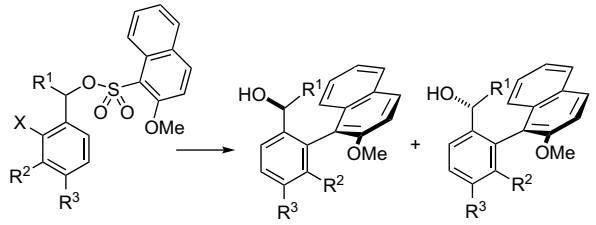


1-6 7 8-13

1, **8** (R^1 = Me, R^2 = R^3 = H, X = Br) **8** (82%)
2, **9** (R^1 = Me, R^2 = R^3 = H, X = I) **9** (66%)
3, **10** (R^1 = R^2 = Me, R^3 = H, X = Br) **10** (70%)
4, **11** (R^1 = Me, R^2 = H, R^3 = F, X = Br) **11** (65%)
5, **12** (R^1 = Me, R^2 = H, R^3 = CO_2Me, X = Br) **12** (70%)
6, **13** (R^1 = *i*-Pr, R^2 = R^3 = H, X = Br) **13** (60%)

Scheme 2. Preparation of radical precursors **8**–**13**.

unambiguously assigned by X-ray analysis (Fig. 1).[16] As expected, reaction with iodide **9** under optimized conditions (Bu_3SnH, 1.5 equiv; V-40, 1.0 equiv; benzene reflux) gave the same selectivity. The two diastereoisomers **14a** and **14b** were isolated in 20% and 36% yield, respectively. Reaction of **9** with $(Me_3Si)_3SiH$ in benzene in the presence of pyridine and catalytic amounts of I_2 with dioxygen as an initiator at rt did not result in product formation.[17]



8-13 14a-18a 14b-18b

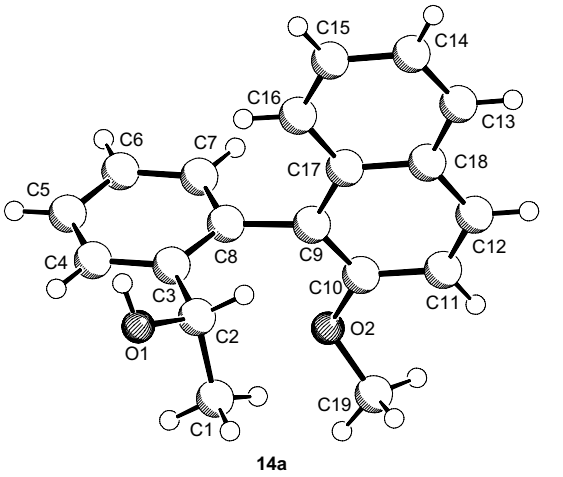
Scheme 3. Atroposelective radical aryl migration. Conditions: Bu_3SnH (1.5 equiv), V-40 (1.0 equiv), syringe pump, 7 h, refluxing benzene. Only one enantiomer drawn. For specification of R^1, R^2, and R^3 see Scheme 2 and Table 1.

To improve atroposelectivity, we replaced the methyl group at the benzylic position by a sterically more demanding isopropyl group (→**13**). However, selectivity could not be improved. The two isomers **18a** and **18b** were formed as a 1:1.8 mixture of diastereoisomers in 60% combined yield. The relative configuration of **18b** was assigned by X-ray analysis (Fig. 2). Since the two isomers **a** and **b** of **14** and **18** showed characteristic behavior during SiO_2-chromatography (isomer **a** eluted far faster than **b**), the relative configuration of the isomers of all other products (**15**–**17**) was assigned in analogy. The assignment of the relative configuration was further supported by the characteristic chemical shifts of the benzylic OH proton of the isomeric biaryls in the ^{1}H NMR spectra.

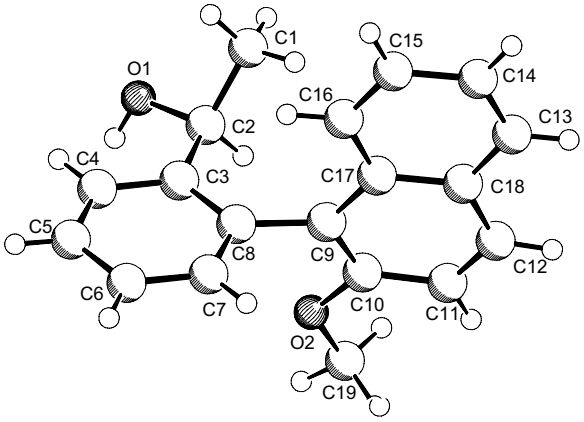
To influence atroposelectivity, we also tested a system bearing a methyl substituent at the *ortho*-position of the attacking aryl radical. Disappointingly, an even lower selectivity was obtained for

Table 1
Diastereoselective radical aryl migration with sulfonates **8**–**13** (S.M.=starting material)

S.M.	R^1	R^2	R^3	**a** (yield)	**b** (yield)
8	Me	H	H	**14a** (30%)	**14b** (54%)
9	Me	H	H	**14a** (20%)	**14b** (36%)
10	Me	Me	H	**15a** (21%)	**15b** (32%)
11	Me	H	F	**16a** (19%)	**16b** (40%)
12	Me	H	CO_2Me	**17a** (23%)	**17b** (43%)
13	*i*-Pr	H	H	**18a** (21%)	**18b** (39%)



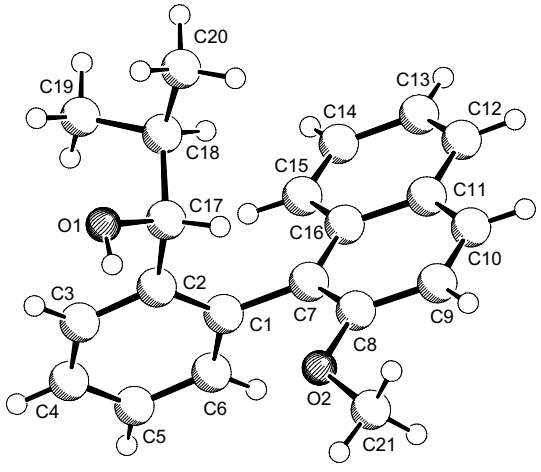
14a



14b

Figure 1. Molecular structure of biaryls **14a** and **14b**.

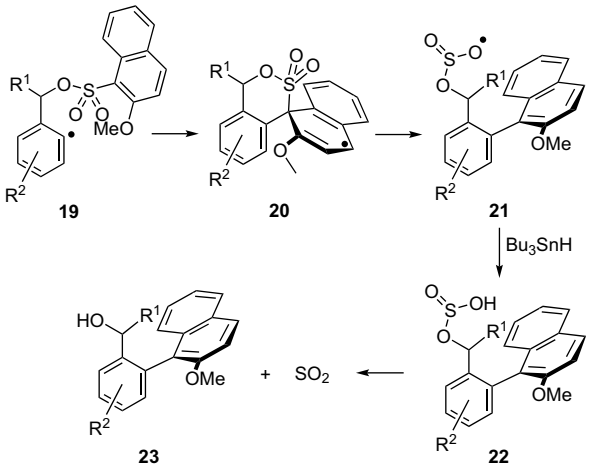
radical aryl migration reaction with sulfonate **10**. Biaryls **15a** and **15b** were isolated in 21% and 32% yield, respectively. It is obvious that a substituent in *meta*-position to the attacking radical should not alter the selectivity to a large extent. In fact, the fluorinated sulfonate **11** delivered the diastereoisomers **16a** and **16b** in a 1:2 atroposelectivity in 60% combined yield. A similar result was achieved with ester **12** (**17a**: 23%, **17b**: 43%).



18b

Figure 2. Molecular structure of biaryl **18b**.

