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ORIGINAL PAPER

Enantioselective synthesis of 1-arylethanediols by rhodium-catalyzed transfer hydrogenation of α-tosyloxyarylketones

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Abstract Catalytic transfer hydrogenation of α-tosyloxyarylketones mediated by a chiral rhodium complex using an azeotropic mixture of formic acid/triethylamine afforded the corresponding 1-arylethanediol monotosylates in excellent yield with high enantioselectivity.

Keywords 1-Arylethanediol · Rhodium · Asymmetric transfer hydrogenation · α-Tosyloxyarylketone

Introduction

Asymmetric transfer hydrogenation (ATH) has been broadening its applications to enantioselective hydrogenation of unsaturated carbonyl and imine groups [1–3]. The catalysts generally consist of bidentate ligands based on 1,2-aminoalcohols or diamines, bound to ruthenium, rhodium, or iridium. The transfer reaction is routinely carried out under isopropanol/base or a formic acid/triethylamine mixture as hydrogen donors. It has been proved that (1*S*,2*S*)- or (1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine (TsDPEN) is an excellent ligand for the catalytic transfer hydrogenation of aryl ketones [1]. The TsDPEN-Ru catalysts efficiently reduced activated ketones, such as arylketones, α-, and β-ketoesters, α,β-unsaturated ketones, 1,2-diketones with high optical and chemical yields, while Rh-catalysts are preferable, notably in the reduction of α-chloroketones [4, 5]. In general, ATH rather offers an operational simplicity, since the reaction does not involve molecular hydrogen and is insensitive to air oxidation, so it is particularly valuable in scale-up synthesis of active pharmaceutical ingredients [6].

Previously, we have reported the asymmetric transfer hydrogenation of 2-tosyloxy-1-(4-hydroxyphenyl)ethanone derivatives with TsDPEN-Rh-catalyst in formic acid/triethylamine and their further applications to the synthesis of β-adrenergic agonists [7]. This represented a simple and highly efficient procedure for the preparation of chiral alcohols from α-tosyloxyketones under catalytic transfer hydrogenation. Indeed, α-sulfonyloxyketones are particularly interesting as versatile intermediates for the preparation of a large group of anti-depressants and α- and β-adrenergic drugs [8, 9]. However, they have not received much attention in asymmetric transfer hydrogenation to date [10, 11]. Herein, we report the asymmetric transfer hydrogenation of various α-tosyloxyarylketones with structural diversity, which may provide their facile entry to many biologically active compounds containing 1,2-aminoalcohol functionality.

Results and discussion

The starting α-tosyloxyketones **2a–2t** were conveniently prepared by α-sulfonyloxylation of the corresponding arylketones **1a–1t**, which are either commercially available or easily accessible in a few steps, with [hydroxy(tosyloxy)iodo]benzene in refluxing acetonitrile [12]. The compounds **1l–1n** were conveniently obtained starting from

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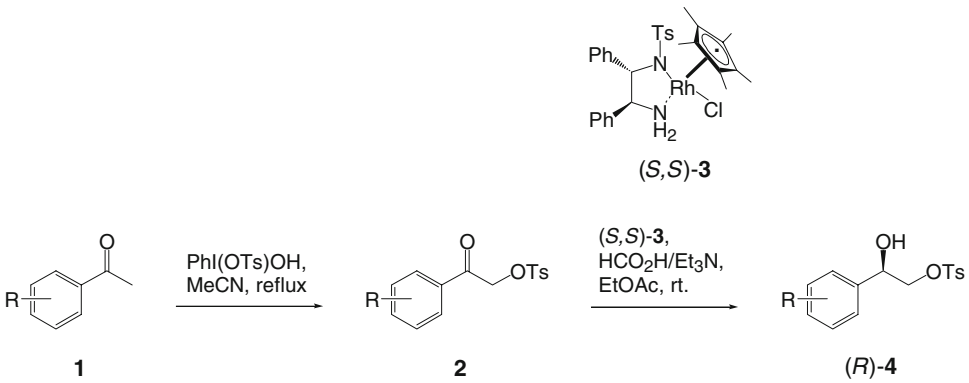
Scheme 1



