Highly Enantioselective Rh-catalyzed Transfer Hydrogenation of α-Functionalized Arylketones

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Asymmetric transfer hydrogenation of α-functionalized arylketones has been studied. The chiral Rh-catalyst effectively performed in transfer hydrogenation of α-mesyloxyketones with an azeotropic mixture of formic acid/triethylamine to produce optically active 1-arylethandiols with excellent enantioselectivity.

Key Words: Asymmetric transfer hydrogenation, α-Mesyloxy arylketone, Arylethandiol

Introduction

To date, 1,2-aminoalcohols have been identified as rich resources in organic synthesis and pharmaceutical industry. The aminoalcohols are often found not only in the structural units of many building blocks, chiral auxiliaries, and ligands in organic transformations,[1] but also in the structural motif of many biologically active compounds. In particular, optically active 2-amino-1-arylethanols are of great importance as selective serotonin reuptake inhibitors, α/β-adrenegic agonists and NR1/2B subtype NMDA receptor antagonists in the therapy of depression, asthma, diabetes, and obesity.[2]

Accordingly, a number of studies have disclosed the methods comprising oxazaborolidine-catalyzed reduction of ketones,[3] asymmetric hydrogenation of aminoketones,[4] asymmetric epoxidation of allylic alcohols[5] and asymmetric dihydroxylation of styrenes.[6] Recently, the β-agonists have been prepared through microbial reduction of α-azido and-bromoketones[7] or lipase-mediated resolution of α-azidoalcohols.[8] It has been also noted that optically enriched cyanohydrin or nitroaldol leads to the synthesis of the β-agonists from the corresponding benzaldehydes.[9] Interestingly, most of the reported methods involves a unique feature, an easy access to versatile synthetic intermediates, thereby securing their wide application to syntheses of aminoalcohols. The varying physiological activity of these molecules can be modulated either by tuning the stereochemistry of functional groups or by variations in the substitution pattern of the aryl moiety.

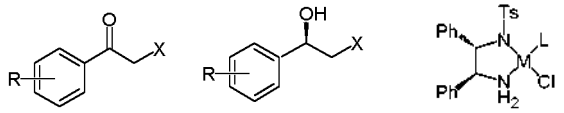
Recently, the application of asymmetric transfer hydrogenation (ATH) has been extended to enantioselective hydrogenation of unsaturated carbonyl and imine groups.[10] The catalysts generally consist of bidentate ligands based on 1,2-aminoalcohols or monosulfonylated diamines, bound to ruthenium, rhodium, or iridium. It has been proved that (*1S,2S*) or (*1R,2R*)-*N*-(*p*-toluenesulfony)-1,2-diphenylethylenediamine (TsDPEN) is an excellent ligand for the catalytic transfer hydrogenation of arylketones,[10a] where the reaction is routinely carried out with isopropanol/base or a formic acid/triethylamine mixture as hydrogen donors. The latter is more versatile as it results in an essentially irreversible reaction.[10b] The ATH, rather, offers an operational simplicity, since the reaction does not involve molecular hydrogen and is insensitive to air oxidation, and thus is particularly valuable in scale-up syntheses of active pharmaceutical ingredients.[11] Herein, we report an asymmetric transfer hydrogenation of various α-functionalized arylketones, aiming toward their facile entry into many biologically active compounds containing aminoalcohols.

Results and Discussion

A well-defined chiral Rh complex **1**[12] effectively performed in transfer hydrogenation of α-functionalized arylketones (substrate/catalyst molar ratio = 1,000) with an azeotopic mixture of formic acid/triethylamine (molar ratio = 5/2) to produce optically active 1-arylethanols, as shown in Table 1. Although, α-chloroketone (**3a**) by (*R,R*)-**1** was reduced to (*S*)-2-chloro-1-phenylethanol with 96% enantiomeric excess (*ee*), the corresponding bromide (**4a**) was reduced to (*S*)-2-bromoethanol with as low as 29% *ee*. The successful reduction of α-hydroxy group (**5a**) with 98% *ee* is notable, since it is capable of binding to the metal center of the catalyst, with no apparent direct contact between the hydroxyl group and the metal leading to deactivation of the catalyst.[13] The high level of enantioselection for α-sulfonyloxyketones (97% for **6a** and 95% *ee* for **7a**) was sustained and thus indicated that these compounds are also good substrates for transfer hydrogenation. Notably, the Rh-catalyst **1** is preferable to the Ru-catalyst **2** in the reduction of α-functionalized ketone (entries 5 and 6, Table 1).[14-16]

Next, we estimated the efficiency of the Rh-catalyst **1** within both chloroketones and the corresponding α-sulfonyloxyketones possessing substituted aryl groups (entries 7-12). The Rh-catalyst cleanly reduced all aryl substrates and formation of by-products such as 1,3-oxolane[15a,b] and formate/epoxide[15] were not observed within this examination. Even the *ee* values of α-tosyloxyketones were comparable to those reported in α-chloroketones,[14a] and among all compounds studied α-mesyloxyketones gave the best enantioselectivities.

Table 1. Asymmetric transfer hydrogenation of α-functionalized arylketones.



ketone: X = Cl (3)
X = Br (4)
X = OH (5)
X = OMs (6)
X = OTs (7)
R = H (a); *p*-OMe (b); *p*-Cl (c)

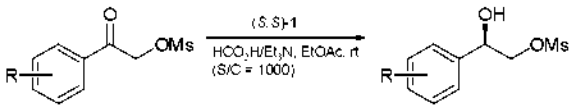
8

1: (*S,S*)-TsDPEN-Rh-Cp*
2: (*S,S*)-TsDPEN-Ru-*p*-cymene

entry[a]	ketone	cat.	time (h)[b]	8	
				yield[c]	ee[d] (R/S)[e]
1	**3a**	(*R,R*)-**1**	1	99	97 (S)[f]
2	**4a**	(*R,R*)-**1**	24[g]	53	29 (S)
3	**5a**	(*S,S*)-**1**	5	56	98 (R)
4	**6a**	(*S,S*)-**1**	0.5	98	97 (R)
5	**7a**	(*R,R*)-**1**	4	97	95 (S)
6	**7a**	(*S,S*)-**2**	72[g]	66	87 (R)
7	**3b**	(*R,R*)-**1**	2	94	94 (S)[f]
8	**3c**	(*R,R*)-**1**	2	90	92 (S)[f]
9	**6b**	(*S,S*)-**1**	4	93	97 (R)
10	**6c**	(*S,S*)-**1**	0.5	97	95 (R)
11	**7b**	(*S,S*)-**1**	18	92	94 (R)
12	**7c**	(*S,S*)-**1**	2	94	93 (R)

Cp* = pentamethylcyclopentadienyl.
[a]Reaction conditions: substrate 1 mmol (S/C = 1,000), HCO_2H/Et_3N (molar ratio = 5/2, 0.2 mL), EtOAc (2 mL). [b]Time taken to reach a complete conversion unless otherwise specified. [c]Isolated yield (%). [d]The *ee* values were measured by chiral HPLC analysis. [e]The absolute configuration was determined by comparing the sign of the specific rotation with the literature data. [f]Data taken from ref. 14a-b. [g]The reaction was not completed at the indicated time.

Table 2. Asymmetric transfer hydrogenation of α-mesyloxy arylketones **6** with (*S,S*)-**1**.