We suggest the following mechanism for the radical aryl migration reaction (Scheme 4). Aryl radical **19** undergoes intramolecular *ipso* attack at the naphthyl group of the sulfonate to form a stabilized radical of type **20** (only one resonance structure drawn). Since only moderate selectivities were obtained we do not want to speculate about the low energy transition state for the formation of the major isomer **b**. Rearomatization then affords the alkoxysulfonyl radical **21**, which is probably slowly reduced with tin hydride to give **22**.[11b] SO_2 extrusion eventually leads to **23**. Large amounts of tin hydride (1.5 equiv) and V-40 (1.0 equiv) were necessary in order to get quantitative conversion in these aryl migration reactions. We believe that the reduction of the alkoxysulfonyl radical **21** with tin hydride is a very inefficient reaction that probably leads to chain termination. Moreover, compounds of type **22** can presumably also react with tin hydride in an ionic reaction consuming additional tin hydride. As already observed for aryl migration reactions to alkyl radicals, aryl transfers were not successful with $(Me_3Si)_3SiH$ as also observed in the present study for aryl migrations to aryl radicals (see above). We believe that the alkoxysulfonyl radical **21** is not reduced with $(Me_3Si)_3SiH$.



Scheme 4. Proposed mechanism of biaryl formation.

In summary, we presented first examples on atroposelective radical aryl migration reactions from sulfur in sulfonates to aryl radicals. The starting sulfonates were readily prepared. Although the present study was conducted with racemic sulfonates, enantiomerically pure radical precursor can be prepared from the corresponding alcohols that are accessible via various methods. The aryl migration reaction delivered the axially chiral biaryls in good yields. However, only moderate atroposelectivity was achieved. It is important to note that the two diastereoisomers formed were readily separated.

3. Experimental section

3.1. General

All reactions involving air or moisture sensitive reagents or intermediates were carried out in heat gun dried glassware under an argon atmosphere and were performed using standard Schlenk techniques. All solvents for extraction and flash chromatography were distilled before use. Acetic acid was purchased from Merck and used as received.

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker DPX 300 (at 300 K) or a Varian Inova 500 (at 298 K) spectrometer. Chemical shifts δ in parts per million are referenced to the solvent residual peak or $SiMe_4$ (δ=0 ppm) as an internal standard. IR spectra were recorded on a Digilab FTS 4000 equipped with a MKII Golden Gate Single Reflection ATR System. ESI-MS and HRMS were performed using a Bruker MicroTof. We were not able to get mass spectra of compounds **7**–**13**. TLC was carried out on Merck silica gel 60 F_{254} plates; detection by UV or dipping into a solution of $Ce(SO_4)_2\cdot H_2O$ (10 g), phosphormolybdic acid hydrate (25 g), concd H_2SO_4 (60 mL) and H_2O (0.94 L) or $NaHCO_3$ (5.0 g), $KMnO_4$ (1.5 g) and H_2O (0.20 L) followed by heating. Flash chromatography (FC) was carried out on Merck or Fluka silica gel 60 (40–63 μm) with an argon pressure of about 0.1–0.5 bar.

3.2. General procedure (GP1) for the $NaBH_4$ reduction

The acetophenone derivative was dissolved in ethanol and cooled to 0 °C. $NaBH_4$ was added in one portion. The suspension was stirred for 10 min at 0 °C, then allowed to warm to rt and stirred at that temperature for 12 h. After addition of satd aq NH_4Cl most of the ethanol was evaporated in vacuo. Diethylether was added to the remaining solution, which was subsequently washed with satd aq NH_4Cl and brine. The organic phase was dried ($MgSO_4$), evaporated, and FC finally yielded the desired alcohol.

3.3. 1-(2-Bromophenyl)ethanol (1)

Prepared according to GP1 using 2′-bromoacetophenone (5.00 mL, 37.1 mmol), $NaBH_4$ (5.60 g, 148 mmol, 4 equiv) in ethanol (150 mL). Purification by FC (pentane/diethylether 8:1) afforded 1-(2-bromophenyl)ethanol (**1**, 7.32 g, 36.4 mmol, 98%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, J=7.7, 1.7 Hz, 1H, C*H*CBr), 7.49 (dd, J=7.7, 1.2 Hz, 1H, C*H*CCBr), 7.32 (m, 1H, CH_{aryl}), 7.11 (ddd, J=7.8, 7.5, 1.8 Hz, 1H, CH_{aryl}), 5.20 (q, J=6.3 Hz, 1H, C*H*OH), 2.66 (br s, 1H, O*H*), 1.44 (d, J=6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6 (C), 132.4 (CH), 128.5 (CH), 127.7 (CH), 126.6 (CH), 121.5 (C), 68.9 (CH), 23.5 (CH_3); IR (neat, cm^{-1}) 3323 br m, 2976 m, 1568 m, 1469 m, 1429 m, 1369 m, 1199 m, 1128 m, 1091 s, 1024 s, 1005 s, 899 m, 752 s; HRMS (ESI) calcd for $[M+Na]^+$: 222.9729; found: 222.9755; Anal. calcd for C_8H_9BrO: C 47.79, H 4.51; found: C 47.76, H 4.53.

3.4. 1-(2-Iodophenyl)ethanol (2)

Prepared according to GP1 using 2′-iodoacetophenone (0.30 mL, 2.1 mmol), $NaBH_4$ (0.32 g, 8.5 mmol, 4 equiv) in ethanol (21 mL). Purification by FC (pentane/diethylether 5:1) afforded 1-(2-iodophenyl)ethanol (**2**, 0.52 g, 2.1 mmol, 99%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J=7.9 Hz, 1H, C*H*CI), 7.50 (dd, J=7.8, 1.3 Hz, 1H, C*H*CCI), 7.34 (dd, J=7.6, 7.5 Hz, 1H, CH_{aryl}), 6.93 (ddd, J=7.7, 7.5, 1.3 Hz, 1H, CH_{aryl}), 5.00 (q, J=6.3 Hz, 1H, C*H*OH), 2.66 (m, 1H, O*H*), 1.39 (d, J=6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4 (C), 139.0 (CH), 128.9 (CH), 128.5 (CH), 126.2 (CH), 97.0 (C), 73.4 (CH), 23.7 (CH_3); IR (neat, cm^{-1}) 3320 br m, 2973 m, 1566 m, 1464 m, 1430 m, 1198 m, 1125 m, 1088 m, 1066 m, 1003 s, 898 m, 752 s; HRMS (ESI) calcd for $[M+Na]^+$: 270.9590; found: 270.9596; Anal. calcd for C_8H_9IO: C 38.73, H 3.66; found: C 38.64, H 3.72.

3.5. 1-(2-Bromo-3-methylphenyl)ethanol (3)

To a solution of 2-bromo-3-methylbenzoic acid (0.50 g, 2.3 mmol) in methanol (6 mL) 2,2-dimethoxypropane (1.4 mL, 11 mmol, 5 equiv) and hydrochloric acid (12 M, 0.39 mL, 4.7 mmol, 2 equiv) were added. The reaction mixture was heated at reflux over night, cooled and most of the solvent was removed in vacuo. The residue was taken up in diethylether and washed with water. The organic extract was dried over $MgSO_4$ and evaporated to dryness to give methyl 2-bromo-3-methylbenzoate (0.50 g, 2.2 mmol, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, J=7.5 Hz, 1H, C*H*CCO), 7.33 (d, J=7.5 Hz, 1H, C*H*CCH$_3$), 7.22 (dd, J=7.5, 7.5 Hz, 1H, CHC*H*CH), 3.92 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3).

The methylester derivative (1.1 g, 4.8 mmol) was dissolved in toluene (25 mL), cooled to −78 °C and diisobutylalumium hydride (DIBAL, 1 M in heptane; 5.6 mL, 5.6 mmol, 1.2 equiv) was added via syringe pump over 1 h. After additional stirring for 1 h at −78 °C the reaction mixture was poured into a suspension of ice water and dichloromethane and stirred for 30 min. The mixture was extracted with diethylether (3×50 mL) and the combined organic layers were washed with brine and dried (Na_2SO_4). The residue was purified by FC (pentane/diethylether 20:1→6:1) to yield 2-bromo-3-methylbenzaldehyde (0.63 g, 3.2 mmol, 69%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.3 (s, 1H, C*H*O), 7.65 (ddd, *J*=7.7, 1.9, 0.52 Hz, 1H, C*H*CCO), 7.40 (ddd, *J*=7.5, 1.8, 0.60 Hz, 1H, C*H*CCH$_3$), 7.25 (dd, *J*=7.6, 7.6 Hz, 1H, CHC*H*CH), 2.40 (s, 3H, C*H*$_3$).

