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Enantioselective α-tosyloxylation of ketones catalyzed by spirobiindane scaffold-based chiral iodoarenes

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ABSTRACT

Enantiomerically pure iodoarene (*S*)-**2** and its derivatives (*S*)-**3** to (*S*)-**18** with a spirobiindane scaffold have been synthesized. The evaluation of these new chiral iodoarenes as catalysts in the enantioselective α-tosyloxylation of ketones was performed using *m*-CPBA as a stoichiometric oxidant, and the synthetically useful α-tosyloxylated ketones were obtained in up to 58% enantiomeric excess (ee).

1. Introduction

Over the past three decades, hypervalent iodine reagents have been widely used in organic synthesis due to their attractive features such as low toxicity, stability toward atmospheric oxygen and moisture, excellent selectivity, and versatile reactivities.[1] In recent years, the use of chiral hypervalent iodine reagents for asymmetric transformations has also attracted much attention and there have been some successful examples mainly for intramolecular reactions. Kita and co-workers reported the enantioselective intramolecular oxidative dearomatization of naphthol derivatives to construct a chiral *ortho*-spirolactone structure (up to 86% ee) using a Zhou ligand-based chiral λ^3-iodane compound **A** (Scheme 1).[2] Ishihara and co-workers improved the enantioselectivity of this oxidative spirolactonization reaction to 92% ee by using **B** as a highly effective precatalyst.[3] Very recently, Fujita et al. realized the asymmetric oxylactonization of *ortho*-alk-1-enylbenzoate (up to 98% ee) by using a lactate-derived λ^3-iodane reagent **C**.[4]

However, chiral hypervalent iodine reagents induced intermolecular transformations still remain a challenging task although many efforts have been devoted to this subject.[5] One typical example was the pioneering work of Wirth and co-workers in a chiral Koser-type reagent mediated enantioselective α-tosyloxylation of ketones. In this reaction, the α-(tosyloxy)propiophenone **1a** can be obtained in up to 40% ee by using a stoichiometric amount of chiral Koser-type reagent **D** (Scheme 2).[6] Since the λ^3-iodane reagents must be used in a stoichiometric amount and the preparation of this reagent requires an additional oxidative transformation from the parent iodoarene, Wirth et al. then developed the chiral iodoarenes catalyzed asymmetric α-tosyloxylation of ketones using *m*-CPBA as a stoichiometric oxidant; the best result was obtained with 39% ee when chiral iodoarene **E** was used as the catalyst (Scheme 3).[7] Therefore, it is still desirable to search for new chiral iodoarenes as catalysts in order to improve the enantioselectivity of this reaction. Herein, in a continuation of our ongoing research on hypervalent iodine chemistry,[8] we report the synthesis of new chiral iodoarenes with rigid spirobiindane backbones and their applications in the asymmetric α-tosyloxylation of ketones using *m*-CPBA as the stoichiometric oxidant to produce α-tosyloxylated ketones in up to 58% ee, which constitutes the highest asymmetric induction in chiral iodoarene catalyzed α-tosyloxylation of ketones so far.

2. Results and discussion

2.1. The Optimization of the asymmetric α-tosyloxylation of 1

Due to the unique rigid structure of the spirobiindane scaffold, the spirobiindane backbone-based chiral ligands have been extensively used in transition metal catalyzed asymmetric transformations over the past ten years.[9] Our idea was to synthesize a series of spirobiindane backbone-based chiral iodoarenes and to use them as catalysts in the asymmetric α-tosyloxylation of ketones. At first, we chose to synthesize the simplest compound (*S*)-**2** as the catalyst. The synthesis of this compound was accomplished from the enantiomerically pure (*S*)-1,1′-spirobiindane-7,7′-diol **2a** by using a seven-step synthetic procedure (Scheme 4). Diol (*S*)-**2a** was first converted into diamine (*S*)-**2c** via a three-step transformation.[2] Monoacetylization of diamine (*S*)-**2c** with acetic anhydride and acetic acid yielded compound (*S*)-**2d**. After an extensive investigation, compound (*S*)-**2d** was efficiently deaminated by treating it with $NaNO_2$ and hypophosphorous acid in 5 M HCl to generate (*S*)-**2e**. Compound (*S*)-**2e** was then hydrolyzed under acid conditions to give the monoamine (*S*)-**2f**. Diazotization-iodination of (*S*)-**2f** with $NaNO_2$ and KI

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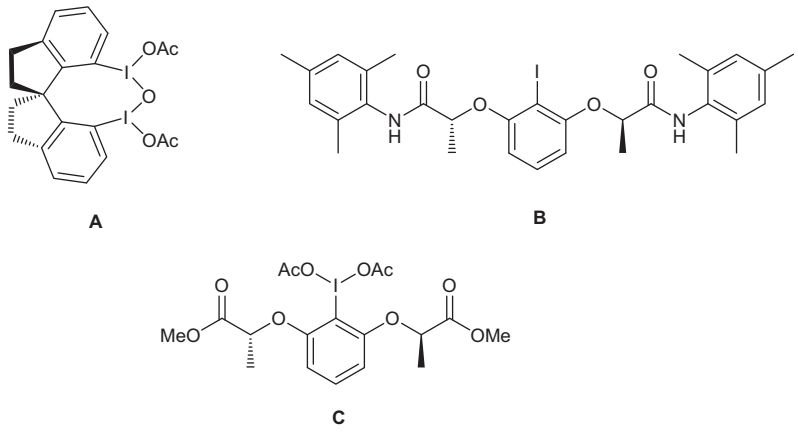
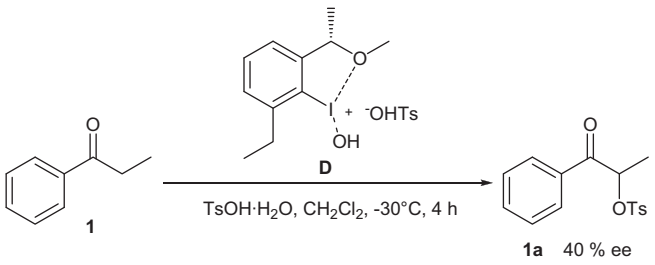
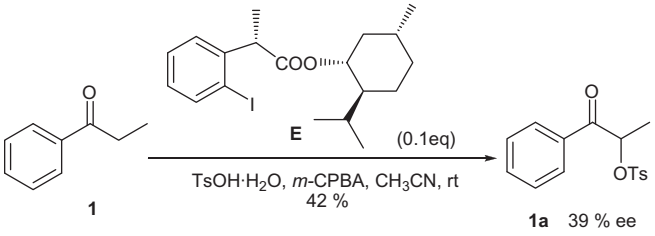


Scheme 1. Selected examples of chiral λ^3-iodane reagents and iodoarenes.