6 (*R*)-**8**

entry[a]	ketone	R	time (h)[b]	(*R*)-**8**	
				yield (%)	ee
1	**6d**	*o*-Cl	0.5	90	77
2	**6e**	*m*-Cl	0.5	95	97
3	**6f**	*o*-OMe	12	92	88
4	**6g**	*m*-OMe	0.5	97	97
5	**6h**	*p*-OAc	0.5	97	97
6	**6i**	*p*-OTBS	0.5	68	98
7	**6j**	*m*-CF_3	0.5	91	94
8	**6k**	*p*-CF_3	0.5	98	96
9	**6l**	*p*-F	0.5	94	96
10	**6m**	*p*-NO_2	0.5	90	88
11	**6n**	*p*-Bu^t	2	85	99
12[b]	**6o**	*p*-$N(Ms)_2$	8	50	96
13[b]	**6p**	*p*-NHMs	5	62	-[c]
14	**6q**	3',4'-Cl_2	1	99	94
15	**6r**	3',4'-C_4H_4	0.5	96	99
16	**6s**	3',4'-$O(CH_2)_2O$	2	92	97
17	**6t**	3'-NO_2-4'-OMe	0.5	90	92
18	**6u**	3'-CH_2OMe-4'-OMe	2	93	95
19	**6v**	2'-OMe-5'-Me	20	91	90

[a]Unless otherwise indicated, reaction conditions are as follows: ketone (**6**, 1 mmol), (*S,S*)-**1** (S/C = 1,000), HCO_2H/Et_3N (molar ratio = 5/2, 0.2 mL), EtOAc (2-5 mL). [b]DMF was used instead of EtOAc. [c]Separation failed.

For example, mesyloxyketones **6b** and **6c** were reduced to the (*R*)-alcohols in 97 and 95% *ee*, respectively, whereas the corresponding chloroketones (entries 7-8) gave the (*S*)-alcohols with the slightly lower *ee* values. This outcome represents the best level of enantioselection ever made in the asymmetric transfer hydrogenation of α-functionalized aryketones.

The α-sulfonyloxyketones have been utilized, indeed, as versatile intermediates for the preparation of a large group of antidepressants and α/β-adrenegic drugs.[16] To date, however, α-sulfonyloxyketones have not attracted much attention in asymmetric transfer hydrogenation.[15] While α-chloroketones are recognized as preferable substrates in the Rh-catalyzed transfer hydrogenation,[14] the ketones suffer from severe drawbacks for commercial applications; they cause irritation to skin and eyes and are photo-labile.[3d] Furthermore, the reduced halohydrin is a poor leaving group, and thus, far, it has been routinely transformed to either styrene oxide[14a,b] for subsequent regioselective ring-opening with amine or to an iodide[3b] for amine displacement. Thus, we readily undertook the asymmetric transfer hydrogenation of various α-mesyloxylketones, aiming toward their facile entry into many biologically active compounds containing 1,2-aminoalcohols.

Previously, the α-mesyloxyketone derivatives **6** were easily prepared in 52-92% yield by the α-sulfonyloxylation[18] of the corresponding arylketones or silyl enol ether with [hydroxy(mesyloxy)iodo]benzene, where the starting arylketones are either commercially available or are easily accessible in a few steps. The *ee* values were measured by chiral HPLC analysis using a Daicel Chiralcel OD-H column. The racemic alcohols (±)-**8** were prepared by sodium borohydride reduction of **6** in THF, and used as standards for *ee* determination. The absolute configuration was determined by comparing the sign of the specific rotation with the literature data. So far, we have examined various substrates differentiated by electronically and sterically demanding groups using the same protocol. All the products gave excellent enantioselectivity with high yield and the results are summarized in Table 2.

For a given catalytic system, the selectivity was not much sensitive to the phenyl ring substituents except *ortho*-substitution. The reduction of *o*-chloroacetophenone (**6d**) showed a decreased enantioselectivity comparing to those of the corresponding congeners (**6c** and **6e**). Consistent with this observation, an *o*-methoxy group (entry 3, Table 2) significantly decreased the enantioselectivity, whereas both *m*- and *p*-methoxyacetophenones (**6b** and **6g**) were reduced with 97% *ee*. Apparently, the introduction of *o*-substituents brings about

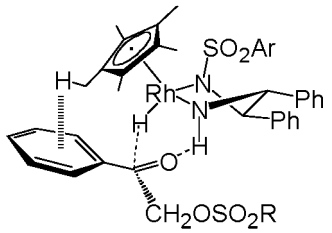


Figure 1. General sense of asymmetric transfer hydrogenation of α-sulfonyloxy arylketones with (*S,S*)-**1**.

steric demands that disturb the compact preorganization toward catalytic complex structure.

The presence of an electron-withdrawing group on the phenyl ring (entries 8-10) has generally facilitated the hydride transfer due to the polar character of the reducing species involved, whereas **6b** was completed only after 4 h. Likewise, the reduction of *o*-substituted acetophenones, such as 2-methoxyphenylethanone derivatives (entries 3 and 19) was particularly sluggish. While, the arylketone derivatives with electron-donating substituents proceeded in a more precisely controlled manner to provide a higher *ee*. The facial selectivity was elevated to 99% *ee* in the cases of 4-*t*-butylphenylethanone (**6n**) and 2-naphthylethanone (**6r**), whereas 4-nitrophenylethanone (**6m**) showed decreased enantioselectivity with 88% *ee*. This result indicated that an attractive interaction between arene ligand and aryl substrate is favorable, presumably due to the contribution of a relatively electron-rich aryl substrate.

Recent studies have suggested that for the origin of enantioselectivity in ATH, electrostatic interactions are of importance, particularly as illustrated in terms of arene-aryl interactions between arene ligand and aryl substrate in the favored transition state[19] and by the dispersion effects arising from between the aryl substrate and the amine ligand in the disfavored transition state.[20] Interestingly, the even bulkier *p*-tosyloxymethyl group in **7** behaves as methyl in acetophenone and is still free from the metal center, so the sense of asymmetric induction has not been changed as observed. The enriched enantioselectivities from **6** compared to those of **3** suggest that there is perhaps facial discrimination between the two substrates.[21] At present, the reason is unclear; however, a plausible explanation could be that there is an additional electrostatic repulsion between the sulfonamide of the ligand and the sulfonate of the substrate, forcing the sulfonyloxymethyl group into the less hindered region in the favored transition state, as depicted in Figure 1. Thus, it is assumed that even a slight change in the substrate forces the complex to be more correctly preorganized toward the reduction. The overall results again suggest that the reduction of α-functionalized arylketone derivatives operates through a general sense of symmetric transfer hydrogenation in the same direction.

Experimental Section

General. The catalyst (*S,S*)-**1** was prepared from the reaction of dichloro(pentamethylcyclopentadienyl)rhodium (III) dimmer and (*1S,2S*)-*N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine in dichloromethane in the presence of triethylamine, according to the literature procedure.[12] It should be noted that the catalyst was used without any purification, so the catalyst includes an equal molar of hydrochloride/triethylamine salt. This catalyst mixture is very stable and insensitive to atmospheric manipulations, and does not show any deterioration in the catalytic activity comparing to that prepared from recrystalization. The formic acid/triethylamine (molar ratio = 5/2) azeotrope was prepared by the double distillation of the mixtures, according to the literature procedure.[22]

The starting arylketones are either commercially available or easily accessible in a few steps. The *p*-OAc and *p*-OTBS ketones (for entries 5 and 6, Table 2) were conveniently obtained from *p*-hydroxyacetophenone, and 2'-OMe-5'-Me ketone[23] (for entry 19) was prepared via acetylation of 1-methoxy-4-methylbenzene with acetic acid in the presence of $LiClO_4$. Surprisingly, the reaction of *p*-aminoacetophenone with methanesulfonyl chloride in the presence of triethylamine afforded *p*-N(Ms)$_2$ ketone (for entry 12) instead of *p*-NHMs ketone.[24] However, in the presence of pyridine, the reaction furnished *p*-NHMs ketone (for entry 13).[25]

The α-mesyloxyketones **6** were easily prepared in 52-92% yield by α-sulfonyloxylation of the corresponding arylketones (**6a-6o** and **6q-6v**) or silyl enol ether (**6p**) with [hydroxy(mesyloxy)iodo]benzene, according to the literature procedure.[18] Overall, the catalytic reactions with (*S,S*)-**1** were effectively performed in transfer hydrogenation of α-mesyloxyketones **6** (substrate/catalyst molar ratio = 1,000) with an azeotopic mixture of formic acid/triethylamine (molar ratio = 5/2) to produce optically active 1-arylethanols (*R*)-**8**. The *ee* value was measured by chiral HPLC analysis using Daicel Chiralcel OD-H column. The racemic alcohol (±)-**8** were prepared by sodium borohydride reduction of **6** in THF, and used as standards for *ee* determination.