The aldehyde derivative (0.53 g, 2.7 mmol) was dissolved in tetrahydrofuran (15 mL) and the solution was heated to 80 °C. MeMgCl (3.0 M in tetrahydrofuran; 1.4 mL, 4.1 mmol, 1.5 equiv) was added dropwise and the suspension was heated to reflux for another 3 h. After cooling to rt, the reaction mixture was hydrolyzed with satd aq NH_4Cl and extracted with dichloromethane (3×30 mL). The combined organic layers were dried over $MgSO_4$ and the solvents were removed in vacuo. FC (pentane/diethylether 3:1) finally yielded 1-(2-bromo-3-methylphenyl)ethanol (**3**) as a colorless oil (0.55 g, 2.6 mmol, 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (br d, *J*=7.7 Hz, 1H, C*H*$_{aryl}$), 7.21 (dd, *J*=7.6, 7.5 Hz, 1H, C*H*$_{aryl}$), 7.13 (dd, *J*=7.4, 1.2 Hz, 1H, C*H*$_{aryl}$), 5.27 (q, *J*=6.4 Hz, 1H, C*H*OH), 2.41 (s, 3H, C*H*$_3$), 2.28 (br s, 1H, O*H*), 1.45 (d, *J*=6.4 Hz, 3H, OCHC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1 (C), 138.3 (C), 129.6 (CH), 127.3 (CH), 124.3 (C), 123.9 (CH), 69.5 (CH), 23.7 (CH_3), 23.5 (CH_3); IR (neat, cm^{-1}) 3285 br m, 2971 m, 1445 m, 1410 m, 1367 m, 1331 m, 1267 m, 1107 s, 1061 s, 1009 s, 856 m, 775 s, 709 s; HRMS (ESI) calcd for $[M+Na]^+$: 236.9885; found: 236.9888; Anal. calcd for $C_9H_{11}BrO$: C 50.26, H 5.22; found: C 50.33, H 5.22.

3.6. 1-(2-Bromo-4-fluorophenyl)ethanol (4)

Prepared according to GP1 using 2′-bromo-4′-fluoroacetophenone (0.50 g, 2.3 mmol), $NaBH_4$ (0.35 g, 9.2 mmol, 4 equiv) in ethanol (20 mL). Purification by FC (pentane/diethylether 5:1) afforded 2′-bromo-4′-fluoroacetophenone (**4**) as a colorless oil (0.50 g, 2.3 mmol, 99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, *J*=8.3, 6.4 Hz, 1H, C*H*$_{aryl}$), 7.22 (dd, *J*=8.2, 2.4 Hz, 1H, C*H*$_{aryl}$), 7.02 (ddd, *J*=8.2, 8.1, 2.4 Hz, 1H, C*H*$_{aryl}$), 5.14 (q, *J*=6.3 Hz, 1H, C*H*OH), 2.85 (br s, 1H, O*H*), 1.40 (d, *J*=6.3 Hz, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3 (d, ^1J(C,F)=250 Hz, C), 140.5 (d, ^4J(C,F)=3.4 Hz, C), 127.6 (d, ^3J(C,F)=8.4 Hz, CH), 121.3 (d, ^3J(C,F)=9.5 Hz, C), 119.61 (d, ^2J(C,F)=24.4 Hz, CH), 114.8 (d, ^2J(C,F)=20.8 Hz, CH), 68.5 (CH), 23.7 (CH_3); IR (neat, cm^{-1}) 3348 br m, 2976 m, 1597 m, 1484 s, 1369 m, 1225 m, 1095 m, 1011 m, 869 m, 632 s; HRMS (ESI) calcd for $[M+Na]^+$: 240.9635; found: 240.9624; Anal. calcd for C_8H_8BrFO: C 43.86, H 3.68; found: C 43.93, H 3.59.

3.7. Methyl 3-bromo-4-(1-hydroxyethyl)benzoate (5)

4-Ethylbenzoic acid (1.76 g, 11.7 mmol) was treated according to a procedure reported by Fleifel[18] with nitric acid (65%, 7.8 mL), distilled water (5.9 mL), acetic acid (100%, 35 mL) and bromine (663 μL, 12.9 mmol, 1.1 equiv). A solution of $AgNO_3$ (1.98 g, 11.7 mmol) in water (5.9 mL) was added via syringe pump over 1 h and the reaction mixture was stirred for 3 h at rt. The suspension was then poured into ice cold water and the precipitate was collected. The solid residue, which consisted of the organic acid and silver bromide, was treated with Na_2CO_3 and the silver bromide was filtered off. The aqueous phase was acidified with hydrochloric acid (12 M) and the precipitate formed was filtered off. The colorless solid product 3-bromo-4-ethylbenzoic acid (2.56 g, 11.2 mmol, 96%) was dried and recrystallized from ethanol.

To a solution of 3-bromo-4-ethylbenzoic acid (2.16 g, 9.48 mmol) in methanol (25 mL) 2,2-dimethoxypropane (5.8 mL, 47 mmol, 5 equiv) and hydrochloric acid (12 M, 1.6 mL, 19 mmol, 2 equiv) were added. The reaction mixture was heated at reflux over night, cooled and most of the solvent was removed in vacuo. The residue was taken up in diethylether and washed with water. The organic extract was dried over $MgSO_4$ and evaporated to dryness to give methyl 3-bromo-4-ethylbenzoate (1.71 g, 7.07 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (s, 1H, C*H*CCBr), 7.88 (dd, *J*=7.9, 1.2 Hz, 1H, C*H*$_{aryl}$), 7.27 (d, *J*=7.9 Hz, 1H, C*H*$_{aryl}$), 3.90 (s, 3H, OC*H*$_3$), 2.78 (q, *J*=7.5 Hz, 1H, C*H*$_2$), 1.23 (t, *J*=7.5 Hz, 1H, C*H*$_3$).

According to a procedure reported by Wakselman[19] the methylester derivative (1.71 mg, 7.07 mmol) was dissolved in acetic acid (175 mL) and a solution of CrO_3 (1 M; 1.77 g, 17.7 mmol, 2.5 equiv) in acetic acid and water (95:5) was added dropwise via syringe pump over 1 h. After being stirred at rt over night, the reaction mixture was diluted with water (800 mL) and extracted with diethylether (3×100 mL). The combined organic layers were washed with satd aq NaOH, dried over $MgSO_4$ and the solvent was evaporated.

Crude methyl 4-acetyl-3-bromobenzoate (1.61 g, 6.27 mmol) was reduced according to GP1 using $NaBH_4$ (308 mg, 8.15 mmol, 1.3 equiv) in methanol (56 mL). Purification by FC (pentane/diethylether 20:1→3:1) afforded methyl 3-bromo-4-(1-hydroxy-ethyl)-benzoate (**5**) as a colorless oil (679 mg, 2.63 mmol, 37% over two steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, *J*=1.6 Hz, 1H, C*H*CBr), 7.96 (dd, *J*=8.1, 1.6 Hz, 1H, C*H*CO$_2$CH$_3$), 7.66 (d, *J*=7.81 Hz, 1H, C*H*CCOH), 5.24 (q, *J*=6.4 Hz, 1H, C*H*OH), 3.90 (s, 3H, OC*H*$_3$), 2.33 (br s, 1H, O*H*), 1.46 (d, *J*=6.4 Hz, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.7 (C), 149.7 (C), 133.8 (CH), 130.5 (C), 128.9 (CH), 126.6 (CH), 121.3 (C), 69.1 (CH), 52.3 (CH_3), 23.5 (CH_3); IR (neat, cm^{-1}) 3395 br m, 2976 m, 1724 s, 1707 s, 1560 m, 1435 m, 1390 m, 1285 s, 1254 s, 1198 m, 1099 m, 1038 m, 765 m; HRMS (ESI) calcd for $[M+Na]^+$: 280.9784; found: 280.9782; Anal. calcd for $C_{10}H_{11}BrO_3$: C 46.36, H 4.28; found: C 46.59, H 4.48.