1-(4-hydroxyphenyl)ethanone, and **1t** was prepared via acetylation of 1-methoxy-4-methylbenzene with acetic acid in the presence of $LiClO_4$ [13]. Thus, we extended Rh-catalyzed transfer hydrogenation of α-tosyloxyarylketones by a substituent variation in the aryl part, as shown in Scheme 1.

Here, the sense of asymmetric induction has not been changed as observed with α-chloroarylketones, and the results are summarized in Table 1. The reduction of *o*-substituted acetophenones (**2b** and **2i**) showed a decrease in enantioselectivity, while *m*- and *p*-substituted derivatives (**2c–2d** and **2j–2k**) regained. The observation suggests that the introduction of *o*-substituents brings about steric demand to disturb toward catalytic complex structure. The ketones with electron-withdrawing groups such as *p*-F (**2g**) and $–CF_3$ (**2h**) showed a decreased enantioselectivity. However, *p*-OMe substrate (**2k**) was cleanly reduced to afford (*R*)-**4k** in 94% *ee* by (*S,S*)-**3** at *S*/*C* = 1,000, while 15% *ee* was previously observed with the same catalyst at *S*/*C* = 200 [7, 11]. The high enantioselectivity was also observed in the cases of *p*-OBn (**2l**), –OTBS (**2m**) and –OAc (**2n**). The substrates with electron-donating substituents proceeded in a more precisely controlled manner to provide a higher *ee*. This informs us that an attractive interaction between arene ligand and aryl substrate is favorable, presumably due to the contribution of a relatively electron-rich aryl substrate.

While α -chloroketones are addressed as superior substrates in the Rh-catalyzed transfer hydrogenation [4, 5], they suffer from severe drawbacks for commercial applications, causing irritation to the skin and eyes and being light-sensitive [14]. Furthermore, the chloride in a reduced halohydrin is a poor leaving group; so far, it routinely transformed either to styrene oxide [4, 5] for subsequent regioselective ring-opening with amine or to iodide [15] for amine displacement.

In this study, we have achieved a highly enantioselective transfer hydrogenation of α-tosyloxyarylketones to produce optically active 1-arylethanediol monotosylates. The products mostly exist in a crystalline solid; so far, they are

Table 1 Rhodium catalyzed transfer hydrogenation of α-tosyloxyketones **2**

Entry[a]	R	Time/h[b]	Conv/%	**4**			
				Yield/%[c]	*ee*[d]	$[\alpha]_D^{25}$/cm^2 g^{-1}	(*R*)/(*S*)[e]
2a	H	4	100	97	95	−51.1	*R*
		4	100	95	95	+51.2	*S*[f]
2b	*o*-Cl	24	65	42	62	−37.8	*R*
2c	*m*-Cl	2	100	99	95	−42.1	*R*
2d	*p*-Cl	2	100	94	93	−44.8	*R*
2e	*o*-Br	24	32	12	85	−37.7	*R*
2f	*m*-CF_3	2	100	96	88	−31.6	*R*
2g	*p*-F	1	100	98	93	−34.8	*R*
2h	*p*-NO_2	2	100	95	69	−23.6	*R*
2i	*o*-OMe	4	100	99	85	−47.9	*R*
2j	*m*-OMe	2	100	96	94	−37.5	*R*
2k	*p*-OMe	18	100	92	94	−50.7	*R*
		18	100	94	94	+50.9	*S*[f]
2l	*p*-OBn	18	95	85	95	−42.5	*R*
2m	*p*-OTBS	2	90	60	96	−37.3	*R*
2n	*p*-OAc	2	100	95	96	−41.2	*R*
2o	*p*-Me	2	100	97	98	−47.8	*R*
2p	3′,4′-C_4H_4	3	100	98	92	−50.0	*R*
2q	3′,4′-$O(CH_2)_2O$	5	100	94	–[g]	−36.9	*R*
2r	3′,4′-$(OMe)_2$	8	100	94	90	−27.0	*R*
2s	3′-NO_2-4′-OMe	3	100	98	84	−36.3	*R*
2t	2′-OMe-5′-Me	9	87	77	90[h]	+32.8	*S*[f]