(*S,S*)-TsDPEN-RhCl-Cp* [(*S,S*)-1]. Into a 25 mL two-neck flask capped with septa and an argon balloon system was charged 100 mg (0.16 mmol) of dichloro(pentamethylcyclopentadienyl)rhodium(III) dimer and 120 mg (0.32 mmol) of (*1S,2S*)-(+)-*N*-*p*-tosyl-1,2-diphenylethylenediamine. Under argon atmosphere, dry dichloromethane (5 mL) was added, followed by the addition of 90 μL of dry triethylamine (0.65 mmol) to the flask. The resulting mixture was allowed to stir 2 h at ambient temperature. The solvent was stripped off using reduced pressure (aspirator) under inert atmosphere. The residue was dried under high vacuum for 2 h. After scratching with spatula, the bright orange powder (190 mg) was transferred into a vial. This was stored under argon and used for catalytic reactions.

Preparation of HCO_2H/Et_3N azeotrope. The formic acid/triethylamine (molar ratio = 5/2) azeotrope was prepared by the double distillation of the mixtures.

α-Sulfonyloxylation of arylketones. Representative procedure for the preparation of 1-phenyl-2-(methylsulfonyloxy) ethanone (6a): A mixture of [hydroxy(methylsulfonyloxy) iodo]benzene (3.15 g, 9.96 mmol) and acetophenone (1.02 g, 8.49 mmol) in acetonitrile (25 mL) was stirred under reflux for 2 h. After cooling to rt, the reaction mixture was concentrated in vacuo. The resulting mixture was diluted with ethyl

acetate (30 mL) and then was washed with sat. $NaHCO_3$ (2 × 10 mL) and brine (10 mL). The organic phase was dried over Na_2SO_4 and concentrated to give a residue. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 3/1) to give 1.68 g (92%) of 1-phenyl-2-(methylsulfonyloxy)ethanone (**6a**) as a solid: mp 77-78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (2H, d, J = 7.2 Hz), 7.65 (1H, t, J = 7.3 Hz), 7.51 (2H, t, J = 7.4 Hz), 5.52 (2H, s), 3.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0, 134.4, 133.3, 129.0, 127.7, 70.2, 39.1; EIMS (70 eV) *m/z* (rel intensity) 214 (M^+, 7), 105 (M^--CH_2OMs, 100).

1-(4-Methoxyphenyl)-2-(methylsulfonyloxy)ethanone (6b): Yield 42%; mp 115-116 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (2H, d, J = 6.9 Hz), 6.97 (2H, d, J = 7.0 Hz), 5.46 (2H, s), 3.89 (3H, s), 3.28 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 164.4, 130.1, 126.3, 114.2, 70.0, 55.5, 39.1; EIMS (70 eV) *m/z* (rel intensity) 244 (M^-, 11), 135 (M^--CH_2OMs, 100), 107 (61), 92 (68).

1-(4-Chlorophenyl)-2-(methylsulfonyloxy)ethanone (6c): Yield 90%; mp 110-112 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (2H, d, J = 8.3 Hz), 7.50 (2H, d, J = 8.3 Hz), 5.47 (2H, s), 3.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.0, 141.0, 131.6, 129.4, 129.1, 69.9, 39.1; EIMS (70 eV) *m/z* (rel intensity) 250 (M^-, 3), 48 (M^+, 7), 139 (M^--CH_2OMs, 100), 111 (66).

1-(2-Chlorophenyl)-2-(methylsulfonyloxy)ethanone (6d): Yield 74%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67-7.63 (1H, m), 7.53-7.37 (3H, m), 5.40 (2H, s), 3.24 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 134.6, 133.4, 131.7, 130.7, 130.1, 127.2, 72.0, 39.0; EIMS (70 eV) *m/z* (rel intensity) 250 (M^+, 1), 248 (M^-, 2), 152 (17), 139 (M^+-CH_2OMs, 100), 111 (56).

1-(3-Chlorophenyl)-2-(methylsulfonyloxy)ethanone (6e): Yield 93%; mp 88-90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (1H, s), 7.76 (1H, d, J = 7.7 Hz), 7.62 (1H, d, J = 8.0 Hz), 7.47 (1H, t, J = 8.0 Hz), 5.47 (2H, s), 3.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.0, 135.4, 134.7, 134.3, 130.3, 127.8, 125.8, 69.9, 39.1; EIMS (70 eV) *m/z* (rel intensity) 250 (M^+, 3), 248 (M^-, 6), 152 (46), 139 (M^+-CH_2OMs, 100), 111 (73).

1-(2-Methoxyphenyl)-2-(methylsulfonyloxy)ethanone (6f): Yield 65%; mp 92-93 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (1H, d, J = 7.8 Hz), 7.57 (1H, t, J = 7.7 Hz), 7.07 (1H, t, J = 7.8 Hz), 7.01 (1H, d, J = 8.4 Hz), 5.42 (2H, s), 3.96 (3H, s), 3.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.7, 159.5, 135.6, 130.9, 123.3, 121.1, 111.5, 74.2, 75.6, 39.0; EIMS (70 eV) *m/z* (rel intensity) 244 (M^-, 30), 135 (M^+-CH_2OMs, 100), 92 (30).

1-(3-Methoxyphenyl)-2-(methylsulfonyloxy)ethanone (6g): Yield 87%; mp 84-85 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.40 (3H, m), 7.19-7.16 (1H, m), 5.49 (2H, s), 3.86 (3H, s), 3.27 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.9, 159.9, 134.5, 130.0, 120.8, 120.0, 111.9, 70.3, 55.4, 39.0; EIMS (70 eV) *m/z* (rel intensity) 244 (M^-, 46), 135 (M^--CH_2OMs, 100), 107 (75), 92 (43).

1-(4-Acetoxyphenyl)-2-(methylsulfonyloxy)ethanone (6h): Yield 70%; mp 90-91 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (2H, d, J = 8.4 Hz), 7.27 (2H, d, J = 8.2 Hz), 5.49 (2H, s), 3.29 (3H, s), 2.34 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.9, 168.6, 155.3, 130.9, 129.5, 122.3, 69.9, 39.2, 21.1; EIMS (70 eV) *m/z* (rel intensity) 272 (M^+, 4), 163 (M^--CH_2OMs, 87), 121 (100).

1-(4-tert-Butyldimethylsilyloxyphenyl)-2-(methylsulfonyloxy)ethanone (6i): Yield 55%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (2H, d, J = 8.6 Hz), 6.91 (2H, d, J = 8.6 Hz), 5.46 (2H, s), 3.28 (3H, s), 0.99 (9H, s), 0.24 (6H ,s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.5, 161.4, 130.0, 126.8, 120.4, 70.0, 39.2, 25.5, 18.2, -4.3; EIMS (70 eV) *m/z* (rel intensity) 344 (M^-, 6), 259 (23), 235 (M^--CH_2OMs, 85), 153 (100).

1-(3-Trifluoromethylphenyl)-2-(methylsulfonyloxy)ethanone (6j): Yield 85%; mp 76-78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (1H, s), 8.09 (1H, d, J = 7.9 Hz), 7.91 (1H, d, J = 7.9 Hz), 7.69 (1H, t, J = 7.8 Hz), 5.52 (2H, s), 3.28 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.0, 133.9, 130.9, 130.8, 130.7, 129.8, 124.7, 124.6, 69.9, 39.0; EIMS (70 eV) *m/z* (rel intensity) 173 (M^--CH_2OMs, 100), 145 (44).