Scheme 2. Enantioselective α-tosyloxylation of propiophenone **1** using reagent **D**.



Scheme 3. Chiral iodoarene **E** catalyzed enantioselective α-tosyloxylation of **1**.

under acidic conditions provided the desired chiral iodoarene (*S*)-**2** in high yields.[10]

With the chiral iodoarene (*S*)-**2** in hand, we then tested its chiral inducing ability as a catalyst in the α-tosyloxylation of **1**. The reaction was first performed in CH_3CN at room temperature with 10 mol % of (*S*)-**2**, 1.5 equivalents of *m*-CPBA and 1.5 equiv of *p*-TsOH·H_2O. After 42 h, the tosyloxylated product **1a** was obtained in 30% ee (Scheme 5).

2.1.1. Solvent screening study of asymmetric α-tosyloxylation of 1 using (*S*)-2 as a catalyst

The effect of solvent was examined under the reaction conditions shown in Scheme 5 except CH_3CN was replaced by other organic solvents (Table 1). Among the solvents screened, the chlorinated hydrocarbons were not good solvents for this reaction, only affording **1a** in up to 21% ee (Table 1, entries 1–4). For the ether solvents, the reactions gave much higher enantioselectivities with the ee values in a range of 40–47% (entries 5–9). The use of EtOAc led to the highest ee value of 53% (entry 10). Other ester solvents were also checked, but none showed superior results compared with EtOAc (entries 11–17 vs entry 10). The reaction was also carried out in CH_3NO_2, but only yielded **1a** in 12% ee (entry 18). The more polar solvents such as HFIP and DMF were also employed but no reaction occurred. Hence, EtOAc was the solvent of choice in the following investigation. The reaction was also carried out in EtOAc at 0 °C, but no enhancement of the enantioselectivity was observed (entry 19).

2.1.2. Evaluation of spirobiindane scaffold-based chiral iodoarenes (*S*)-3 to (*S*)-18 in the asymmetric α-tosyloxylation of 1 in EtOAc

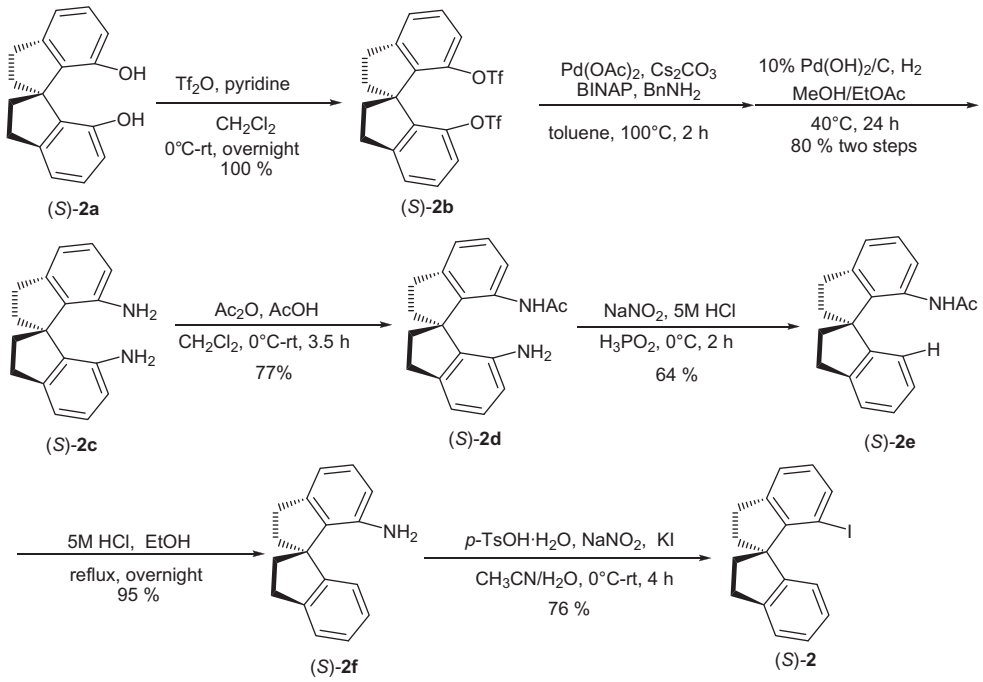
In order to further improve the enantioselectivity, the derivatives of (*S*)-**2** with various substituents at the 6, 7′, and 4 positions were synthesized (see the Experimental Section for the detailed procedures) (Scheme 6).

In the report of Wirth, the introduction of substituents at the *ortho*-position significantly improved the enantioselectivities.[7] Herein, the R^1 substituted chiral iodoarenes (*S*)-**3** to (*S*)-**9** were first evaluated in the α-tosyloxylation of **1** (Table 2, entries 1–7); however for us, such an advantageous effect was not observed. The installation of a methyl group at the *ortho*-position decreased the ee value from 53% to 20% (Table 2, entry 1). Changing the methyl group to an ethyl group led to a slight increase in the stereoselectivity (32% ee). When catalyst (*S*)-**5** bearing a phenyl group was employed, the ee value of **1a** was 20% (entry 3). The presence of a chlorine atom at the *ortho*-position produced **1a** with 45% ee whereas the introduction of a bromine atom resulted in the same ee value as that obtained with (*S*)-**2** (entries 4 and 5). The carboxylic acid and carboxylic acid methyl ester groups were also introduced at the 6-position; the use of catalysts (*R*)-**8** and (*R*)-**9** resulted in very poor enantioselectivities (entries 6 and 7).

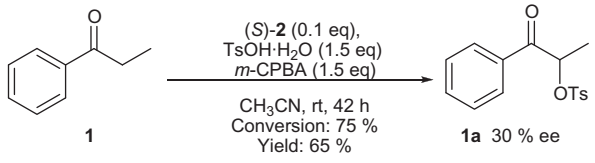
As for the 7′-position, the amide group was first introduced as the potential coordination site, however, catalyst (*S*)-**10** only provided **1a** in 34% ee (entry 8). The sulfonamide group was also checked but the reaction gave a poor enantioselectivity. The use of dimethylamino and diethylamino groups also led to low selectivities (entries 10–11). A phenyl group was then installed and **1a** was obtained in 22% ee (entry 12). A carboxylic acid group was introduced, but the reaction only provided **1a** in 33% ee (entry 13). The diiodo-catalyst (*S*)-**17** was employed as well, and the reaction afforded **1a** with an ee value of 21% (entry 15). As for the 4-position phenyl group substituted compound (*S*)-**18**, the reaction produced **1a** in a slight lower ee value compared with that of (*S*)-**2** (entry 16).