[a] Unless otherwise indicated, reaction conditions are as follows: ketone **2** (1 mmol), (*S,S*)-**3** (*S*/*C* = 1,000), HCO_2H/Et_3 N (molar ratio = 5/2, 0.2 cm^3), 2 cm^3 EtOAc

[b] Time taken to reach the conversion specified

[c] Isolated yield

[d] The % *ee* values were measured using a chiral stationary phase

[e] The absolute configuration was determined by comparing the sign of the specific rotation with the literature data

[f] (*R,R*)-**3** was used instead of (*S,S*)-**3**

[g] Separation failed

[h] Measured as the corresponding acetate

easy to handle and/or enrich optical purity, if necessary. This may provide new opportunities for industrial synthesis of active pharmaceutical ingredients, in particular, optically active 2-amino-1-arylethanols with structural diversity.

Experimental

The catalytic reactions were carried out under an argon atmosphere with oven-dried glassware. The reactions were monitored by TLC using silica gel plates, and the products were purified by flash column chromatography on silica gel (230–400 mesh). Melting points were measured on an electrothermal apparatus. NMR spectra were recorded at 300 MHz for ^{1}H and 75 or 125 MHz for ^{13}C. Mass spectra were recorded on a GC/MS operating system at an ionization potential of 70 eV. Optical rotations were measured on a high-resolution digital polarimeter. The *ee* values of the samples were determined by HPLC analysis using Daicel Chiralcel OD-H chiral column [250 × 4.6 mm, ethanol/*n*-hexane (v/v) = 1-5/99-95, flow rate 0.5–1.2 cm^3/min].

The starting α-tosyloxyketones **2a-2t** were conveniently prepared by α-tosyloxylation of the corresponding acetophenones **1a-2t** with [hydroxy(tosyloxy)iodo]benzene in refluxing acetonitrile [7, 10–12, 14]. The chiral rhodium complex (*S,S*)-**3** was prepared from the reaction of dichloro(pentamethylcyclopentadienyl)rhodium (III) dimer (99%) and (1*S*,2*S*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine (98%) in dichloromethane in the presence of triethylamine, according to [16]. The formic acid/triethylamine (molar ratio = 5/2) azeotrope was prepared by double distillation of the mixture [17]. All reagent-grade chemicals and anhydrous solvents were purchased from commercial suppliers and used without further purification.

General procedure for asymmetric transfer hydrogenation of α-tosyloxyarylketones

Using the protocol previously described [7], the reduction of 1 mmol of ketone with (*S,S*)-**3** (*S*/*C* = 1,000) was carried out using a formic acid/triethylamine mixture (molar ratio = 5/2, 0.2 cm^3) in 2 cm^3 ethyl acetate for the time indicated in Table 1 at ambient temperature to afford the corresponding alcohol. The Rh-catalyst effectively performed in transfer hydrogenation of α-tosyloxyketones **2a-2t** to produce optically active α-tosyloxyalcohols **4a-4t**.

(S)-1-Phenyl-2-(p-tolylsulfonyloxy)ethanol
(**4a**, $C_{15}H_{16}O_4S$)
Yield: 95%; white solid; mp 69–71 °C; $[\alpha]_D^{25}$ +51.2 cm^2 g^{-1} (*c* 2.52, $CHCl_3$); 95% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.4 Hz, 2H), 7.36–7.27 (m, 7H), 4.99 (d, J = 8.7 Hz, 1H), 4.17 (dd, J = 10.2, 3.3 Hz, 1H), 4.07 (dd, J = 10.2, 8.7 Hz, 1H), 2.55 (d, J = 3.0 Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 138.1, 132.6, 129.9, 128.6, 128.5, 126.1, 74.3, 71.9, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 292 (7) $[M]^+$; HRMS Calcd for $C_{15}H_{16}O_4S$: 292.0769, found 292.0769.