1-(4-Trifluoromethylphenyl)-2-(methylsulfonyloxy)ethanone (6k): Yield 63%; mp 109-110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (2H, d, J =8.2 Hz), 7.79 (2H, d, J = 8.3 Hz), 5.50 (2H, s), 3.29 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.4, 136.0, 128.2, 126.2, 126.1, 69.9, 39.2; EIMS (70 eV) *m/z* (rel intensity) 282 (M^+, 1), 263 (32), 173 (M^+-CH_2OMs, 100), 145 (100).

1-(4-Fluorophenyl)-2-(methylsulfonyloxy)ethanone (6l): Yield 84%; mp 90-91 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96-7.91 (2H, m), 7.27-7.17 (2H, m), 5.47 (2H, s), 3.28 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.5, 167.4, 130.6, 129.9, 116.4, 69.9, 39.2; EIMS (70 eV) *m/z* (rel intensity) 232 (M^-, 2), 123 (M^+-CH_2OMs, 100), 95 (25).

1-(4-Nitrophenyl)-2-(methylsulfonyloxy)ethanone (6m): Yield 84%; mp 128-129 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.37 (2H, d, J = 8.7 Hz), 8.17 (2H, d, J = 8.8 Hz), 5.76 (2H, s), 3.29 (3H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.0, 150.3, 138.3, 129.5, 124.1, 71.5, 37.4; EIMS (70 eV) *m/z* (rel intensity) 150 (M^+-CH_2OMs, 100), 104 (27), 96 (20).

1-(4-*tert*-Butylphenyl)-2-(methylsulfonyloxy)ethanone (6n): Yield 75%; mp 43-44 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (2H, d, J = 8.4 Hz), 7.52 (2H, d, J = 8.5 Hz), 5.50 (2H, s), 3.28 (3H, s), 1.35 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.6, 158.4, 130.8, 127.7, 125.9, 70.2, 39.1, 35.2, 30.9; EIMS (70 eV) *m/z* (rel intensity) 270 (M^+, 21), 255 (20), 161 (M^+-CH_2OMs, 100).

1-(4-*N,N*-bis-Methylsulfonylaminophenyl)-2-(methylsulfonyloxy)ethanone (6o): Yield 44%; mp 186-188 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.02 (2H, d, J = 8.5 Hz), 7.69 (2H, d, J = 8.5 Hz), 5.69 (2H, s), 3.51 (6H, s), 3.24 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) δ 191.0, 138.5, 134.7, 131.5, 129.0, 71.4, 43.2, 37.4; EIMS (70 eV) *m/z* (rel intensity) 385 (M^+, 1), 276 (M^--CH_2OMs, 100), 198 (99), 182 (19).

1-(3,4-Dichlorophenyl)-2-(methylsulfonyloxy)ethanone (6q): Yield 68%; mp 100-101 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (1H, s), 7.72 (1H, d, J = 8.4 Hz), 7.61 (1H, d, J = 8.3 Hz), 5.43 (2H, s), 3.27 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 139.1, 133.9, 132.8, 131.1, 129.7, 126.7, 69.7, 39.1; EIMS (70 eV) *m/z* (rel intensity) 286 (M^+, 2), 284 (M^-, 9), 282 (M^-, 11), 177 (M^--CH_2OMs, 13), 175 (M^--CH_2OMs, 77), 173 (M^--CH_2OMs, 100), 145 (17).

1-(Naphthalen-2-yl)-2-(methylsulfonyloxy)ethanone (6r): Yield 80%; mp 105-106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ

8.36 (1H, s), 7.96-7.86 (4H, m), 7.66-7.55 (2H, m), 5.63 (2H, s), 3.30 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.9, 135.9, 132.2, 130.6, 129.7, 129.5, 129.1, 129.0, 127.8, 127.2, 122.8, 70.2, 39.1; EIMS (70 eV) *m/z* (rel intensity) 264 (M^-, 82), 155 (M^--CH_2OMs, 93), 141 (33), 126 (100).

1-(2,3-Dihydrobenzo[1,4]dioxin-6-yl)-2-(methylsulfonyloxy)ethanone (6s): Yield 80%; mp 136-137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.39 (1H, s), 6.95 (1H, d, J = 8.2 Hz), 5.43 (2H, s), 4.35-4.28 (4H, m), 3.27 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 149.1, 143.7, 127.0, 121.9, 117.7, 117.2, 70.0, 64.7, 64.0, 39.2; EIMS (70 eV) *m/z* (rel intensity) 272 (M^-, 7), 163 (M^+-CH_2OMs, 100), 135 (11), 107 (10).

1-(3-Nitro-4-methoxyphenyl)-2-(methylsulfonyloxy)ethanone (6t): Yield 87%; mp 119-120 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (1H, d, J = 2.2 Hz), 8.12 (1H, d, J = 8.9 and 2.0 Hz), 7.22 (1H, d, J = 8.9 Hz), 5.45 (2H, s), 4.07 (3H, s), 3.28 (3H, s); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.4, 155.7, 139.1, 133.9, 125.9, 124.9, 114.6, 71.1, 57.4, 37.4; EIMS (70 eV) *m/z* (rel intensity) 289 (M^-, 48), 181 (100), 164 (22), 105 (30).

1-(3-Methoxymethyl-4-methoxyphenyl)-2-(methylsulfonyloxy)ethanone (6u): Yield 58%; mp 77-78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.86 (2H, m), 6.95 (1H, d, J = 8.4 Hz), 5.48 (2H, s), 4.49 (2H, s), 3.92 (3H, s), 3.46 (3H, s), 3.27 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.6, 161.6, 129.4, 128.2, 127.5, 126.0, 110.1, 70.1, 68.8, 58.6, 55.7, 39.1; EIMS (70 eV) *m/z* (rel intensity) 288 (M^+, 6), 179 (M^--CH_2OMs, 100), 119 (7).

1-(2-Methoxy-5-methylphenyl)-2-(methylsulfonyloxy)ethanone (6v): Yield 61%; mp 91-92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (1H, s), 7.36 (1H, d, J = 8.5 Hz), 6.90 (1H, d, J = 8.5 Hz), 5.40 (2H, s), 3.92 (3H, s), 3.27 (3H, s), 2.32 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.8, 157.6, 136.2, 130.9, 130.5, 122.9, 111.4, 74.3, 55.6, 39.0, 20.1; EIMS (70 eV) *m/z* (rel intensity) 258 (M^+, 93), 150 (100), 91 (54).

α-Sulfonyloxylation of silyl enol ether. Representative procedure for the preparation of 1-(4-*N*-methylsulfonylaminophenyl)-2-(methylsulfonyloxy)ethanone (6p): To a solution of 1-(4-*N*-methylsulfonylaminophenyl)-2-ethanone (426 mg, 2 mmol) in anhydrous dichloromethane (2 mL) at 0 °C was added DIPEA (0.52 mL, 3 mmol) via a syringe. To this solution, TBSOTf (0.42 mL, 2.4 mmol) was slowly added via a syringe. The resulting mixture was stirred for 30min at 0 °C and then allowed to warm to room temperature. To this mixture was added [hydroxy(mesyloxy)iodo]benzene (948 mg, 3 mmol) and then the resulting mixture was stirred for 1h. The white precipitate was filtered and then washed with dichloromethane to give 351 mg (57 %) of 1-(4-*N*-methylsulfonylaminophenyl)-2-(methylsulfonyloxy)ethanone (**6p**) as a solid: mp 183 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.43 (1H, s), 7.92 (2H, d, J = 8.7 Hz), 7.29 (2H, d, J = 8.7 Hz), 5.63 (2H, s), 3.27 (3H, s), 3.11 (3H, s); EIMS (70 eV) *m/z* (rel intensity) 307 (M^+, 2), 198 (M^+-CH_2OMs, 100), 119 (15).