2.1.3. The variation of the sulfonic acid in the asymmetric α-sulfoxylation of 1 using (*S*)-2 as a catalyst in EtOAc

A series of sulfonic acids were then examined instead of *p*-TsOH·H_2O as the source of the sulfonate nucleophile (Table 3).



Scheme 4. Synthesis of chiral iodoarene (*S*)-**2**.



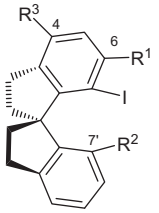
Scheme 5. (*S*)-**2** catalyzed α-tosyloxylation of **1** in CH_3CN.

The use of 4-methoxy and 4-chloro benzenesulfonic acid hydrate in this reaction led to similar results as those obtained with *p*-TsOH·H_2O, whereas using 4-nitrobenzenesulfonic acid hydrate greatly decreased the selectivity (Table 3, entries 1–3). Benzenesulfonic acid was also checked and the corresponding sulfonyloxylated product **1e** was obtained in low selectivity (entry 4). 2,4,6-Tri(iso-propyl)benzenesulfonic acid was used as a sterically congested nucleophile and the reaction yielded **1f** with an ee value of 50% (entry 5). The reaction using naphthalene-2-sulfonic acid hydrate was carried out, and produced 1-oxo-1-phenylpropan-2-yl naphthalene-2-sulfonate **1g** in 49% ee (entry 6). Two aliphatic sulfonic acids were also employed and the reactions provided the

Table 1
Solvent screening study using catalyst (*S*)-**2** in the α-tosyloxylation of **1**[a]

Entry	Solvent	Time (h)	Conversion (%)	Yield[b] (%)	ee[c] (%) (abs. config.)[e]
1	CH_2Cl_2	42	77	25	19 (*S*)
2	$CHCl_3$	42	48	23	21 (*S*)
3	CCl_4	42	70	10	15 (*S*)
4	CH_3CCl_3	42	33	20	20 (*S*)
5	THF	42	25	10	47 (*S*)
6	Ether	42	70	38	40 (*S*)
7	Ethylene glycol dimethyl ether	42	46	32	41 (*S*)
8	Methyl-*tert*-butyl ether	42	40	30	41 (*S*)
9	1,4-dioxane	42	60	53	40 (*S*)
10	EtOAc	42	63	53	53 (*S*)[f]
11	Methyl butyrate	42	50	36	44 (*S*)
12	Methyl acetate	42	55	39	42 (*S*)
13	Butyl acetate	42	60	48	49 (*S*)
14	γ-Butyrolactone	42	50	17	35 (*S*)
15	Butyl butyrate	42	60	42	38 (*S*)
16	Diethyl carbonate	42	50	38	36 (*S*)
17	CF_3COOEt	42	36	36	17 (*S*)
18	CH_3NO_2	42	64	46	12 (*S*)
19[d]	EtOAc	42	25	16	51 (*S*)

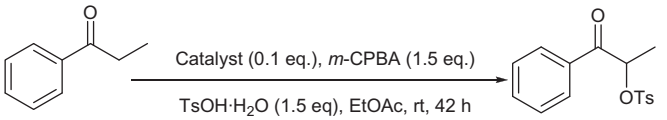
[a] 0.5 mmol of **1** was used.
[b] Isolated yield.
[c] Determined by HPLC.
[d] The reaction was carried out at 0 °C.
[e] See Experimental Section for details.
[f] $[\alpha]_D^{25} = -5.2$ (*c* 0.5, $CHCl_3$).



(*S*)-**3** $R^1 = CH_3$, $R^2 = R^3 = H$
(*S*)-**4** $R^1 = C_2H_5$, $R^2 = R^3 = H$
(*S*)-**5** $R^1 = C_6H_5$, $R^2 = R^3 = H$
(*S*)-**6** $R^1 = Cl$, $R^2 = R^3 = H$
(*S*)-**7** $R^1 = Br$, $R^2 = R^3 = H$
(*R*)-**8** $R^1 = COOH$, $R^2 = R^3 = H$
(*R*)-**9** $R^1 = COOMe$, $R^2 = R^3 = H$
(*S*)-**10** $R^1 = H$, $R^2 = NHAc$, $R^3 = H$
(*S*)-**11** $R^1 = H$, $R^2 = NHSO_2CH_3$, $R^3 = H$
(*S*)-**12** $R^1 = H$, $R^2 = N(CH_3)_2$, $R^3 = H$
(*S*)-**13** $R^1 = H$, $R^2 = N(C_2H_5)_2$, $R^3 = H$
(*S*)-**14** $R^1 = H$, $R^2 = Ph$, $R^3 = H$
(*S*)-**15** $R^1 = H$, $R^2 = COOH$, $R^3 = H$
(*S*)-**16** $R^1 = H$, $R^2 = OMe$, $R^3 = H$
(*S*)-**17** $R^1 = H$, $R^2 = I$, $R^3 = H$
(*S*)-**18** $R^1 = R^2 = H$, $R^3 = C_6H_5$,

Scheme 6. Structures of chiral iodoarenes (*S*)-**3** to (*S*)-**18**.