(R)-1-(2-Chlorophenyl)-2-(p-tolylsulfonyloxy)ethanol
(**4b**, $C_{15}H_{15}ClO_4S$)
Yield: 42%; yellow oil; $[\alpha]_D^{25}$ −37.8 cm^2 g^{-1} (*c* 2.45, $CHCl_3$); 62% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 7.34–7.23 (m, 5H), 5.35 (dd, J = 8.1, 3.0 Hz, 1H), 4.27 (dd, J = 10.5, 2.7 Hz, 1H), 3.98 (dd, J = 10.5, 8.4 Hz, 1H), 2.77 (d, J = 3.6 Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 135.6, 132.5, 131.8, 129.9, 129.4, 129.4, 127.98, 127.8, 127.2, 72.7, 68.8, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 141 (100) $[M–CH_2OTs]^+$, 143 (35) $[M–CH_2OTs]^+$.

(R)-1-(3-Chlorophenyl)-2-(p-tolylsulfonyloxy)ethanol
(**4c**, $C_{15}H_{15}ClO_4S$)
Yield: 99%; pale yellow oil; $[\alpha]_D^{25}$ –42.1 cm^2 g^{-1} (*c* 0.98, $CHCl_3$); 95% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.1 Hz, 2H), 7.35–7.18 (m, 6H), 4.96 (dt, J = 8.1, 3.3 Hz, 1H), 4.14 (dd, J = 10.5, 3.3 Hz, 1H), 4.02 (dd, J = 10.5, 8.4 Hz, 1H), 2.61 (d, J = 3.6 Hz, 1H), 2.46 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.2, 140.3, 138.5, 137.4, 134.6, 132.3, 129.9, 129.9, 128.5, 127.9, 126.3, 124.3, 71.8, 71.2, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 141 (100) $[M–CH_2OTs]^+$, 143 (28) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{15}H_{15}ClO_4S$: C, 55.13; H, 4.63. Found: C, 55.27, H, 4.76.

(R)-1-(4-Chlorophenyl)-2-(p-tolylsulfonyloxy)ethanol
(**4d**, $C_{15}H_{15}ClO_4S$)
Yield: 94%; white solid; mp 91–92 °C; $[\alpha]_D^{25}$ −44.8 cm^2 g^{-1} (*c* 2.52, $CHCl_3$); 93% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.1 Hz, 2H), 7.35–7.23 (m, 6H), 4.96 (dt, J = 8.1, 3.3 Hz, 1H), 4.14 (dd, J = 10.5, 3.3 Hz, 1H), 4.02 (dd, J = 10.5, 8.1 Hz, 1H), 2.59 (d, J = 3.3 Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 136.7, 134.2, 132.4, 129.9, 128.7, 127.8, 127.5, 73.9, 71.25, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 141 (100) $[M–CH_2OTs]^+$, 143 (60) $[M–CH_2OTs]^+$.

(R)-1-(2-Bromophenyl)-2-(p-tolylsulfonyloxy)ethanol
(**4e**, $C_{15}H_{15}BrO_4S$)
Yield: 12%; yellow oil; $[\alpha]_D^{25}$ −37.7 cm^2 g^{-1} (*c* 0.28, $CHCl_3$); 85% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.34–7.30 (m, 3H), 7.17 (t, J = 7.7 Hz, 1H), 5.31–5.29 (m, 1H), 4.27 (dd, J = 10.5, 2.6 Hz, 1H), 3.97 (dd, J = 10.5, 8.3 Hz, 1H), 2.86 (bs, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 137.1, 132.7,

132.56, 129.9, 129.8, 128.1, 128.0, 127.8, 121.8, 72.7, 71.0, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 370 (19) $[M]^+$, 372 (21) $[M]^+$; HRMS Calcd for $C_{15}H_{15}BrO_4S$: 369.9874, found 369.9875.