Representative procedure for the synthesis of (*R*)-1-phenyl-2-(methylsulfonyloxy)ethanol (entry 4, Table 1): 0.8 mg (equivalent to 0.001 mmol) of (*S,S*)-**1** mixture and 215 mg (1 mmol) of 1-phenyl-2-(methylsulfonyloxy)ethanone (**6a**) was taken into a two-neck flask. After displacement of air with argon, ethyl acetate (2 mL) was added via syringe. While stirring the reaction mixture, 0.2 mL of HCO_2H/Et_3N (5:2) mixture was added. The combined contents were stirred for 0.5 h. The reaction mixture was diluted with ethyl acetate (10 mL) and washed with water (3 × 5 mL). The organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated, and then the residue was purified by column chromatography on silica with a solvent mixture of chloroform/ethyl acetate (10/1) to give 212 mg (98%) of (*R*)-1-phenyl-2-(methylsulfonyloxy) ethanol as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.30 (5H, m), 5.03-4.98 (1H, m), 4.31 (1H, dd, J = 10.8 and 3.7 Hz), 4.25 (1H, dd, J = 10.8 and 7.8 Hz), 3.15 (1H, d, J = 3.4 Hz), 2.99 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 128.6, 128.5, 126.1, 73.9, 71.9, 37.4; EIMS (70 eV) *m/z* (rel intensity) 216 (M^-, 1), 186 (36), 107 (M^--CH_2OMs, 100), 79 (36); $[\alpha]_D^{29}$ -50.3 (*c* 1.10, $CHCl_3$); 97.3% *ee*.

(*R*)-1-(4-Methoxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 9, Table 1): Yield 93%; mp 72-73 °C; 1H NMR (300 MHz, $CDCl_3$) δ 7.31 (2H, d, J = 8.7 Hz), 6.91 (2H, d, J = 8.4 Hz), 4.99 (1H, dd, J = 7.5 and 4.5 Hz), 4.30 (1H, dd, J = 11.1 and 4.5 Hz), 4.26-4.23 (1H, m), 3.81 (3H, s), 3.04 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 130.3, 127.5, 114.1, 73.8, 71.7, 55.3, 37.6; EIMS (70 eV) *m/z* (rel intensity) 246 (M^-, 27), 229 (56), 137 (M^--CH_2OMs, 100), 121 (23); $[\alpha]_D^{25}$ -51.0 (*c* 1.09, $CHCl_3$); 97.2% *ee*.

(*R*)-1-(4-Chlorophenyl)-2-(methylsulfonyloxy)ethanol (entry 10, Table 1): Yield 97%; mp 84-85 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.31 (4H, m), 5.04-4.99 (1H, m), 4.30 (1H, dd, J = 10.8 and 3.5 Hz), 4.23 (1H, dd, J = 10.8 and 8.0 Hz), 3.08 (1H, d, J = 3.5 Hz), 3.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8, 134.3, 128.8, 127.5, 73.5, 71.3, 37.6; EIMS (70 eV) *m/z* (rel intensity) 250 (M^+, 1), 143 (M^+-CH_2OMs, 37), 141 (M^+-CH_2OMs, 100), 113 (19), 77 (44); $[\alpha]_D^{28}$ -44.7 (*c* 1.02, $CHCl_3$); 95.2% *ee*.

(*R*)-1-(2-Chlorophenyl)-2-(methylsulfonyloxy)ethanol (entry 1, Table 2): Yield 90%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (1H, d, J = 8.2 Hz), 7.37-7.24 (3H, m), 5.45-5.42 (1H, m), 4.44 (1H, dd, J = 10.9 and 2.6 Hz), 4.22 (1H, dd, J = 10.9 and 8.1 Hz), 3.22 (1H, d, J = 3.0 Hz), 3.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7, 131.7, 129.5, 129.4, 127.7, 127.2, 72.4, 68.8, 37.5; EIMS (70 eV) *m/z* (rel intensity) 252 (M^-, 1), 250 (M^-, 2), 220 (10), 143 (M^+-CH_2OMs, 41), 141 (M^+-CH_2OMs, 100), 113 (13); $[\alpha]_D^{28}$ -53.2 (*c* 1.03, $CHCl_3$); 76.8% *ee*.

(*R*)-1-(3-Chlorophenyl)-2-(methylsulfonyloxy)ethanol (entry 2, Table 2): Yield 95%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (1H, s), 7.32-7.24 (3H, m), 5.04-4.99 (1H, m), 4.32 (1H, dd, J = 10.9 and 3.4 Hz), 4.24 (1H, dd, J = 10.8 and 8.0 Hz), 3.24 (1H, d, J = 3.1 Hz), 3.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 134.6, 129.9, 128.6, 126.3, 124.3, 73.5, 71.3, 37.5; EIMS (70 eV) *m/z* (rel intensity) 250 (M^+, 1), 143 (M^+-CH_2OMs, 45), 141 (M^--CH_2OMs, 100), 113 (42), 77 (60); $[\alpha]_D^{28}$ -39.0 (*c* 1.02, $CHCl_3$); 96.5% *ee*.

(*R*)-1-(2-Methoxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 3, Table 2): Yield 92%; mp 33-34 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (1H, d, J = 7.5 Hz), 7.31 (1H, t, J = 7.9 Hz), 7.00 (1H, t, J = 7.5 Hz), 6.89 (1H, d, J = 8.2 Hz), 5.25 (1H, dd, J = 8.0 and 3.1 Hz), 4.43 (1H, dd, J = 10.7 and 3.1 Hz), 4.31 (1H, dd, J = 10.7 and 8.0 Hz), 3.85 (3H, s), 3.02 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 129.4, 127.3, 126.2, 120.9, 110.3, 72.9, 68.5, 55.3, 37.5; EIMS (70 eV) *m/z* (rel

intensity) 246 (M^-, 4), 137 (M^--CH_2OMs, 100), 107 (36); $[\alpha]_D^{28}$ -50.11 (*c* 1.13, $CHCl_3$); 88.2% *ee*.

(*R*)-1-(3-Methoxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 4, Table 2): Yield 97%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (1H, t, *J* = 8.2 Hz), 6.95-6.83 (3H, m), 5.00-4.96 (1H, m), 4.31 (1H, dd, *J* = 10.8 and 3.6 Hz), 4.25 (1H, dd, *J* = 10.8 and 8.0 Hz), 3.79 (3H, s), 3.20 (1H, d, *J* = 3.5 Hz), 3.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 140.0, 129.7, 118.3, 113.9, 111.6, 73.1, 71.8, 55.1, 37.4; EIMS (70 eV) *m*/*z* (rel intensity) 246 (M^-, 39), 150 (16), 137 (M^+-CH_2OMs, 100), 109 (83), 94 (24); $[\alpha]_D^{28}$ -38.9 (*c* 1.12, $CHCl_3$); 96.7% *ee*.

(*R*)-1-(4-Acetoxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 5, Table 2): Yield 97%; mp 55-56 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (2H, d, *J* = 8.6 Hz), 7.10 (2H, d, *J* = 8.47 Hz), 5.03-5.00 (1H, m), 4.31 (1H, dd, *J* = 10.8 and 3.5 Hz), 4.24 (1H ,dd, *J* = 10.3 and 8.0 Hz), 3.02 (3H, s), 2.93 (1H, d, *J* = 3.1 Hz), 2.30 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 150.9, 136.3, 127.6, 122.2, 74.0, 71.7, 37.8, 21.3; EIMS (70 eV) *m*/*z* (rel intensity) 274 (M^+, 1), 165 (M^--CH_2OMs, 37), 123 (100); $[\alpha]_D^{26}$ -41.3 (*c* 1.05, $CHCl_3$); 97.4% *ee*.