Table 2
The test of spirobiindane scaffold-based chiral iodoarenes (*S*)-**3** to (*S*)-**18** in the asymmetric α-tosyloxylation of **1**[a]



1 **1a**

Entry	Catalysts	Conversion (%)	Yield[b] (%)	ee[c] (%) (abs. config.)
1	(*S*)-**3**	51	41	20 (*S*)
2	(*S*)-**4**	50	39	32 (*S*)
3	(*S*)-**5**	17	13	20 (*S*)
4	(*S*)-**6**	35	27	45 (*S*)
5	(*S*)-**7**	36	40	53 (*S*)
6	(*S*)-**8**	29	15	3 (*R*)
7	(*S*)-**9**	50	32	5 (*R*)
8	(*S*)-**10**	30	26	34 (*S*)
9	(*S*)-**11**	49	39	9 (*S*)
10	(*S*)-**12**	55	40	16 (*S*)
11	(*S*)-**13**	21	13	12 (*S*)
12	(*S*)-**14**	30	24	22 (*S*)
13	(*S*)-**15**	44	27	33 (*S*)
14	(*S*)-**16**	48	30	20 (*S*)
15	(*S*)-**17**	66	48	21 (*S*)
16	(*S*)-**18**	49	28	45 (*S*)

[a] 0.5 mmol of **1** was used.
[b] Isolated yield.
[c] Determined by HPLC.

corresponding sulfonyloxylated products **1h** and **1i** in 46% and 40% ee respectively (entries 7 and 8). Chiral sulfonic acids, such as camphorsulfonic acid were then examined. In Wirth's report, the use of (1*S*)-(−)-10-camphorsulfonic acid as a nucleophile and catalyst **E** led to the formation of **1j** in 44% de. In the case of the opposite enantiomer (1*R*)-(+)-10-camphorsulfonic acid monohydrate, the corresponding α-sulfonyloxylated product **1k** was obtained in a decreased de value of 34%.[7b] In our cases, the employment of (1*S*)-(−)-10-camphorsulfonic acid produced **1j** in 40% de, while the use of (1*R*)-(+)-10-camphorsulfonic acid monohydrate resulted in the formation of **1k** in an increased de value of 49% (entries 9 and 10).

2.2. Substrate scope and mechanism considerations

After the screening of solvent, the test of catalysts and the different sulfonic acids, the optimal asymmetric α-sulfoxylation system employed (*S*)-**2** as the catalyst and *p*-TsOH·H_2O as the nucleophile in EtOAc. A variety of ketones were then tested under these reaction conditions (Table 4). It was found that the electron-deficient propiophenones gave lower enantioselectivities compared with that of 4-nitro propiophenone which provided its tosylated product **21** with 56% ee (Table 4, entries 1–4). Two electron-rich propiophenones were also checked and an ee value of 40% was obtained for both (entries 5 and 6). An elongation of the side chain of propiophenone by one methylene unit led to the highest ee value of 58% (entry 7). Further elongation of the side chain resulted in a decrease in enantioselectivity (entry 8 vs. entry 7). In the case of 1,2-diphenylethanone, the reaction yielded **27** in only 13% ee (entry 9). Substrates bearing another aromatic ring such as naphthalene, furan, and thiophene were transformed into the corresponding α-tosyloxylated products **28**, **29,** and **30** with moderate ee values (entries 10–12). The cyclic substrates 1-tertralone and cyclohexanone were then examined and the reactions afforded **31** and **32** in low selectivities (entries 13 and 14). Two aliphatic ketones were subjected to the reaction as well which afforded their tosylated products **33** and **34** in 22% and 12% ee respectively (entry 15 and 16).

As proposed by Wirth,[7] the mechanism of this asymmetric α-tosyloxylation reaction involved ligand exchange of the Koser-type iodane **F** generated in situ from chiral iodoarene with the enol form of propiophenone to produce intermediate **G** (generation of the stereocentre), which was followed by the nucleophilic attack of TsOH upon the α carbon bearing the iodine (III) structural unit in **G** to yield **1a** with concomitant reductive elimination of the chiral iodoarene (path A, Scheme 7). Alternatively, the reaction might also proceed through intermediate **H**, which then reacted with TsOH via an S_N2' reaction to produce **1a** together with the generation of the stereocenter (path B, Scheme 7).

A reaction model was proposed for rationalizing the steric effects based on the absolute configuration of the tosyloxylated ketone **1a**.[11] Two transition states (**TS**) for enantioselectivity-determining step were proposed (Scheme 8). In the model **TS-1**, there is a repulsive force between the methylene group at the 2′-position of the chiral oxidant and the phenyl ring of propiophenone. On the contrary, no obvious repulsive force was observed in model **TS-2** since the phenyl group of the propiophenone is oriented away from the methylene group. According to the model **TS-2**, the in situ generated chiral Koser-type reagent approaches **1** from its *Re* face to form the reaction intermediate which undergoes nucleophilic attack of TsOH to produce **1a** with an (*S*)-configuration, which is consistent with our experiment results.

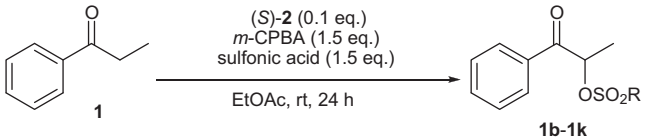
As displayed in the proposed reaction mechanism, the generation of product **1a** requires the enolization of substrate **1** to guarantee the formation of the intermediate **G** or **H**. Also, the enolisation might take place in the tosylated product **1a**, which would lead to racemization. In order to verify this possibility, enantioenriched **1a** (48% ee) was subjected to the optimal reaction conditions in the absence of the chiral iodoarene. It was found that the ee value of **1a** decreased to 39% after 42 h. This result indicated that a slight racemization of **1a** occurred in the reaction, which is in contrast to Wirth's observation (Scheme 9).[7] This is mainly due to the acidity of TsOH ($pK_a = -2.8$), which promoted the enolization of the **1a**.

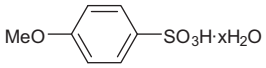
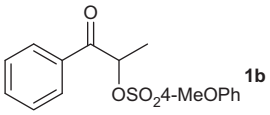
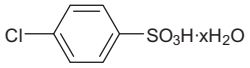
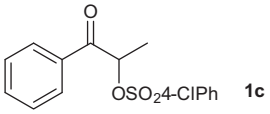
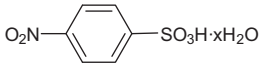
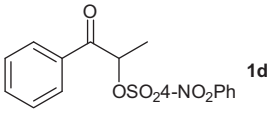
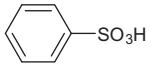
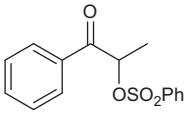
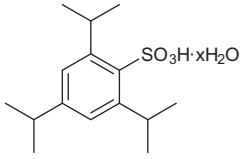
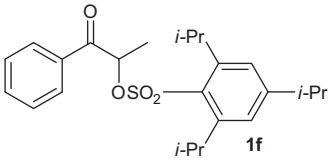
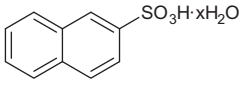
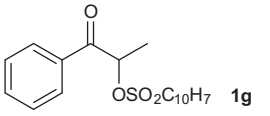
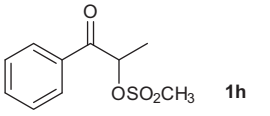
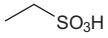
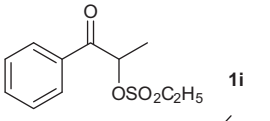
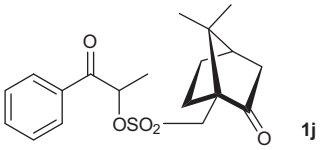
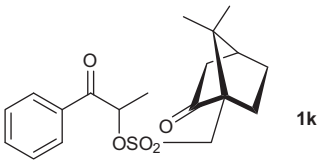
3. Conclusions