3.8. 1-(2-Bromophenyl)-2-methylpropan-1-ol (6)

Isopropyl chloride (0.98 mL, 11 mmol, 1.3 equiv) was added dropwise to a well-stirred suspension of magnesium turnings (0.26 g, 11 mmol, 1.3 equiv) in anhydrous diethylether (20 mL). The reaction mixture was stirred for 1 h and kept at reflux for 90 min. 2-Bromobenzaldehyde (1.0 mL, 8.5 mmol) was added dropwise and the mixture was heated to reflux for another 3 h. After cooling to rt, the reaction mixture was hydrolyzed with hydrochloric acid (6 M). The organic layer was washed with satd aq $NaHSO_3$, satd aq $NaHCO_3$ and water, dried over $MgSO_4$ and the solvent was evaporated in vacuo. The crude alcohol was purified by FC (pentane/diethylether 8:1) to yield 1-(2-bromophenyl)-2-methylpropan-1-ol (**6**) as a colorless oil (0.74 g, 3.3 mmol, 38%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J*=8.0 Hz, 1H, C*H*$_{aryl}$), 7.46 (d, *J*=7.8 Hz, 1H, C*H*$_{aryl}$), 7.30 (dd, *J*=7.6, 7.5 Hz, 1H, C*H*$_{aryl}$), 7.10 (m, 1H, C*H*$_{aryl}$), 4.84 (q, *J*=5.9 Hz, 1H, C*H*OH), 2.39 (br s, 1H, O*H*), 2.03 (m, 1H, C*H*(CH$_3$)$_2$), 0.95 (d, *J*=7.2 Hz, 3H, C(CH$_3$)C*H*$_3$), 0.93 (d, *J*=7.0 Hz, 3H, C(C*H*$_3$)CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9 (C), 132.5 (CH), 128.5 (CH), 128.2 (CH), 127.3 (CH), 122.6 (C), 77.4 (CH), 33.9 (CH), 19.4 (CH_3), 16.8 (CH_3); IR (neat, cm^{-1}) 3389 br m, 2966 m, 1467 m, 1436 m, 1099 m, 1003 s, 751 s; HRMS (ESI) calcd for $[M+Na]^+$: 251.0042; found: 251.022; Anal. calcd for $C_{10}H_{13}BrO$: C 52.42, H 5.72; found: C 52.56, H 5.68.

3.9. 2-Methoxynaphthalene-1-sulfonyl chloride (7)

A solution of chlorosulfonic acid (10.6 mL, 158 mmol, 2.5 equiv) in dichloromethane (30 mL) was added to a solution of 2-methoxynaphthalene (10.0 g, 63.2 mmol) in dichloromethane

(70 mL) at −12 °C over 1 h. The reaction was allowed to warm to 0 °C and stirred at that temperature for 10 min. After warming to rt, the reaction was stopped upon addition of ice cold water and the aqueous layer was extracted with dichloromethane (3×100 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to dryness to afford the sulfonyl chloride **7** as a pale yellow solid (4.36 g, 17.0 mmol, 27%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (d, J=8.8 Hz, 1H, CH_{aryl}), 8.11 (d, J=9.2 Hz, 1H, CH_{aryl}), 7.81 (d, J=8.1 Hz, 1H, CH_{aryl}), 7.67 (ddd, J=8.8, 7.0, 1.3 Hz, 1H, CH_{aryl}), 7.47 (ddd, J=8.1, 7.0, 1.0 Hz, 1H, CH_{aryl}), 7.32 (d, J=9.2 Hz, 1H, CH_{aryl}), 4.14 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0 (C), 139.0 (CH), 130.0 (CH), 129.4 (C), 129.0 (CH), 128.6 (C), 125.1 (CH), 123.2 (CH), 113.2 (CH), 57.5 (CH_3). One quaternary carbon was not detected. IR (neat, cm^{-1}) 1509 m, 1468 m, 1365 s, 1283 m, 1248 m, 1171 s, 1153 s, 1061 m, 1027 m, 811 s, 761 m, 748 m, 658 m; Anal. calcd for $C_{11}H_9ClO_3S$: C 51.47, H 3.53; found: C 51.62, H 3.64.

3.10. General procedure (GP2) for the sulfonylation

According to a procedure reported by Tanabe[14] the alcohol was dissolved in dichloromethane and treated with NEt_3 and $NMe_3 \cdot HCl$. The reaction mixture was cooled to 0 °C and the sulfonyl chloride was added slowly as a dichloromethane solution (0.5 mL CH_2Cl_2). The reaction was stirred for 1 h at that temperature, was then allowed to warm up to rt and stirred for additional 3 h at rt. The reaction was stopped upon addition of water and the aqueous layer was extracted with dichloromethane (three times). The combined organic layers were washed with brine and dried over $MgSO_4$. The solvents were removed in vacuo and FC finally yielded the desired sulfonate.

3.11. 1-(2-Bromophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (8)

According to GP2 1-(2-bromophenyl)ethanol (**1**, 200 mg, 1.00 mmol) was treated with NEt_3 (207 μL, 1.49 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (95 mg, 1.0 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 382 mg, 1.49 mmol, 1.5 equiv) in dichloromethane (9 mL). FC (pentane/diethylether 3:1; 1 vol % NEt_3) gave the sulfonate **8** as a colorless oil (345 mg, 0.821 mmol, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (dd, J=9.0, 0.7 Hz, 1H, CH_{aryl}), 7.92 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.71 (dd, J=8.1, 1.3 Hz, 1H, CH_{aryl}), 7.58 (m, 1H, CH_{aryl}), 7.42–7.35 (m, 2H, CH_{aryl}), 7.26 (dd, J=8.0, 1.2 Hz, 1H, CH_{aryl}), 7.14–7.04 (m, 2H, CH_{aryl}), 7.00 (ddd, J=8.0, 7.4, 1.7 Hz, 1H, CH_{aryl}), 6.01 (q, J=6.5 Hz, 1H, C$HOSO_2$R), 3.88 (s, 3H, OCH_3), 1.57 (d, J=6.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5 (C), 139.5 (C), 136.7 (CH), 132.1 (CH), 131.1 (C), 129.2 (CH), 128.9 (CH), 128.7 (C), 128.5 (CH), 127.6 (CH), 127.3 (CH), 124.4 (CH), 124.3 (CH), 120.7 (C), 117.2 (C), 112.8 (CH), 79.1 (CH), 56.9 (CH_3), 23.1 (CH_3).

3.12. 1-(2-Iodophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (9)

According to GP2 1-(2-iodophenyl)ethanol (**2**, 200 mg, 0.806 mmol) was treated with NEt_3 (168 μL, 1.21 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (77 mg, 0.81 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 309 mg, 1.21 mmol, 1.5 equiv) in dichloromethane (8 mL). FC (pentane/diethylether 3:1; 1 vol % NEt_3) gave the sulfonate **9** as a colorless oil (249 mg, 0.532 mmol, 66%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.78 (d, J=9.2 Hz, 1H, CH_{aryl}), 7.58 (d, J=8.0 Hz, 1H, CH_{aryl}), 7.47–7.36 (m, 2H, CH_{aryl}), 7.28–7.20 (m, 2H, CH_{aryl}), 7.02–6.93 (m, 2H, CH_{aryl}), 6.66 (ddd, J=7.7, 7.4, 1.6 Hz, 1H, CH_{aryl}), 5.71 (q, J=6.4 Hz, 1H, C$HOSO_2$R), 3.73 (s, 3H, OCH_3), 1.42 (d, J=6.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5 (C), 142.5 (C), 138.7 (CH), 136.8 (CH), 131.0 (C), 129.4 (CH), 128.9 (CH), 128.7 (C), 128.5 (CH), 128.1 (CH), 127.2 (CH), 124.4 (2×CH), 117.1 (C), 112.8 (CH), 95.8 (C), 83.7 (CH), 56.9 (CH_3), 23.2 (CH_3).