(R)-1-(3-Trifluoromethylphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4f**, $C_{16}H_{15}F_3O_4S$)
Yield: 96%; white solid; mp 89–92 °C; $[\alpha]_D^{25}$ −31.6 $cm^2\ g^{-1}$ (*c* 2.42, $CHCl_3$); 88% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, $J = 8.4$ Hz, 2H), 7.58–7.43 (m, 4H), 7.33 (d, $J = 8.14$ Hz, 2H), 5.05 (dt, $J = 8.1$, 3.3 Hz, 1H), 4.16 (dd, $J = 10.5$, 3.6 Hz, 1H), 4.05 (dd, $J = 10.5$, 8.1 Hz, 1H), 2.89 (d, $J = 3.3$ Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 139.3, 132.3, 131.4, 131.1, 129.9, 129.6, 129.1, 127.8, 125.2, 123.0, 73.8, 71.3, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 360 (14) $[M]^+$; HRMS Calcd for $C_{16}H_{15}F_3O_4S$: 360.0643, found 360.0644.

(R)-1-(4-Fluorophenyl)-2-(p-tolylsulfonyloxy)ethanol (**4g**, $C_{15}H_{15}FO_4S$)
Yield: 98%; white solid; mp 66–68 °C; $[\alpha]_D^{25}$ −34.8 $cm^2\ g^{-1}$ (*c* 1.59, $CHCl_3$); 93% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, $J = 8.2$ Hz, 2H), 7.35–7.28 (m, 4H), 7.01 (t, $J = 8.6$ Hz, 2H), 4.96 (dt, $J = 8.2$, 3.0 Hz, 1H), 4.11 (dd, $J = 10.5$, 3.5 Hz, 1H), 4.02 (dd, $J = 10.2$, 8.3 Hz, 1H), 2.68 (d, $J = 3.1$ Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.5, 144.8, 136.8, 132.1, 130.0, 127.5, 125.4, 114.9, 74.1, 69.1, 21.0 ppm; MS (EI, 70 eV) *m/z* (%) 125 (100) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{15}H_{15}FO_4S$: C, 58.05; H, 4.87. Found: C, 58.47; H, 5.01.

(R)-1-(4-Nitrophenyl)-2-(p-tolylsulfonyloxy)ethanol (**4h**, $C_{15}H_{15}NO_6S$)
Yield: 95%; white solid; mp 174–175 °C; $[\alpha]_D^{25}$ −23.6 $cm^2\ g^{-1}$ (*c* 1.06, acetone); 69% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, $J = 8.6$ Hz, 2H,), 7.75 (d, $J = 8.1$ Hz, 2H), 7.52 (d, $J = 8.5$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 5.13–5.10 (m, 1H), 4.20 (dd, $J = 10.6$, 3.4 Hz, 1H), 4.10–4.04 (m, 1H), 2.82 (d, $J = 3.1$ Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.3, 146.8, 144.8, 131.9, 129.9, 127.5, 123.1, 73.7, 69.0, 21.0 ppm; MS (EI, 70 eV) *m/z* (%) 152 (74) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{15}H_{15}NO_6S$: C, 53.40; H, 4.48. Found: C, 53.97; H, 5.04.