In conclusion, we have synthesized the spirobiindane scaffold-based chiral iodoarene (*S*)-**2** and its derivatives (*S*)-**3** to (*S*)-**18**. The solvent screening study of asymmetric α-tosyloxylation of **1** using (*S*)-**2** as catalyst was conducted and EtOAc was found to be the optimum solvent. The evalution of chiral iodoarenes (*S*)-**3** to

(*S*)-**18** in asymmetric α-tosyloxylation of **1** in EtOAc was performed, and no advantageous effect for enantioselectivity was observed using these catalysts. The results of varying the sulfonic acid in the asymmetric reaction indicated that *p*-TsOH·H_2O still remained the nucleophile of choice. The best result was obtained with 58% ee when phenyl propyl ketone was used as the substrate; this is the highest ee value achieved so far for the iodoarene catalyzed α-tosyloxylation of aromatic ketones.

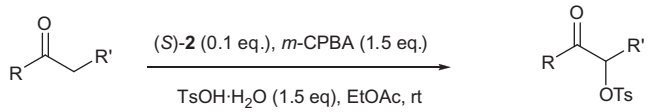
Table 3
(*S*)-**2** Catalyzed α-sulfonyloxylation of **1** using different sulfonic acids[a]



Entry	Sulfonic acid	Product	Conversion (%)	Yield[b] (%)	ee[c] (%)
1		 **1b**	34	22	48
2		 **1c**	52	41	50
3		 **1d**	40	32	13
4[d]		 **1e**	41	25	23
5		 **1f**	40	29	50[d]
6		 **1g**	32	24	49
7[d]		 **1h**	30	18	46
8[e]		 **1i**	39	29	40
9	(1*S*)-(−)-10-Camphorsulfonic acid monohydrate	 **1j**	40	15	40 (de)
10	(1*R*)-(+)-10-Camphorsulfonic acid	 **1k**	48	11	49 (de)

[a] 0.5 mmol of **1** was used.
[b] Isolated yield.
[c] Determined by HPLC, absolute configuration unknown.
[d] $[\alpha]_D^{25} = -4.8$ (*c* 0.5, $CHCl_3$)
[e] 1.5 equiv of water were added.

Table 4
α-Tosyloxylation of ketones using catalyst (*S*)-**2** in EtOAc[a]



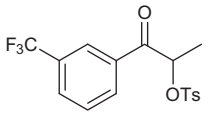
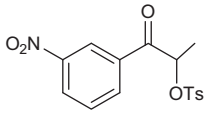
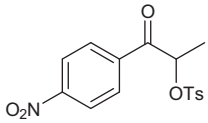
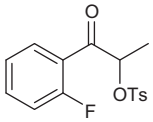
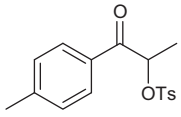
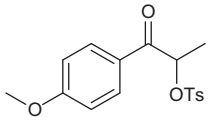
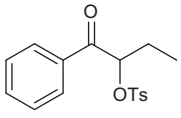
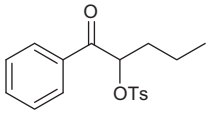
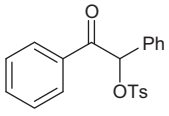
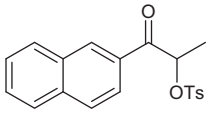
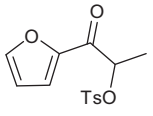
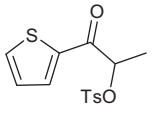
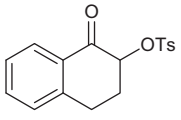
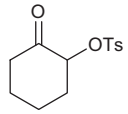
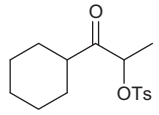
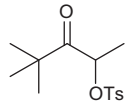
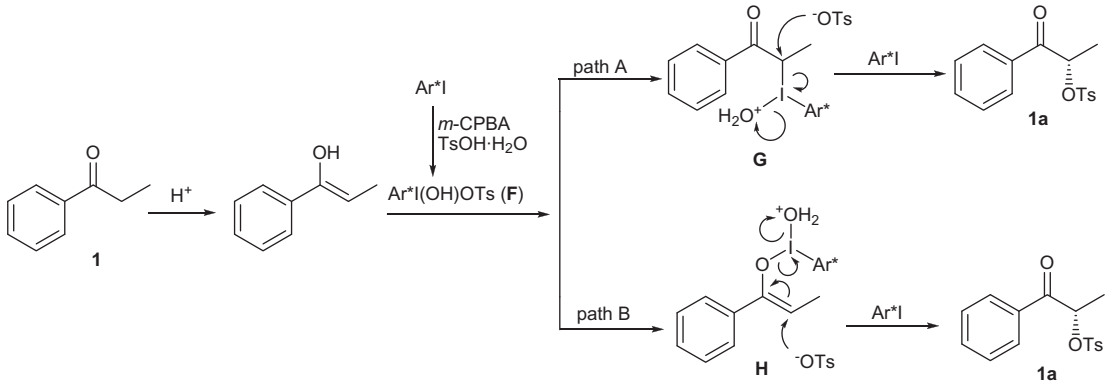
Entry	Product	Time (h)	Conversion (%)	Yield[b] (%)	ee[c] (%)
1	 **19**	24	21	14	30
2	 **20**	20	35	18	23
3	 **21**	21	30	16	56
4	 **22**	24	46	20	42
5	 **23**	24	35	28	40
6	 **24**	24	82	8	40
7	 **25**	20	32	25	58
8	 **26**	25	26	20	39
9	 **27**	24	29	16	13
10	 **28**	24	48	32	45
11	 **29**	24	67	37	52
12	 **30**	24	50	14	49
13	 **31**	24	45	13	8