3.13. 1-(2-Bromo-3-methylphenyl)ethyl 2-methoxynaphthalene-1-sulfonate (10)

According to GP2 1-(2-bromo-3-methylphenyl)ethanol (**3**, 150 mg, 0.701 mmol) was treated with NEt_3 (146 μL, 1.05 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (67 mg, 0.70 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 269 mg, 1.05 mmol, 1.5 equiv) in dichloromethane (7 mL). FC (pentane/diethylether 3:1 → 1:1; 1 vol % NEt_3) gave the sulfonate **10** as a colorless oil (213 mg, 0.492 mmol, 70%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (d, J=9.0 Hz, 1H, CH_{aryl}), 7.91 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.71 (d, J=8.1 Hz, 1H, CH_{aryl}), 7.56 (ddd, J=8.8, 6.9, 1.4 Hz, 1H, CH_{aryl}), 7.38 (ddd, J=7.8, 6.9, 0.9 Hz, 1H, CH_{aryl}), 7.23 (m, 1H, CH_{aryl}), 7.10 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.00–6.93 (m, 2H, CH_{aryl}), 6.11 (q, J=6.5 Hz, 1H, C$HOSO_2$R), 3.88 (s, 3H, OCH_3), 2.22 (s, 3H, CCH_3), 1.56 (d, J=6.5 Hz, 3H, CHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4 (C), 139.9 (C), 136.9 (C), 136.6 (CH), 131.1 (C), 130.0 (CH), 128.8 (CH), 128.7 (C), 128.4 (CH), 126.8 (CH), 125.0 (CH), 124.4 (CH), 124.3 (CH), 123.4 (C), 117.4 (C), 112.9 (CH), 79.8 (CH), 56.9 (CH_3), 23.5 (CH_3), 23.0 (CH_3).

3.14. 1-(2-Bromo-4-fluorophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (11)

According to GP2 1-(2-bromo-4-fluorophenyl)ethanol (**4**, 200 mg, 0.913 mmol) was treated with NEt_3 (190 μL, 1.37 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (87 mg, 0.91 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 351 mg, 1.37 mmol, 1.5 equiv) in dichloromethane (10 mL). FC (pentane/diethylether 5:1 → 1:1; 1 vol % NEt_3) gave the sulfonate **11** as a colorless oil (260 mg, 0.594 mmol, 65%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (d, J=8.6 Hz, 1H, CH_{aryl}), 7.81 (d, J=9.2 Hz, 1H, CH_{aryl}), 7.60 (d, J=8.1 Hz, 1H, CH_{aryl}), 7.46 (m, 1H, CH_{aryl}), 7.33–7.16 (m, 2H, CH_{aryl}), 7.02 (d, J=9.2 Hz, 1H, CH_{aryl}), 6.88 (dd, J=8.2, 2.6 Hz, 1H, CH_{aryl}), 6.67 (ddd, J=8.5, 8.4, 2.6 Hz, 1H, CH_{aryl}), 5.87 (q, J=6.5 Hz, 1H, C$HOSO_2$R), 3.80 (s, 3H, OCH_3), 1.44 (d, J=6.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.4 (d, ^1J(C,F)=251.6 Hz, C), 158.5 (C), 136.8 (CH), 135.5 (d, ^4J(C,F)=3.6 Hz, C), 131.0 (CH), 130.1 (C), 129.0 (C), 128.9 (CH), 128.8 (CH), 128.6 (d, ^3J(C,F)=12.4 Hz, CH), 124.4 (d, ^3J(C,F)=11.7 Hz, C), 120.7 (C), 119.1 (d, ^2J(C,F)=24.5 Hz, CH), 117.2 (CH), 114.6 (d, ^2J(C,F)=21.3 Hz, CH), 112.8 (CH), 78.5 (CH), 57.0 (CH_3), 23.1 (CH_3).

3.15. Methyl 3-bromo-4-(1-{[2-methoxy-1-naphthylsulfonyl]-oxy}ethyl)benzoate (12)

According to GP2 methyl 3-bromo-4-(1-hydroxyethyl)benzoate (**5**, 122 mg, 0.473 mmol) was treated with NEt_3 (99 μL, 0.71 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (45 mg, 0.47 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 181 mg, 0.709 mmol, 1.5 equiv) in dichloromethane (5 mL). FC (pentane/diethylether 8:1 → 1:1; 1 vol % NEt_3) gave the sulfonate **12** as a colorless oil (158 mg, 0.331 mmol, 70%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (d, J=8.9 Hz, 1H, CH_{aryl}), 7.95 (m, 2H, CH_{aryl}), 7.72 (m, 2H, CH_{aryl}), 7.59 (m, 1H, CH_{aryl}), 7.47 (d, J=8.2 Hz, 1H, CH_{aryl}), 7.39 (dd, J=7.6, 7.4 Hz, 1H, CH_{aryl}), 7.13 (dd, J=9.2, 1.8 Hz, 1H, CH_{aryl}), 6.02 (q, J=6.5 Hz, 1H, C$HOSO_2$R), 3.91 (s, 3H, OCH_3), 3.88 (s, 3H, COOCH_3), 1.58 (d, J=6.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2 (C), 158.5 (C), 144.3 (C), 136.9 (CH), 133.3 (CH), 131.0 (2×C), 129.6 (CH), 128.7 (C), 128.6 (CH), 128.3 (CH), 127.5 (CH), 124.6 (CH), 124.3 (CH), 120.5 (C), 117.1 (C), 112.9 (CH), 78.5 (CH), 57.0 (CH_3), 52.4 (CH_3), 22.7 (CH_3).

3.16. 1-(2-Bromophenyl)-2-methylpropyl 2-methoxynaphthalene-1-sulfonate (13)

According to GP1 2-(2-bromophenyl)-2-methylpropan-1-ol (**6**, 250 mg, 1.10 mmol) was treated with NEt_3 (229 μL, 1.65 mmol, 1.5 equiv), $NMe_3 \cdot HCl$ (105 mg, 1.10 mmol), and 2-methoxynaphthalene-1-sulfonyl chloride (**7**, 421 mg, 1.65 mmol, 1.5 equiv) in dichloromethane (10 mL). FC (pentane/diethylether 5:1→2:1; 1 vol% NEt_3) gave the sulfonate **13** as a colorless oil (295 mg, 0.658 mmol, 60%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (d, *J*=9.0 Hz, 1H, C*H*$_{aryl}$), 7.76 (d, *J*=9.1 Hz, 1H, C*H*$_{aryl}$), 7.59 (d, *J*=8.1 Hz, 1H, C*H*$_{aryl}$), 7.50 (m, 1H, C*H*$_{aryl}$), 7.30 (m, 1H, C*H*$_{aryl}$), 7.10 (m, 2H, C*H*$_{aryl}$), 6.93 (d, *J*=9.1 Hz, 1H, C*H*$_{aryl}$), 6.88–6.73 (m, 2H, C*H*$_{aryl}$), 5.62 (q, *J*=6.9 Hz, 1H, C*H*OSO$_2$R), 3.83 (s, 3H, OC*H*$_3$), 2.05 (m, 1H, C*H*(CH$_3$)$_2$), 1.00 (d, *J*=6.7 Hz, 3H, CH(CH$_3$)C*H*$_3$), 0.75 (d, *J*=6.9 Hz, 3H, CH(C*H*$_3$)CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0 (C), 142.9 (C), 138.9 (CH), 132.4 (CH), 130.0 (CH), 129.4 (C), 129.0 (CH), 128.5 (C), 128.4 (CH), 128.3 (C), 128.2 (CH), 127.2 (CH), 125.0 (CH), 123.1 (CH), 122.5 (C), 113.3 (CH), 77.3 (CH), 57.4 (CH$_3$), 33.9 (CH), 19.3 (CH$_3$), 16.6 (CH$_3$).