(R)-1-(2-Methoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4i**, $C_{16}H_{18}O_5S$)
Yield: 99%; white solid; mp 53–55 °C; $[\alpha]_D^{25}$ −47.9 $cm^2\ g^{-1}$ (*c* 2.54, $CHCl_3$); 85% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, $J = 8.1$ Hz, 2H), 7.38–7.24 (m, 4H), 6.95 (t, $J = 7.5$ Hz, 1H), 6.82 (d, $J = 8.1$ Hz, 1H), 5.17 (dd, $J = 8.1$, 3.3 Hz, 1H), 4.28 (dd, $J = 10.2$, 3.3 Hz, 1H), 4.05 (dd, $J = 10.2$, 8.1 Hz, 1H), 3.77 (s, 3H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 144.7, 132.8, 129.7, 129.3, 127.9, 127.4, 126.1, 120.8, 110.3, 73.0, 68.2, 55.2, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 322 (60) $[M]^+$.

(R)-1-(3-Methoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4j**, $C_{16}H_{18}O_5S$)
Yield: 96%; white solid; mp 52–54 °C; $[\alpha]_D^{25}$ −37.5 $cm^2\ g^{-1}$ (*c* 2.56, $CHCl_3$); 94% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.27–7.22 (m, 1H), 6.88–6.82 (m, 3H), 4.95 (d, $J = 8.7$, 3.0 Hz, 1H), 4.15 (dd, $J = 10.5$, 3.3 Hz, 1H), 4.04 (dd, $J = 10.5$, 8.7 Hz, 1H), 2.53 (d, $J = 3.3$ Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.8, 145.7, 239.8, 132.5, 129.9, 129.7, 127.9, 118.4, 114.0, 111.5, 74.3, 71.8, 55.2, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 322 (46) $[M]^+$.

(R)-1-(4-Methoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4k**, $C_{16}H_{18}O_5S$)
Yield: 92%; white solid; mp 71–72 °C; $[\alpha]_D^{25}$ −50.7 $cm^2\ g^{-1}$ (*c* 0.79, $CHCl_3$); 94% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.3$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.23 (d, $J = 6.9$ Hz, 2H), 6.86 (d, $J = 6.8$ Hz, 2H), 4.92 (dd, $J = 8.4$, 3.5 Hz, 1H), 4.11 (dd, $J = 10.3$, 3.5 Hz, 1H), 4.03 (dd, $J = 10.4$, 8.5 Hz, 1H), 3.79 (s, 3H), 2.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.7, 145.0, 132.6, 130.3, 129.9, 127.9, 127.4, 114.0, 74.2, 71.4, 55.2, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 322 (44) $[M]^+$; HRMS Calcd for $C_{16}H_{18}O_5S$: 322.0875, found 322.0875.

(R)-1-(4-Benzyloxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4l**, $C_{22}H_{22}O_5S$)
Yield: 85%; white solid; mp 91–92 °C; $[\alpha]_D^{28}$ −42.5 $cm^2\ g^{-1}$ (*c* 0.79, $CHCl_3$); 95% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.4$ Hz, 2H), 7.43–7.31 (m, 6H), 7.23 (d, $J = 8.8$ Hz, 2H), 6.93 (d, $J = 8.8$ Hz, 2H), 5.05 (s, 2H), 4.92 (dt, $J = 8.3$, 3.0 Hz, 1H), 4.11 (dd, $J = 10.3$, 3.5 Hz, 1H), 4.02 (dd, $J = 10.3$, 8.5 Hz, 1H), 2.47 (d, $J = 3.0$ Hz, 1H), 2.44 (s, 3H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.9, 145.0, 136.7, 132.6, 130.5, 129.9, 128.5, 128.0, 127.9, 127.5, 127.4, 114.9, 74.2, 71.4, 69.9, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 398 (1) $[M]^+$; HRMS Calcd for $C_{16}H_{18}O_5S$: 398.1188, found 398.1191.