(*R*)-1-(4-*tert*-Butyldimethylsilyloxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 6, Table 2): Yield 68%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (2H, d, *J* = 8.5 Hz), 6.65 (2H, d, *J* = 8.0 Hz), 4.80-4.77 (1H, m), 4.12-4.06 (2H, m), 2.84 (3H, s), 2.40 (1H, s), 0.75 (9H, s), 0.00 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 135.4, 131.8, 124.8, 78.4, 76.2, 42.0, 30.0, 22.6, 0.00; EIMS (70 eV) *m*/*z* (rel intensity) 346 (M^-, 4, 237 (M^--CH_2OMs, 100), 193 (27), 153 (87); $[\alpha]_D^{26}$ -35.2 (*c* 1.02, $CHCl_3$); 97.6% *ee*.

(*R*)-1-(3-Trifluoromethylphenyl)-2-(methylsulfonyloxy)ethanol (entry 7, Table 2): Yield 91%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (1H, s), 7.59 (2H, d, *J* = 7.4 Hz), 7.51 (1H, t, *J* = 7.5 Hz), 5.12-5.09 (1H, m), 4.35 (1H, dd, *J* = 10.9 and 3.4 Hz), 4.26 (1H, dd, *J* = 10.9 and 8.0 Hz), 3.43 (1H, d, *J* = 2.8 Hz), 3.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 129.2, 128.8, 125.2, 124.9, 122.6, 121.6, 73.1, 70.9, 37.1; EIMS (70 eV) *m*/*z* (rel intensity) 175 (M^--CH_2OMs, 100), 127 (45); $[\alpha]_D^{28}$ -33.3 (*c* 1.10, $CHCl_3$); 94.1% *ee*.

(*R*)-1-(4-Trifluoromethylphenyl)-2-(methylsulfonyloxy)ethanol (entry 8, Table 2): Yield 98%; mp 72-73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (2H, d, *J* = 8.1 Hz), 7.54 (2H, d, *J* = 8.1 Hz), 5.14-5.11 (1H, m), 4.36 (1H, dd, *J* = 10.8 and 3.3 Hz), 4.27 (1H, dd, *J* = 11.1 and 8.1 Hz), 3.06 (3H, s), 2.88 (1H, d, *J* = 3.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.1, 126.5, 125.8, 125.7, 124.9, 122.7, 73.3, 71.6, 37.7; EIMS (70 eV) *m*/*z* (rel intensity) 284 (M^+, 2), 254 (55), 175 (M^--CH_2OMs, 100), 147 (51), 127 (100); $[\alpha]_D^{25}$ -37.7 (*c* 1.16, $CHCl_3$); 95.9% *ee*.

(*R*)-1-(4-Fluorophenyl)-2-(methylsulfonyloxy)ethanol (entry 9, Table 2): Yield 94%; mp 70-71 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.34 (2H, m), 8.07 (2H, t, *J* = 8.7 Hz), 5.06-5.01 (1H, m), 4.31 (1H, dd, *J* = 10.9 and 3.7 Hz), 4.24 (1H, dd, *J* = 10.9 and 8.0 Hz), 3.04 (3H, s), 2.96 (1H, d, *J* = 3.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 134.1, 128.0, 127.9, 115.8, 115.5, 73.7, 71.4, 37.6; EIMS (70 eV) *m*/*z* (rel intensity) 234 (M^-,1), 204 (11), 125 (M^+-CH_2OMs, 100), 97 (36); $[\alpha]_D^{28}$ -47.1 (*c* 1.05, $CHCl_3$); 96.2% *ee*.

(*R*)-1-(4-Nitrophenyl)-2-(methylsulfonyloxy)ethanol (entry 10, Table 2): Yield 90%; mp 97-98 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.22 (2H, d, *J* = 8.6 Hz), 7.69 (2H, d, *J* = 8.8 Hz), 5.04-5.00 (1H, m), 4.30 (1H, dd, *J* = 10.4 and 4.0 Hz), 4.24 (1H, dd, *J* = 10.4 and 6.4 Hz), 3.12 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) δ 148.6, 146.9, 127.8, 123.3, 73.6, 69.4, 36.7; EIMS (70 eV) *m*/*z* (rel intensity) 152 (M^--CH_2OMs, 100), 106 (8), 94 (8), 77 (10); $[\alpha]_D^{28}$ -35.9 (*c* 0.51, Acetone); 87.6% *ee*.

(*R*)-1-(4-*tert*-Butylphenyl)-2-(methylsulfonyloxy)ethanol (entry 11, Table 2): Yield 85%; mp 75-76 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (2H, d, *J* = 8.4 Hz), 7.32 (2H, d, *J* = 8.3 Hz), 5.02 (1H, dd, *J* = 7.5 and 3.7 Hz), 4.34-4.31 (1H, m), 4.28 (1H, dd, *J* = 10.9 and 7.8 Hz), 3.03 (3H, s), 1.31 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.8, 135.3, 125.9, 125.7, 73.9, 72.0, 37.6, 34.6, 31.2; EIMS (70 eV) *m*/*z* (rel intensity) 272 (M^-, 7), 242 (12), 163 (M^--CH_2OMs, 100), 133 (19), 91 (27); $[\alpha]_D^{25}$ -47.9 (*c* 0.98, $CHCl_3$); 99.0 % *ee*.

(*R*)-1-[4-*N*,*N*-Bis(methylsulfonyl)aminophenyl]-2-(methylsulfonyloxy)ethanol (entry 12, Table 2): Yield 50%; mp 126-128 °C; ^{1}H NMR (300 MHz, acetone-d_6) δ 7.61 (2H, d, *J* = 8.4 HZ), 7.51 (2H, d, *J* = 8.4 Hz), 5.16-5.09 (1H, m), 4.36 (1H, dd, *J* = 10.5 and 3.6 Hz), 4.29 (1H, dd, *J* = 10.5 and 7.0 Hz), 3.49 (6H, s), 3.05 (3H, s), 2.86 (1H, s); ^{13}C NMR (75 MHz, acetone-d_6) δ 143.0, 134.0, 131.1, 127.7, 74.4, 70.9, 42.5, 36.5; EIMS (70 eV) *m*/*z* (rel intensity) 278 (M^+-CH_2OMs, 85), 200 (100), 182 (48), 133 (10); $[\alpha]_D^{26}$ -28.8 (*c* 0.52, acetone); 96.4% *ee*

(*R*)-1-(4-*N*-Methylsulfonylaminophenyl)-2-(methylsulfonyloxy)ethanol (entry 13, Table 2): Yield 62%; mp 126-127 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.59 (1H, bs), 7.47 (2H, d, *J* = 8.5 Hz), 7.35 (2H, d, *J* = 8.7 Hz), 5.04-4.98 (1H, m), 4.33-4.21 (2H, m), 3.09 (3H, s), 2.98 (3H, s), 2.85 (1H, bs); EIMS (70 eV) *m*/*z* (rel intensity) 309 (M^+, 5), 200 (M^+-CH_2OMs, 100), 184 (50); $[\alpha]_D$ -89.6 (*c* 0.96, acetone).

(*R*)-1-(3,4-Dichlorophenyl)-2-(methylsulfonyloxy)ethanol (entry 14, Table 2): Yield 99%; mp 72-74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (1H, d, *J* = 1.7 Hz), 7.46 (1H, d, *J* = 8.3 Hz), 7.26 (1H, dd, *J* = 8.3 and 1.7 Hz), 5.03-5.00 (1H, m), 4.32 (1H, dd, *J* = 10.9 and 3.3 Hz), 4.22 (1H, dd, *J* = 10.9 and 8.2 Hz), 3.06 (3H, s), 2.95 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 133.0, 132.6, 130.7, 128.2, 125.4, 73.2, 71.0, 37.7; EIMS (70 eV) *m*/*z* (rel intensity) 288 (M^+, 1), 286 (M^-, 3), 284 (M^-, 4), 254 (22), 179 (M^+-CH_2OMs, 11), 177 (M^+-CH_2OMs, 67), 175 (M^+-CH_2OMs, 100), 147 (16); $[\alpha]_D^{25}$ -37.5 (*c* 0.97, $CHCl_3$); 93.8% *ee*.