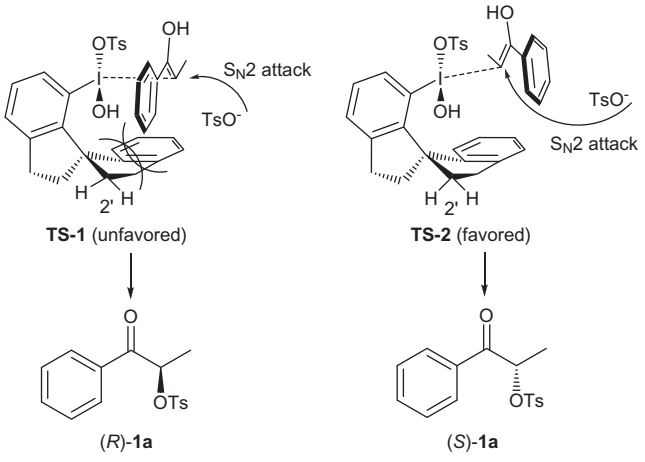
Table 4 (*continued*)

Entry	Product	Time (h)	Conversion (%)	Yield[b] (%)	ee[c] (%)
14	 **32**	24	17	10	18
15	 **33**	20	25	16	22
16	 **34**	24	32	10	12

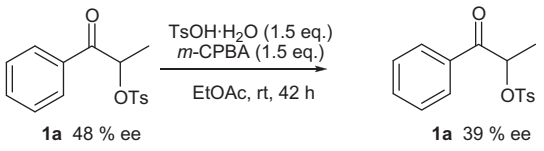
[a] 0.5 mmol of substrates were used.
[b] Isolated yield.
[c] Determined by HPLC; absolute configuration unknown.



Scheme 7. The possible reaction pathway.



Scheme 8. The proposed reaction model.



Scheme 9. The racemization of **1a**.

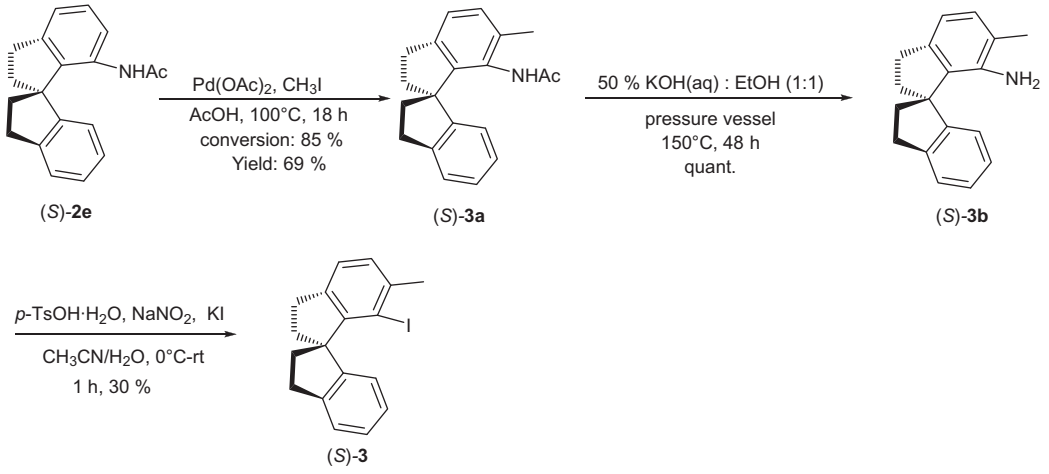
4. Experimental

4.1. General remarks

The ^{1}H NMR spectra were recorded at 400 or 300 MHz and ^{13}C NMR spectra were measured at 100 or 75 MHz using a Bruker AV400 or AV300 instrument with $CDCl_3$ as the solvent. The ^{19}F NMR spectrum was recorded at 376 MHz still using a Bruker AV400 instrument with $CDCl_3$ as the solvent. IR spectra were recorded on a FT-IR Bruker EQUINOX55 spectrometer in KBr pellets. High resolution mass spectral analyses (HRMS) were performed on high resolution ESI–FTICR or ESI-QTOF mass spectrometers. High performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC–20AT with a UV detector SPD–20A and chiral column of Daicel CHIRALCEL CHIRALPAK AD–H (4.6 mm × 25 cm). Optical rotations were measured on a Perkin Elmer 341 MC polarimeter. All solvents used were purified following the standard methods. Petroleum ether (PE) had a range of boiling point 60–90 °C.

4.2. Preparation of chiral iodoarenes (*S*)-3 to (*S*)-18

4.2.1. Preparation of (*S*)-3

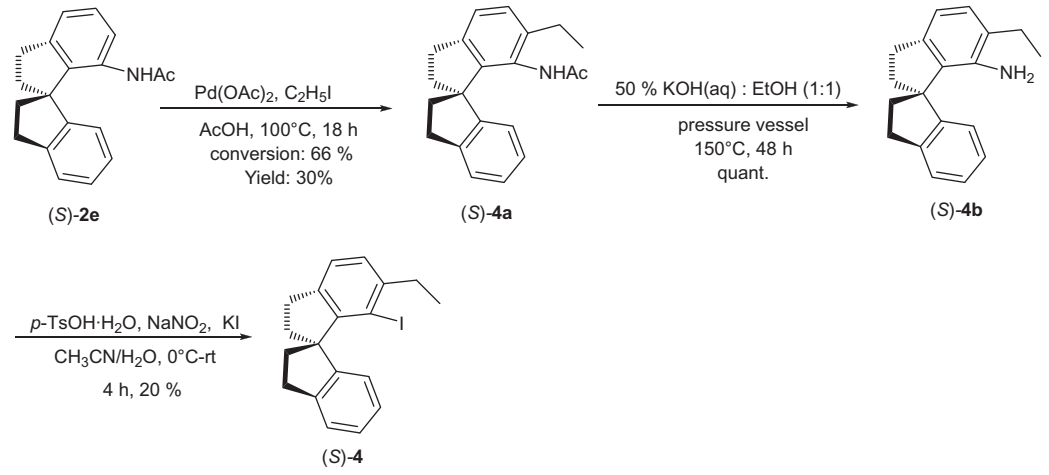


4.2.1.1. Compound (*S*)-3a. To a solution of (*S*)-**2e** (291 mg, 1.05 mmol), $Pd(OAc)_2$ (354 mg, 1.58 mmol), and AcOH (1.8 g, 30 mmol) was added CH_3I (1.363 g, 9.6 mmol). The reaction mixture was then stirred at 100 °C for 18 h. The PdI_2 precipitate was removed by filtration and the filtrate was concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE–EtOAc, 90:10) to afford the product (*S*)-**3a** as a colorless solid (211 mg, 69%).