(R)-1-(4-tert-Butyldimethylsilyloxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4m**, $C_{21}H_{30}O_5SSi$)
Yield: 60%; yellow oil; $[\alpha]_D^{29}$ −37.3 $cm^2\ g^{-1}$ (*c* 1.02, $CHCl_3$); 96% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.6$ Hz, 2H), 7.16 (d, $J = 8.3$ Hz, 2H), 6.79 (d, $J = 8.6$ Hz, 2H), 4.92–4.89 (m, 1H), 4.11 (dd, $J = 10.3$, 3.3 Hz, 1H), 4.02 (dd, $J = 10.3$, 8.5 Hz, 1H), 2.48 (d, $J = 2.8$ Hz, 1H), 2.44 (s, 3H), 0.96 (s, 9H), 0.17 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 145.0, 132.6, 130.8, 129.9, 127.9,

127.4, 120.2, 74.3, 71.5, 25.6, 21.6, 18.1, −4.4 ppm; MS (EI, 70 eV) *m/z* (%) 422 (1) $[M]^+$; HRMS Calcd for $C_{21}H_{30}O_5SSi$: 422.1583, found 422.1587.

(R)-1-(4-Acetoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4n**, $C_{17}H_{18}O_6S$)
Yield: 95%; pale yellow oil; $[\alpha]_D^{25}$ −41.2 $cm^2\ g^{-1}$ (*c* 1.09, $CHCl_3$); 96% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.6$ Hz, 2H), 7.33 (d, $J = 8.7$ Hz, 2H), 7.06 (d, $J = 8.6$ Hz, 2H), 4.99 (dt, $J = 8.5$, 3.2 Hz, 1H), 4.12 (dd, $J = 10.4$, 3.3 Hz, 1H), 4.01 (dd, $J = 10.4$, 8.5 Hz, 1H), 2.61 (d, $J = 3.2$ Hz, 1H), 2.45 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 150.6, 145.1, 145.7, 132.4, 129.9, 127.9, 127.3, 121.8, 74.1, 74.3 21.6, 21.0 ppm; MS (EI, 70 eV) *m/z* (%) 165 (39) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{17}H_{18}O_6S$: C, 58.27; H, 5.18. Found: C, 60.01, H, 5.08.

(R)-1-(4-Methylphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4o**, $C_{16}H_{18}O_4S$)
Yield: 97%; white solid; mp 85–86 °C; $[\alpha]_D^{25}$ −47.8 $cm^2\ g^{-1}$ (*c* 1.27, $CHCl_3$); 98% *ee*; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, $J = 8.3$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.0$ Hz, 2H), 7.14 (d, $J = 7.7$ Hz, 2H), 4.94–4.92 (m, 1H), 4.12 (dd, $J = 10.4$, 3.2 Hz, 1H), 4.03 (dd, $J = 10.4$, 8.6 Hz, 1H), 2.59 (s, 1H), 2.44 (s, 3H), 2.33 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 138.3, 135.2, 132.0, 129.9, 129.3, 127.9, 126.7, 126.0, 74.3, 71.7, 21.6, 21.1 ppm; MS (EI, 70 eV) *m/z* (%) 121 (100) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.72; H, 5.92. Found: C, 61.98; H, 5.97.

(R)-1-(2-Naphthyl)-2-(p-tolylsulfonyloxy)ethanol (**4p**, $C_{19}H_{18}O_4S$)
Yield: 98%; white solid; mp 116–118 °C; $[\alpha]_D^{25}$ −50.0 $cm^2\ g^{-1}$ (*c* 2.50, $CHCl_3$); 92% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83–7.72 (m, 6H), 7.51–7.47 (m, 2H), 7.38 (d, $J = 8.7$ Hz, 1H), 7.27–7.25 (m, 2H), 5.15 (dd, $J = 8.1$, 3.3 Hz, 1H), 4.25 (dd, $J = 10.5$, 3.6 Hz, 1H), 4.14 (dd, $J = 10.5$, 8.1 Hz, 1H), 2.65 (bs, 1H), 2.41 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 135.6, 133.2, 133.1, 132.5, 129.8, 128.4, 127.9, 127.8, 127.6, 127.3, 126.3, 125.4, 123.6, 74.2, 72.0, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 157 (100) $[M–CH_2OTs]^+$; Anal. Calcd for $C_{19}H_{18}O_4S$: C, 66.65; H, 5.30. Found: C, 66.72; H, 5.81.