(*R*)-1-(Naphthalene-2-yl)-2-(methysulfonyloxy)ethanol (entry 15, Table 2): Yield 96%; mp 124-125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.83 (4H, m), 7.52-7.46 (3H, m), 5.24-5.19 (1H, m), 4.44 (1H, dd, *J* = 11.0 and 3.7 Hz), 4.37 (1H, dd, *J* = 10.9 and 8.0 Hz), 3.04 (3H, s), 2.87 (1H, d, *J* = 3.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 133.3, 133.1, 128.6, 127.9, 127.7, 126.5, 126.4, 125.4, 123.6, 73.8, 72.2, 37.6, 30.9; EIMS (70 eV) *m*/*z* (rel intensity) 266 (M^-, 15), 170 (9), 157 (M^+-CH_2OMs, 100), 129 (86); $[\alpha]_D^{28}$ -51.4 (*c* 0.53, $CHCl_3$); 99.3% *ee*.

(*R*)-1-(2,3-Dihydrobenzo[1,4]dioxin-6-yl)-2-(methylsulfonyloxy)ethanol (entry 16, Table 2): Yield 92%; oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90-6.85 (3H, m), 4.92 (1H, dd, *J* = 7.8 and 3.8 Hz), 4.29-4.22 (6H, m), 3.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.0, 143.9, 131.9, 119.4, 117.7, 115.5, 74.1, 71.8, 64.6, 64.5, 37.8; EIMS (70 eV) *m*/*z* (rel intensity) 274 (M^+, 13), 165 (M^+-CH_2OMs, 100), 137 (56); $[\alpha]_D^{26}$ -41.9 (*c* 1.21,

$CHCl_3$); 97.3% *ee*.

(*R*)-1-(3-Nitro-4-methoxyphenyl)-2-(methylsulfonyloxy) ethanol (entry 17, Table 2): Yield 90%; mp 60-62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (1H, d, J = 2.1 Hz), 7.59 (1H, dd, J = 8.7 and 2.2 Hz), 7.12 (1H, d, J = 8.7 Hz), 5.07-5.05 (1H, m), 4.33 (1H, dd, J = 10.9 and 3.3 Hz), 4.25 (1H, dd, J = 10.9 and 8.0 Hz), 3.97 (3H, s), 3.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 139.7, 132.2, 131.1, 123.8, 114.1, 73.4, 70.8, 56.9, 37.9; EIMS (70 eV) *m*/*z* (rel intensity) 182 (M^+-CH_2OMs, 100), 165 (5), 107 (9); $[\alpha]_D^{26}$ -41.6 (*c* 1.04, $CHCl_3$); 92.0% *ee*.

(*R*)-1-(3-Methoxymethyl-4-methoxyphenyl)-2-(methylsulfonyloxy)ethanol (entry 18, Table 2): Yield 93%; mp 68-69 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (1H, d, J = 1.8 Hz), 7.30 (1H, d, J = 8.4 and 2.1 Hz), 6.87 (1H, d, J = 8.4 Hz), 4.99 (1H, dd, J = 6.6 and 4.8 Hz), 4.48 (2H, s), 4.31-4.27 (2H, m), 3.84 (2H, s), 3.43 (3H, s), 3.04 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.2, 130.1, 127.1, 126.7, 126.6, 110.3, 73.9, 71.8, 69.2, 58.5, 55.5, 37.6; EIMS (70 eV) *m*/*z* (rel intensity) 290 (M^-, 37), 259 (14), 181 (M^+-CH_2OMs, 100), 149 (9); $[\alpha]_D^{25}$ -41.5 (*c* 1.86, $CHCl_3$); 95.4% *ee*.

(*R*)-1-(2-Methoxy-5-methylphenyl)-2-(methylsulfonyloxy) ethanol (entry 19, Table 2): Yield 91%; mp 62-63 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (1H, d, J = 1.9 Hz), 7.09 (1H, dd, J = 8.3 and 2.0 Hz), 6.78 (1H, d, J = 8.3 Hz), 5.21 (1H, dd, J = 8.1 and 3.1 Hz), 4.40 (1H, J = 10.6 and 3.0 Hz), 4.30 (1H, dd, J = 10.7 and 8.1 Hz), 3.82 (3H, s), 3.03 (3H, s), 2.73 (1H, s), 2.29 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 130.2, 129.6, 127.9, 125.7, 110.3, 73.0, 68.6, 55.3, 37.5, 20.4; EIMS (70 eV) *m*/*z* (rel intensity) 260 (M^-, 16), 151 (M^--CH_2OMs, 100), 121 (62), 91 (16); $[\alpha]_D^{28}$ -42.1 (*c* 1.21, $CHCl_3$); 89.6% *ee*.

Conclusion

This work constitutes an extended study of asymmetric reduction of α-functionalized arylketones under transfer hydrogenation conditions. Among them, α-mesyloxy arylketones are the substrates of choice for the assessment of a high level of enantioselection in the Rh-catalyzed transfer hydrogenation. It is assumed that the results from a slight change in the substrate forces the complex to be more correctly oriented toward the reduction. The Rh-catalyst effectively performed in transfer hydrogenation of α-mesyloxyketones containing electronically and sterically demanding groups in an azeotropic mixture of formic acid/triethylamine to produce optically active 1-arylethanediols up to 99% *ee*. This excellent level of enantioselection achieved in the asymmetric transfer hydrogenation of α-functionalized aryketones may provide new opportunities for industrial synthesis of active pharmaceutical ingredients, in particular, optically active 2-amino-1-arylethanols. Further synthetic applications and some mechanistic considerations are in progress.