4.2.1.2. Compound (*S*)-3b. Compound (*S*)-**3a** (183 mg, 0.63 mmol) was dissolved in EtOH (12 mL) and 50% aqueous KOH (12 mL) in a closed vessel. The reaction mixture was then heated to 150 °C for 48 h. After the heating was finished, water (10 mL) was added to the reaction mixture and the resulting mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE–EtOAc, 98:2) to afford the product (*S*)-**3b** as a colorless solid (157 mg, quant.).

4.2.1.3. Compound (*S*)-3. Compound (*S*)-**3** was prepared by the same procedure as that for (*S*)-**2** (30% yield) as a colorless solid; mp: 102–03 °C; $[\alpha]_D^{25} = -87.5$ (*c* 1.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.97–2.14 (m, 2H), 2.28–2.40 (m, 5H), 2.87–2.91 (m, 2H), 3.00–3.04 (m, 2H), 6.86 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 7.06–7.20 (m, 4H); ^{13}C NMR (100 MHz): δ = 28.96, 30.22, 30.88, 35.60, 42.52, 64.61, 100.25, 123.90, 124.36, 124.39, 126.48, 128.30, 140.57, 143.99, 144.06, 149.71, 149.79; IR (KBr): 3418, 3067, 3039, 2944, 2921, 2853, 2841, 1636, 1618, 1558, 1476, 1456, 1443, 1431, 1374, 1320, 1302, 1261, 1221, 1166, 1150, 1097, 1084, 1021, 897, 820, 752, 618, 540, 500 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{21}NI$ $[M+NH_4]^+$: 378.0713, found: 378.0708.

4.2.2. Preparation of (*S*)-4

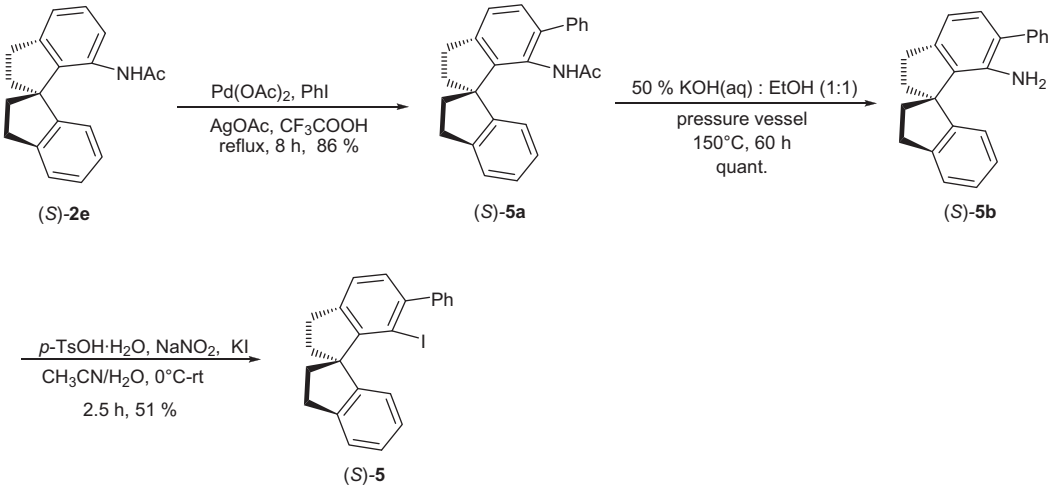


4.2.2.1. Compound (*S*)-4a. To a solution of (*S*)-**2e** (346 mg, 1.25 mmol), $Pd(OAc)_2$ (420 mg, 1.875 mmol) and AcOH (2.16 g, 36 mmol) was added C_2H_5I (1.95 g, 12.5 mmol). The reaction mixture was stirred at 100 °C for 18 h. The PdI_2 precipitate was removed by filtration and the filtrate was concentrated in vacuo to afford the crude product, which was purified by flash column chromatograpy (PE–EtOAc, 90:10) to afford the product (*S*)-**4a** as a colorless solid (113 mg, 30%).

4.2.2.2. Compound (*S*)-4b. Compound (*S*)-**4b** was prepared by the same procedure as that for (*S*)-**3b** (quant.) and obtained as a colorless oil.

4.2.2.3. Compound (*S*)-4. Compound (*S*)-**4** was prepared by the same procedure as that for (*S*)-**2** (20% yield) as a colorless oil; $[\alpha]_D^{25} = -80.3$ (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.10$ (t, $J = 7.6$ Hz, 3H), 1.97–2.05 (m, 1H), 2.08–2.14 (m, 1H), 2.31–2.42 (m, 2H), 2.66 (q, $J = 7.6$ Hz, 2H), 2.86–2.91 (m, 2H), 3.00–3.04 (m, 2H), 6.86 (d, $J = 7.6$ Hz, 1H), 7.00 (d, $J = 7.6$ Hz, 1H), 7.07–7.20 (m, 4H); ^{13}C NMR (100 MHz): $\delta = 14.97$, 30.23, 30.86, 34.43, 35.62, 42.57, 64.79, 99.54, 124.18, 124.35, 124.41, 126.44, 126.49, 127.10, 143.93, 144.25, 145.76, 149.85; IR (KBr):3065, 3039, 2930, 2858, 2845, 1727, 1603, 1587, 1558, 1478, 1451, 1434, 1395, 1371, 1321, 1279, 1262, 1221, 1168, 1085, 1074, 1059, 1022, 885, 824, 807, 775, 748, 760, 721 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{19}H_{20}I$ $[M+H]^+$: 375.0604, found: 375.0616.