3.17. General procedure (GP3) for the aryl migration reaction

The sulfonate was dissolved in benzene (0.03 M) and heated to 80 °C. A solution of Bu_3SnH and V-40 in benzene (1 mL) was added by syringe pump over 7 h. After complete addition stirring was continued at that temperature for 30 min. The solution was then allowed to cool to rt and water and diethylether were added. The organic phase was washed with satd aq NH_4Cl and brine and was dried over $MgSO_4$. The solvents were evaporated and the crude residue was filtered over a KF–SiO_2 column[20] (10:90). FC (SiO_2) finally yielded the desired biaryl.

3.18. 1-[2-(2-Methoxy-1-naphthyl)phenyl]ethanol (14a and 14b)

According to GP3 with 1-(2-bromophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (**8**, 150 mg, 0.356 mmol), Bu_3SnH (144 μL, 0.534 mmol, 1.5 equiv), and V-40 (87 mg, 0.36 mmol, 1.0 equiv) in benzene (12 mL). Purification by FC (pentane/diethylether 20:1→3:1) afforded the separated diastereoisomers **14a** (29.7 mg, 0.107 mmol, 30%) and **14b** (53.5 mg, 0.192 mmol, 54%) as colorless oils.

3.19. 1-[2-(2-Methoxy-1-naphthyl)phenyl]ethanol (14a and 14b)

According to GP3 with 1-(2-iodophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (**9**, 286 mg, 0.612 mmol), Bu_3SnH (247 μL, 0.917 mmol, 1.5 equiv), and V-40 (149 mg, 0.612 mmol, 1.0 equiv) in benzene (20 mL). Purification by FC (pentane/diethylether 20:1→3:1) afforded the separated diastereoisomers **14a** (34 mg, 0.122 mmol, 20%) and **14b** (61 mg, 0.219 mmol, 36%) as colorless oils.

*3.19.1. Diastereoisomer **14a***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J*=9.1 Hz, 1H, C*H*$_{aryl}$), 7.78–7.73 (m, 1H, C*H*$_{aryl}$), 7.67 (dd, *J*=7.7, 0.9 Hz, 1H, C*H*$_{aryl}$), 7.42 (ddd, *J*=7.7, 7.6, 1.4 Hz, 1H, C*H*$_{aryl}$), 7.36–7.14 (m, 5H, C*H*$_{aryl}$), 7.07 (br d, *J*=7.6 Hz, 1H, C*H*$_{aryl}$), 4.42 (q, *J*=6.4 Hz, 1H, C*H*OH), 3.78 (s, 3H, OC*H*$_3$), 1.62 (br s, 1H, O*H*), 1.23 (d, *J*=6.4 Hz, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0 (C), 144.99 (C), 134.1 (C), 133.7 (C), 131.0 (CH), 129.4 (CH), 128.9 (C), 128.2 (CH), 127.9 (CH), 127.3 (CH), 126.7 (CH), 125.4 (CH), 124.7 (CH), 123.6 (CH), 123.2 (C), 113.2 (CH), 67.5 (CH), 56.2 (CH$_3$), 24.1 (CH$_3$); IR (neat, cm^{-1}) 3399 br m, 2968 m, 2923 m, 1621 m, 1592 m, 1508 m, 1464 m, 1331 m, 1259 s, 1063 s, 905 m, 811 m, 758 m, 730 m; HRMS (ESI) calcd for [M+Na]$^+$: 301.1199; found: 301.1209; X-ray crystal structure analysis of **14a**: formula $C_{19}H_{18}O_2$, *M*=278.33, colorless crystal 0.20×0.10×0.07 mm, *a*=19.7811(11), *c*=7.7299(4) Å, *V*=3024.6(3) Å^3, ρ_{calcd}=1.222 g cm^{-3}, μ=0.616 mm^{-1}, empirical absorption correction (0.887≤*T*≤0.958), *Z*=8, tetragonal, space group *I*4 (No. 79), λ=1.54178 Å, *T*=223(2) K, ω and φ scans, 6777 reflections collected (±*h*, ±*k*, ±*l*), [(sin θ)/λ]=0.60 Å^{-1}, 1983 independent (R_{int}=0.038) and 1924 observed reflections [*I*≥2σ(*I*)], 194 refined parameters, *R*=0.034, *wR*^{2}=0.089, Flack parameter 0.2(3), max. (min.) residual electron density 0.11 (−0.12) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

*3.19.2. Diastereoisomer **14b***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J*=9.1 Hz, 1H, C*H*$_{aryl}$), 7.84 (dd, *J*=7.7, 1.5 Hz, 1H, C*H*$_{aryl}$), 7.75 (d, *J*=7.8 Hz, 1H, C*H*$_{aryl}$), 7.50 (ddd, *J*=7.8, 7.7, 1.3 Hz, 1H, C*H*$_{aryl}$), 7.43–7.29 (m, 4H, C*H*$_{aryl}$), 7.26–7.22 (m, 1H, C*H*$_{aryl}$), 7.15 (br d, *J*=7.7 Hz, 1H, C*H*$_{aryl}$), 4.55 (q, *J*=6.4 Hz, 1H, C*H*OH), 3.82 (s, 3H, OC*H*$_3$), 2.57 (br s, 1H, O*H*), 1.26 (d, *J*=6.4 Hz, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2 (C), 144.6 (C), 134.5 (C), 134.0 (C), 131.0 (CH), 129.4 (CH), 129.2 (C), 128.3 (CH), 127.9 (CH), 127.5 (CH), 126.5 (CH), 125.3 (CH), 125.2 (CH), 123.8 (CH), 123.7 (C), 113.5 (CH), 67.0 (CH), 56.8 (CH$_3$), 22.5 (CH$_3$); IR (neat, cm^{-1}) 3415 br m, 2972 m, 2924 m, 1622 m, 1592 m, 1509 m, 1465 m, 1331 m, 1259 s, 1075 s, 906 m, 812 m, 758 m, 731 m; HRMS (ESI) calcd for [M+Na]$^+$: 301.1199; found: 301.1220; X-ray crystal structure analysis of **14b**: formula $C_{19}H_{18}O_2$, *M*=278.33, colorless crystal 0.30×0.15×0.10 mm, *a*=25.3009(7), *b*=7.9281(2), *c*=30.0895(9) Å, β=96.208(1)°, *V*=6000.2(3) Å^3, ρ_{calcd}=1.232 g cm^{-3}, μ=0.621 mm^{-1}, empirical absorption correction (0.836≤*T*≤0.941), *Z*=16, monoclinic, space group *C*2/*c* (No. 15), λ=1.54178 Å, *T*=223(2) K, ω and φ scans, 21,629 reflections collected (±*h*, ±*k*, ±*l*), [(sin θ)/λ]=0.60 Å^{-1}, 5284 independent (R_{int}=0.058) and 4150 observed reflections [*I*≥2σ(*I*)], 386 refined parameters, *R*=0.046, *wR*^{2}=0.112, max. (min.) residual electron density 0.17 (−0.15) e Å^{-3}, two almost identical molecules in the asymmetric unit, hydrogen atoms calculated and refined as riding atoms.

3.20. 1-[2-(2-Methoxy-1-naphthyl)-3-methylphenyl]ethanol (15a and 15b)

According to GP3 with 1-(2-bromo-3-methylphenyl)ethyl 2-methoxynaphthalene-1-sulfonate (**10**, 100 mg, 0.230 mmol), Bu_3SnH (93 μL, 0.35 mmol, 1.5 equiv), and V-40 (56 mg, 0.23 mmol, 1.0 equiv) in benzene (8 mL). Purification by FC (pentane/diethylether 10:1→3:1) afforded the separated diastereoisomers **15a** (14.0 mg, 0.0479 mmol, 21%) and **15b** (21.3 mg, 0.073 mmol, 32%) as colorless oils.