(R)-1-(2,3-Dihydrobenzo[1, 4]dioxin-6-yl)-2-(p-tolylsulfonyloxy)ethanol (**4q**, $C_{17}H_{18}O_6S$)
Yield: 94%; pale yellow oil; $[\alpha]_D^{25}$ −36.9 $cm^2\ g^{-1}$ (*c* 1.73, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 6.79 (m, 3H), 4.86 (dd, $J = 8.4$, 3.3 Hz, 1H), 4.23 (s, 4H), 4.10 (dd, $J = 10.5$, 2.7 Hz, 1H), 4.00 (dd, $J = 10.2$, 8.4 Hz, 1H), 2.45 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.6, 144.9, 143.6, 132.9, 129.9, 129.7, 127.8, 120.2, 117.5, 116.1, 75.5, 72.4, 64.2, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 350 (1) $[M]^+$.

(R)-1-(3,4-Dimethoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4r**, $C_{17}H_{20}O_6S$)
Yield: 94%; pale yellow oil; $[\alpha]_D^{25}$ −27.0 $cm^2\ g^{-1}$ (*c* 0.83, $CHCl_3$); 90% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (d, $J = 8.2$ Hz, 2H), 7.75 (d, $J = 8.3$ Hz, 2H), 6.85–6.82 (m, 3H), 4.92 (dd, $J = 8.1$, 3.7 Hz, 1H), 4.12 (dd, $J = 10.4$, 3.7 Hz, 1H), 4.05 (dd, $J = 10.2$, 8.1 Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2,44 (s, 3H) ppm; MS (EI, 70 eV) *m/z* (%) 352 (3) $[M]^+$.

(R)-1-(3-Nitro-4-methoxyphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4s**, $C_{16}H_{17}NO_7S$)
Yield: 98%; white solid; mp 92–93 °C; $[\alpha]_D^{25}$ −36.3 $cm^2\ g^{-1}$ (*c* 2.49, $CHCl_3$); 84% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.54 (d, $J = 8.4$ Hz, 1H), 7.34 (d, $J = 8.1$ Hz, 2H), 7.06 (d, $J = 8.7$ Hz, 1H), 5.00–4.98 (m, 1H), 4.13 (dd, $J = 10.5$, 3.9 Hz, 1H), 4.04 (dd, $J = 10.5$, 7.8 Hz, 1H), 3.96 (s, 3H), 2.73 (bs, 1H), 2.46 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 145.3, 139.3, 132.2, 132.0, 130.8, 130.0, 127.8, 123.5, 113.6, 73.5, 70.4, 56.6, 21.6 ppm; MS (EI, 70 eV) *m/z* (%) 182 (100) $[M–CH_2OTs]^+$.

(S)-1-(2-Methoxy-5-methylphenyl)-2-(p-tolylsulfonyloxy)ethanol (**4t**, $C_{17}H_{20}O_5S$)
Yield: 77%; yellow oil; $[\alpha]_D^{25}$ +32.8 $cm^2\ g^{-1}$ (*c* 1.06, $CHCl_3$); 90% *ee*; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, $J = 8.3$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 1.9$ Hz, 1H), 7.05 (dd, $J = 8.7$, 1.7 Hz, 1H), 6.71 (d, $J = 8.3$ Hz, 1H), 5.15–5.10 (m, 1H), 4.25 (dd, $J = 10.1$, 3.4 Hz, 1H), 4.05 (dd, $J = 10.1$, 8.1 Hz, 1H), 3.73 (s, 3H), 2.82 (d, $J = 5.3$ Hz, 1H), 2.44 (s, 3H), 2.26 (s, 3H) ppm; MS (EI, 70 eV) *m/z* (%) 336 (2) $[M]^+$.

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