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References

1. For reviews, see: (a) Fache, F.; Schulz, E.; Tommasino, L. M.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159; (b) Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835; (c) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, *25*, 117; (d) Juraristi, E.; Quintana, D.; Escalante, J. *Aldrichim. Acta* **1994**, *27*, 3; (e) Cole, D. C. *Tetrahedron* **1994**, *50*, 9517.
2. (a) Agranat, I.; Caner, H.; Caldwell, J. *Nature Rev. Drug Discov.* **2002**, *1*, 753; (b) Pinard, E.; Alanine, A.; Bourson, A.; Büttelmann, B.; Heitz, M.-P.; Mutel, V.; Gill, R.; Trube, G.; Wyler, R. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2615; (c) Kordik, C. P.; Reitz, A. B. *J. Med. Chem.* **1999**, *42*, 181; (d) Amici, M. D.; Micheli, C. D.; Kassi, L.; Carrea, G.; Ottolina, G.; Colombo, G. *Tetrahedron* **2001**, *57*, 1849.
3. (a) Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed. Eng.* **1998**, *37*, 1986; (b) Corey, E. J.; Link, J. O. *J. Org. Chem.* **1991**, *56*, 442; (c) Xing, X.; Ho, P.; Bourquin, G.; Yeh, L.-A.; Cuny, G. D. *Tetrahedron* **2003**, *59*, 9961; (d) Cho, B. T.; Yang, W. K.; Choi, O. K. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1204.
4. Ohkuma, T.; Ishii, D.; Takeno, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 6510.
5. Gao, Y.; Sharpless, K. B. *J. Org. Chem.* **1988**, *53*, 4081.
6. (a) Kumar, P.; Upadhyay, R. K.; Pandey, R. K. *Tetrahedron: Asymmetry* **2004**, *15*, 3955; (b) Weissman, S. A.; Rossen, K.; Reider, P. J. *Org. Lett.* **2001**, *3*, 2513.
7. (a) Goswami, J.; Bezbaruah, R. L.; Goswami, A.; Borthakur, N. *Tetrahedron: Asymmetry* **2001**, *12*, 3343; (b) Yadav, J. S.; Reddy, P. T.; Nanda, S.; Rao, A. B. *Tetrahedron: Asymmetry* **2001**, *12*, 3381; (c) Fardelone, L. C.; Rodrigues, J. A. R.; Moran, P. J. S. *J. Mol. Cat. B: Enzymatic* **2006**, *39*, 9.
8. Kamal, A.; Shaik, A. A.; Sandbhor, M.; Malik, M. S. *Tetrahedron: Asymmetry* **2004**, *15*, 3939.
9. (a) Brown, R. F. C.; Jackson, W. R.; McCarthy, T. D. *Tetrahedron: Asymmetry* **1993**, *4*, 2149; (b) Baeza, A.; Nájera, C.; Sansano, J. M.; Saá, J. M. *Chem. Eur. J.* **2005**, *11*, 3849; (c) Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621; (d) Xiong, Y.; Wang, F.; Huang, X.; Wen, Y.; Feng, X. *Chem. Eur. J.* **2007**, *13*, 829.
10. (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562; (b) Fujii, A.; Hashiguchi, S.;Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 2521; (c) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285; (d) Hashiguchi, S.; Fujii, A.; Haack, K.-J.; Matsumura, K.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 288; (e) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738; (f) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97; (g) Murata, K.; Okano, K.; Miyagi, M.; Iwane, H.; Noyori, R.; Ikariya, T. *Org. Lett.* **1999**, *1*, 1119; (h) Okano, K.; Murata, K.; Ikariya, T. *Tetrahedron Lett.* **2000**, *41*, 9277; (i) Koike, T.; Murata, K.; Ikariya, T. *Org. Lett.* **2000**, *2*, 3833; (j) Gladiali, S.; Alberico, E. *Chem. Soc. Rev.* **2006**, *35*, 226; (k) Palmer, M. J.; Wills, M. *Tetrahedron: Asymmetry* **1999**, *10*, 2045.
11. Farina, V.; Reeves, J. T.; Senanayake, C. H.; Song, J. J. *Chem. Rev.* **2006**, *106*, 2734.
12. (a) Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.* **1998**, 1199; (b) Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.* **1998**, 1201; (c) Murata, K.; Ikariya, T.; Noyori, R. *J. Org. Chem.* **1999**, *64*, 2186.
13. (a) Matharu, D. S.; Morris, D. J.; Kawamoto, A. M.; Clarkson, G. J.; Wills, M. *Org. Lett.* **2005**, *7*, 5489; (b) Matharu, D. S.; Morris, D. J.; Clarkson, G. J.; Wills, M. *Chem. Commun.* **2006**, 3232.
14. (a) Hamada, T.; Torii, T.; Izawa, K.; Noyori, R.; Ikariya, T. *Org. Lett.* **2002**, *4*, 4373; (b) Hamada, T.; Torii, T.; Izawa, K.; Ikariya, T. *Tetrahedron* **2004**, *60*, 7411; (c) Hamada, T.; Torii, T.; Onishi, T.; Izawa, K.; Ikariya, T. *J. Org. Chem.* **2004**, *69*, 7391; (d) Zaidlewicz, M.; Tafelska-Kaczmarek, A.; Prewysz-Kwinto, A. *Tetrahedron: Asymmetry* **2005**, *16*, 3205.
15. (a) Cross, D. J.; Kenny, J. A.; Houson, I.; Campbell, L.; Walsgrove, T.; Wills, K. *Tetrahedron: Asymmetry* **2001**, *12*, 1801; (b)

Peach, P.; Cross, D. J.; Kenny, J. A.; Mann, I.; Houson, I.; Campbell, L.; Walsgrove, T.; Wills, M. *Tetrahedron* **2006**, *62*, 1864; (c) Lee, D.-M.; Lee, J.-C.; Jeong, N.; Lee, K.-I. *Tetrahedron: Asymmetry* **2007**, *18*, 2662; (d) Lee, D.-M.; Kumaraswamy, G.; Lee, K.-I. *Monatsh. Chem.* **2009**, *140*, 73.

16. (a) Kumar, P.; Upadhyay, R. K.; Pandy, R. K. *Tetrahedron: Asymmetry* **2004**, *15*, 3955; (b) Ali, I. S.; Sudalai, A. *Tetrahedron Lett.* **2002**, *43*, 5435; (c) Andersson, P. G.; Schink, H. E.; Österlund, K. *J. Org. Chem.* **1988**, *63*, 8067; (d) Cho, B. T.; Kang, S. K.; Shin, S. H. *Tetrahedron: Asymmetry* **2002**, *13*, 1209; (e) Cho, B. T.; Kang, S. K.; Yang, W. K. *Bull. Korean Chem. Soc.* **2002**, *23*, 1328.
17. Wang, F.; Liu, H.; Cun, L.; Zhu, J.; Deng, J.; Jiang, Y. *J. Org. Chem.* **2005**, *70*, 9424.
18. For recent advances in α-sulfonyloxylation of arylketones, see: (a) Lodaya, J. S.; Koser, G. F. *J. Org. Chem.* **1988**, *53*, 210; (b) Koser, G. F.; Relenyi, A. G.; Kalos, A. N.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1982**, *47*, 2487; (c) Lee, J. C.; Oh, Y. S.; Cho, S. H. *Bull. Korean Chem. Soc.* **1996**, *17*, 989; (d) Moriarty, R. M.; Penmasta, R.; Awasthi, A. K.; Epa, W. R.; Prakash, I. *J. Org. Chem.* **1989**, *54*, 1101; (e) Yamamoto, Y.; Togo, H. *Synlett* **2006**, 798; (f) Ueno, M.; Nabana, T.; Togo, H. *J. Org. Chem.* **2003**, *68*, 6424.
19. (a) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285; (b) Yamakawa, M.; Ito, H.; Noyori, R. *J. Am. Chem. Soc.* **2000**, *122*, 1466; (c) Sandoval, C. A.; Ohkuma, T.; Utsumi, N.; Tsutsumi, K.; Murata, K.; Noyori, R. *Chem. Asian J.* **2006**, *1*, 102.
20. Brandt, P.; Roth, P.; Andersson, P. G. *J. Org. Chem.* **2004**, *69*, 4885.
21. (a) Šterk, D.; Stephan, M.; Mohar, B. *Org. Lett.* **2006**, *8*, 5935; (b) Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem.* **2006**, *71*, 7035; (c) Cheung, F. K.; Lin, C. Minissi, F.; Crivillé, A. L.; Graham, M. A.; Fox, D. J.; Wills, M. *Org. Lett.* **2007**, *9*, 4659.
22. (a) Wagner, K. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 50; (b) Narita, K.; Sekiya, M. *Chem. Pharm. Bull.* **1977**, *25*, 135.
23. Bartoli, G.; Bosco, M.; Marcantoni, E.; Massaccesi, M.; Rinaldi, S.; Sambri, L. *Tetrahedron Lett.* **2002**, *43*, 6331.
24. Zarghi, A.; Rao, P. N. P.; Knaus, E. E. *Bioorg. Med. Chem.* **2007**, *15*, 1056.
25. Chung, J.-U.; Kim, S. Y.; Lim, J.-O.; Choi, H.-K.; Kang, S.-U.; Yoon, H.-S.; Ryu, H.; Kang, D. W.; Lee, J.; Kang, B.; Choi, S.; Toth, A.; Pearce, L. V.; Pavlyukovets, V. A.; Lundberg, D. J.; Blumberg, P. M. *Bioorg. Med. Chem.* **2007**, *15*, 6043.