*3.20.1. Diastereoisomer **15a***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J*=9.1 Hz, 1H, C*H*$_{aryl}$), 7.85 (dd, *J*=7.3, 1.7 Hz, 1H, C*H*$_{aryl}$), 7.57 (d, *J*=7.8 Hz, 1H, C*H*$_{aryl}$), 7.49–7.28 (m, 5H, C*H*$_{aryl}$), 7.08 (d, *J*=7.7 Hz, 1H, C*H*$_{aryl}$), 4.41 (d, *J*=6.4 Hz, 1H, C*H*OH), 3.85 (s, 3H, OC*H*$_3$), 1.83 (s, 3H, C*H*$_3$), 1.56 (br s, 1H, O*H*), 1.22 (d, *J*=6.4 Hz, 3H, OCHC*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2 (C), 144.4 (C), 137.5 (C), 134.2 (C), 133.4 (C), 129.5 (CH), 129.3 (C), 129.2 (CH), 128.2 (CH), 128.1 (CH), 126.8 (CH), 124.6 (CH), 123.9 (CH), 122.7 (CH), 122.4 (C), 113.5 (CH), 67.3 (CH), 56.6 (CH$_3$), 22.4 (CH$_3$), 20.2 (CH$_3$); IR (neat, cm^{-1}) 3415 br m, 2969 m, 2927 m, 2857 m, 1622 m, 1593 m, 1508 m, 1461 m, 1378 m, 1331 m, 1253 s, 1092 m, 1063 s, 1020 m, 907 s, 809 m, 732 s; HRMS (ESI) calcd for [M+Na]$^+$: 315.1356; found: 315.1357.

*3.20.2. Diastereoisomer **15b***

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J*=9.0 Hz, 1H, C*H*$_{aryl}$), 7.85 (dd, *J*=7.4, 1.4 Hz, 1H, C*H*$_{aryl}$), 7.57 (d, *J*=7.8 Hz, 1H, C*H*$_{aryl}$), 7.49–7.28

(m, 5H, CH_{aryl}), 7.08 (d, J=7.8 Hz, 1H, CH_{aryl}), 3.93 (d, J=6.4 Hz, 1H, CHOH), 3.85 (s, 3H, OCH_3), 2.26 (br s, 1H, OH), 1.83 (s, 3H, CH_3), 1.23 (d, J=6.4 Hz, 3H, OCHCH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2 (C), 144.4 (C), 137.5 (C), 134.2 (C), 133.4 (C), 133.4 (C), 129.4 (CH), 129.3 (C), 129.2 (CH), 128.2 (CH), 128.1 (CH), 126.8 (CH), 124.6 (CH), 123.9 (CH), 122.6 (CH), 113.5 (CH), 67.2 (CH), 56.5 (CH_3), 22.4 (CH_3), 20.2 (CH_3); IR (neat, cm^{-1}) 3425 br m, 2965 m, 2928 m, 1622 m, 1593 m, 1508 m, 1461 m, 1377 m, 1331 s, 1254 m, 1147 m, 1063 s, 1019 m, 809 m; HRMS (ESI) calcd for [M+Na]$^+$: 315.1356; found: 315.1343.

3.21. 1-[4-Fluoro-2-(2-methoxynaphthyl)phenyl]ethanol (16a and 16b)

According to GP3 with 1-(2-bromo-4-fluorophenyl)ethyl 2-methoxynaphthalene-1-sulfonate (**11**, 151 mg, 0.344 mmol), Bu_3SnH (139 μL, 0.516 mmol, 1.5 equiv), and V-40 (84 mg, 0.34 mmol, 1.0 equiv) in benzene (12 mL). Purification by FC (pentane/diethylether 20:1→2:1) afforded the separated diastereoisomers **16a** (20.0 mg, 0.068 mmol, 19%) and **16b** (41.1 mg, 0.139 mmol, 40%) as colorless oils.

3.21.1. Diastereoisomer *16a*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.84 (dd, J=6.2, 3.3 Hz, 1H, CH_{aryl}), 7.72 (dd, J=8.7, 5.9 Hz, 1H, CH_{aryl}), 7.41–7.32 (m, 3H, CH_{aryl}), 7.26–7.15 (m, 2H, CH_{aryl}), 6.87 (dd, J=9.1, 2.7 Hz, 1H, CH_{aryl}), 4.45 (q, J=6.3 Hz, 1H, CHOH), 3.83 (s, 3H, OCH_3), 1.56 (br s, 1H, OH), 1.26 (d, J=6.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9 (d, ^1J(C,F)=246 Hz, C), 154.0 (C), 141.0 (d, ^4J(C,F)=3.1 Hz, C), 136.1 (C), 133.3 (C), 129.8 (CH), 128.9 (C), 128.1 (CH), 127.2 (d, ^3J(C,F)=8.6 Hz, CH), 127.1 (CH), 124.4 (CH), 123.8 (CH), 121.1 (C), 117.5 (d, ^2J(C,F)=20.8 Hz, CH), 115.1 (d, ^2J(C,F)=21.0 Hz, CH), 113.1 (CH), 66.9 (CH), 56.2 (CH_3), 24.3 (CH_3); IR (neat, cm^{-1}) 3410 br m, 2934 m, 2841 m, 1611 m, 1593 m, 1510 m, 1333 m, 1259 s, 1176 m, 1062 s, 907 m, 809 m, 731 m, 632 s; HRMS (ESI) calcd for [M+Na]$^+$: 319.1105; found: 319.1103.

3.21.2. Diastereoisomer *16b*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.84 (m, 1H, CH_{aryl}), 7.70 (dd, J=8.7, 5.9 Hz, 1H, CH_{aryl}), 7.42–7.32 (m, 3H, CH_{aryl}), 7.25–7.14 (m, 2H, CH_{aryl}), 6.87 (dd, J=9.2, 2.8 Hz, 1H, CH_{aryl}), 4.51 (q, J=6.5 Hz, 1H, CHOH), 3.85 (s, 3H, OCH_3), 2.40 (br s, 1H, OH), 1.26 (d, J=6.5 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9 (d, ^1J(C,F)=247 Hz, C), 153.2 (C), 140.7 (d, ^4J(C,F)=3.1 Hz, C), 136.6 (d, ^3J(C,F)=8.0 Hz, C), 133.3 (C), 129.9 (CH), 129.3 (C), 128.0 (CH), 127.2 (d, ^3J(C,F)=8.5 Hz, CH), 126.8 (CH), 124.9 (CH), 124.0 (CH), 122.5 (d, ^4J(C,F)=1.5 Hz, C), 117.5 (d, ^2J(C,F)=20.8 Hz, CH), 115.1 (d, ^2J(C,F)=20.9 Hz, CH), 113.4 (CH), 66.5 (CH), 56.8 (CH_3), 22.7 (CH_3); IR (neat, cm^{-1}) 3415 br m, 2970 m, 2935 m, 2842 m, 1621 m, 1593 m, 1510 m, 1470 m, 1333 m, 1265 s, 1176 m, 1063 m, 1020 m, 886 m, 809 m; HRMS (ESI) calcd for [M+Na]$^+$: 319.1105; found: 319.1106.

3.22. Methyl 4-(1-hydroxyethyl)-3-(2-methoxy-1-naphthyl)benzoate (17a and 17b)

According to GP3 with methyl 3-bromo-4-(1-{[2-methoxy-1-naphthylsulfonyl]oxy}ethyl) benzoate (**12**, 261 mg, 0.546 mmol), Bu_3SnH (221 μL, 0.819 mmol, 1.5 equiv), and V-40 (133 mg, 0.546 mmol, 1.0 equiv) in benzene (18 mL). Purification by FC (pentane/diethylether 10:1→1:1) afforded the separated diastereoisomers **17a** (43 mg, 0.128 mmol, 23%) and **17b** (79 mg, 0.235 mmol, 43%) as colorless oils.

3.22.1. Diastereoisomer *17a*

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, J=8.2, 1.8 Hz, 1H, CH_{aryl}), 7.94 (d, J=9.1 Hz, 1H, CH_{aryl}), 7.89–7.80 (m, 3H, CH_{aryl}), 7.41–7.30 (m, 3H, CH_{aryl}), 7.17 (m, 1H, CH_{aryl}), 4.53 (q, J=6.4 Hz, 1H, CHOH), 3.88 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 1.67 (br s, 1H, OH), 1.30 (d, J=6.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (C), 154.2 (C), 150.3 (C), 134.3 (C), 133.4 (CH), 132.5 (CH), 129.8 (CH), 129.4 (CH), 129.3 (C), 128.9 (C), 127.0 (CH), 125.6 (CH), 125.3 (C), 124.4 (CH), 123.8 (CH), 122.1 (C), 113.1 (CH), 67.3 (CH), 56.2 (CH_3), 52.0 (CH_3), 24.2 (CH_3); IR (neat, cm^{-1}) 3420 br m, 2950 m, 2930 m, 1712 s, 1623 m, 1595 m, 1510 m, 1438 m, 1289 m, 1251 s, 1222 m, 1123 m, 1060 m, 1005 m, 905 m, 821 m, 732 s; HRMS (ESI) calcd for [M+Na]$^+$: 359.1254; found: 359.1253.

3.22.2. Diastereoisomer *17b*

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (dd, J=8.2, 1.8 Hz, 1H, CH_{aryl}), 7.95 (d, J=9.0 Hz, 1H, CH_{aryl}), 7.90–7.82 (m, 3H, CH_{aryl}), 7.44–7.31 (m, 3H, CH_{aryl}), 7.19 (m, 1H, CH_{aryl}), 4.62 (q, J=6.3 Hz, 1H, CHOH), 3.89 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 2.44 (br s, 1H, OH), 1.24 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9 (C), 153.3 (C), 149.9 (C), 134.7 (C), 133.8 (C), 132.4 (CH), 129.9 (CH), 129.5 (CH), 129.3 (2×C), 128.0 (CH), 126.8 (CH), 125.6 (CH), 124.9 (CH), 124.0 (CH), 122.6 (C), 113.4 (CH), 66.9 (CH), 56.8 (CH_3), 52.0 (CH_3), 22.7 (CH_3); IR (neat, cm^{-1}) 3425 br m, 2972 m, 2936 m, 1717 s, 1593 m, 1509 m, 1436 m, 1293 m, 1265 s, 1215 m, 1079 m, 1065 m, 1004 m, 906 m, 809 m, 729 s; HRMS (ESI) calcd for [M+Na]$^+$: 359.1254; found: 359.1259.

3.23. 1-[2-(2-Methoxy-1-naphthyl)phenyl]-2-methyl propan-1-ol (18a and 18b)

According to GP3 with 1-(2-bromophenyl)-2-methylpropyl 2-methoxynaphthalene-1-sulfonate (**13**, 156 mg, 0.348 mmol), Bu_3SnH (141 μL, 0.522 mmol, 1.5 equiv), and V-40 (85 mg, 0.35 mmol, 1.0 equiv) in benzene (12 mL). Purification by FC (pentane/diethylether 20:1→2:1) afforded the separated diastereoisomers **18a** (13.4 mg, 0.044 mmol, 21%) and **18b** (25.0 mg, 0.818 mmol, 39%) as colorless oils.

3.23.1. Diastereoisomer *18a*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J=9.0 Hz, 1H, CH_{aryl}), 7.84 (m, 1H, CH_{aryl}), 7.68 (dd, J=7.7, 1.0 Hz, 1H, CH_{aryl}), 7.50 (ddd, J=7.8, 7.6, 1.2 Hz, 1H, CH_{aryl}), 7.43–7.21 (m, 5H, CH_{aryl}), 7.16 (dd, J=7.6, 1.1 Hz, 1H, CH_{aryl}), 3.92 (d, J=7.7 Hz, 1H, CHOH), 3.81 (s, 3H, OCH_3), 2.03 (m, 1H, CH(CH_3)$_2$), 1.66 (br s, 1H, OH), 0.84 (d, J=6.6 Hz, 3H, CH(CH_3)CH_3), 0.63 (d, J=6.8 Hz, 3H, CH(CH_3)CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3 (C), 143.5 (C), 135.5 (C), 133.9 (C), 131.1 (CH), 129.4 (C), 129.3 (CH), 128.3 (CH), 127.8 (CH), 127.2 (CH), 126.3 (CH), 126.3 (CH), 125.6 (CH), 124.0 (C), 123.8 (CH), 113.5 (CH), 77.3 (CH), 56.9 (CH_3), 32.7 (CH), 19.3 (CH_3), 19.2 (CH_3); IR (neat, cm^{-1}) 3435 br m, 2968 m, 1623 m, 1593 m, 1509 m, 1464 m, 1382 m, 1333 m, 1247 s, 1064 s, 1004 s, 905 m, 802 s; HRMS (ESI) calcd for [M+Na]$^+$: 329.1523; found: 329.1518.

3.23.2. Diastereoisomer *18b*

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J=9.0 Hz, 1H, CH_{aryl}), 7.87–7.81 (m, 1H, CH_{aryl}), 7.68 (dd, J=7.8 Hz, 1H, CH_{aryl}), 7.51 (ddd, J=7.8, 7.6, 1.1 Hz, 1H, CH_{aryl}), 7.43–7.29 (m, 5H, CH_{aryl}), 7.17 (dd, J=7.6, 1.1 Hz, 1H, CH_{aryl}), 3.93 (d, J=6.6 Hz, 1H, CHOH), 3.84 (s, 3H, OCH_3), 2.48 (br s, 1H, OH), 2.05 (m, 1H, CH(CH_3)$_2$), 0.91 (d, J=6.6 Hz, 3H, CH(CH_3)CH_3), 0.44 (d, J=6.6 Hz, 3H, CH(CH_3)CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3 (C), 143.5 (C), 135.5 (C), 133.9 (C), 131.1 (CH), 129.4 (CH), 129.3 (C), 128.3 (CH), 127.8 (CH), 127.3 (CH), 126.4 (CH), 126.3 (CH), 125.6 (CH), 124.0 (C), 123.8 (CH), 113.5 (CH), 77.3 (CH), 56.9 (CH_3), 32.7 (CH), 19.3 (CH_3), 19.2 (CH_3); IR (neat, cm^{-1}) 3345 br m, 2961 m, 2922 m, 2870 m, 2839 m, 1621 m, 1593 m, 1509 m, 1465 m, 1384 m, 1329 m, 1257 s, 1066 m, 1012 m, 908 s, 809 s, 729 s; HRMS (ESI) calcd for [M+Na]$^+$: 329.1512; found: 329.1512; X-ray crystal structure analysis of **18b**: formula $C_{21}H_{22}O_2$, M=306.39, colorless crystal 0.50×0.20×0.20 mm, a=11.1518(2),

b=26.1286(6), c=12.2533(3) Å, β=104.684(1)°, V=3453.76(13) Å^3, ρ_{calcd}=1.178 g cm^{-3}, μ=0.581 mm^{-1}, empirical absorption correction ($0.760 \leq T \leq 0.893$), Z=8, monoclinic, space group $P2_1/c$ (No. 14), λ=1.54178 Å, T=223(2) K, ω and φ scans, 33,708 reflections collected ($\pm h$, $\pm k$, $\pm l$), [$(\sin\theta)/\lambda$]=0.59 Å^{-1}, 6046 independent (R_{int}=0.043) and 5574 observed reflections [$I \geq 2\sigma(I)$], 423 refined parameters, R=0.043, wR^2=0.122, max. (min.) residual electron density 0.15 (−0.22) e Å^{-3}, two almost identical molecules in the asymmetric unit, hydrogen atoms calculated and refined as riding atoms.

CCDC 689499 (**14b**), 689500 (**18b**), and 689501 (**14a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336 033, E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

We thank the Fonds der Chemischen Industrie and Novartis Pharma AG (Young Investigator Award to A.S.) for financial support.

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