4.2.3. Preparation of (*S*)-5

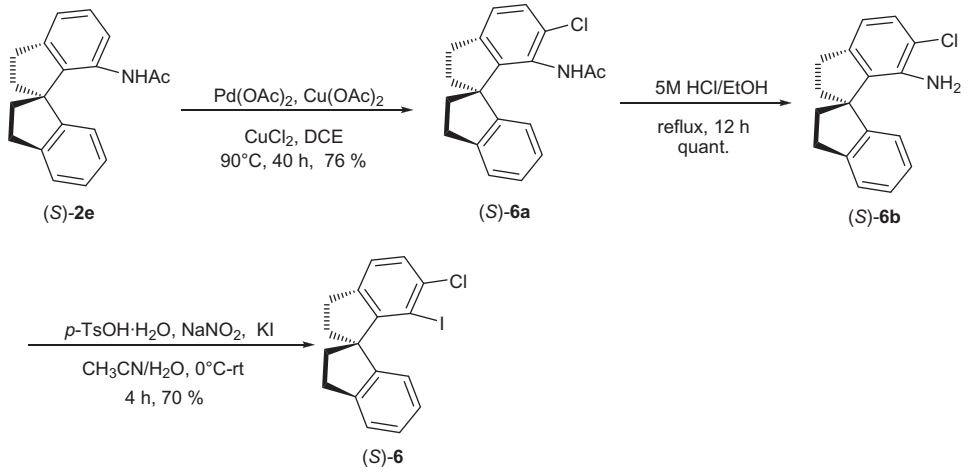


4.2.3.1. Compound (*S*)-5a. Compound (*S*)-**2e** (277 mg, 1 mmol), $Pd(OAc)_2$ (34 mg, 0.15 mmol), AgOAc (199 mg, 1.2 mmol) and PhI (510 mg, 2.5 mmol) were dissolved in TFA (3 mL). The resulting solution was heated for 8 h at 110 °C. The precipitate was removed by filtration and the filtrate was concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE-EtOAc, 90:10) to afford the product (*S*)-**5a** as a colorless solid (304 mg, 86%).

4.2.3.2. Compound (*S*)-5b. Compound (*S*)-**5b** was prepared by the same procedure as that for (*S*)-**3b** (quant.) and obtained as a green solid.

4.2.3.3. Compound (*S*)-5. Compound (*S*)-**5** was prepared by the same procedure as that for (*S*)-**2** (51% yield) as a colorless solid; mp: 80–81 °C; $[\alpha]_D^{25} = -70.9$ (*c* 0.46, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.03$–2.19 (m, 2H), 2.37–2.45 (m, 2H), 2.95–3.05 (m, 4H), 6.95 (d, $J = 6.8$ Hz, 1H), 7.04–7.31 (m, 10 H); ^{13}C NMR (100 MHz): $\delta = 30.38$, 30.85, 35.68, 42.45, 64.86, 97.68, 123.90, 124.38, 124.39, 126.52, 126.56, 127.19, 127.69, 128.65, 129.75, 143.94, 145.40, 145.67, 146.76, 149.59, 150.03; IR (KBr): 3425, 3052, 3015, 2958, 2923, 2850, 1949, 1905, 1885, 1730, 1631, 1468, 1444, 1427, 1380, 1306, 1259, 1167, 1152, 1121, 1102, 1028, 933, 877, 823, 767, 758, 706, 699, 601, 579, 545, 530 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}NI$ $[M+NH_4]^+$: 440.0870, found: 440.0875.

4.2.4. Preparation of (*S*)-6



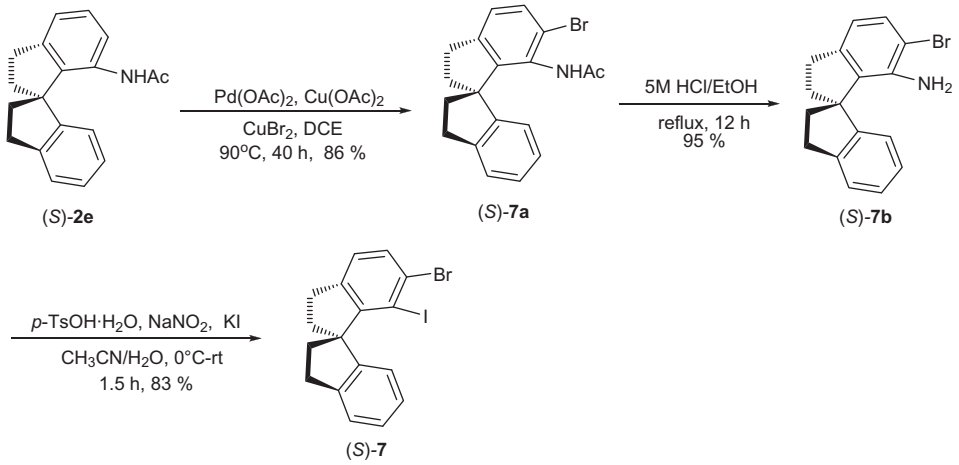
4.2.4.1. Compound (*S*)-6a. Compound (*S*)-**2e** (277 mg, 1 mmol), $Pd(OAc)_2$ (22.4 mg, 0.1 mmol), $Cu(OAc)_2$ (364 mg, 2 mmol) and anhydrous $CuCl_2$ (268 mg, 2 mmol) were added to a 25 mL oven-dried flask under N_2. Next, DCE (10 mL) was added *via* syringe.

The reaction mixture was heated at 90 °C for 40 h. The precipitate was removed by filtration and the filtrate was concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE–EtOAc, 90:10) to afford the product (*S*)-**6a** as a colorless solid (236 mg, 76%).

4.2.4.2. Compound (*S*)-6b. Compound (*S*)-**6b** was prepared by the same procedure as that for (*S*)-**2f** (quant.) and obtained as a colorless solid

4.2.4.3. Compound (*S*)-6. Compound (*S*)-**6** was prepared by the same procedure as that for (*S*)-**2** (70% yield) as a colorless solid; mp:67–68 °C; $[\alpha]_D^{25} = -84.5$ (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.00–2.17 (m, 2H), 2.21–2.38 (m, 2H), 2.87–3.05 (m, 4H), 6.81–6.87 (m, 1H), 7.10–7.26 (m, 5H); ^{13}C NMR (100 MHz): δ = 30.20, 30.86, 35.59, 42.46, 65.07, 97.33, 124.28, 124.44, 125.15, 126.65, 126.75, 127.68, 137.76, 143.96, 144.73, 149.00, 152.32; IR (KBr): 2952, 2924, 2850, 1715, 1581, 1549, 1479, 1458, 1422, 1438, 1385, 1362, 1311, 1260, 1220, 1173, 1131, 1086, 1022, 969, 877, 819, 806, 755, 726, 676, 549 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{18}NClI$ $[M+NH_4]^+$: 398.0167, found: 398.0171.

4.2.5. Preparation of (*S*)-7



4.2.5.1. Compound (*S*)-7a. Compound (*S*)-**2e** (277 mg, 1 mmol), $Pd(OAc)_2$ (22.4 mg, 0.1 mmol), $Cu(OAc)_2$ (364 mg, 2 mmol) and anhydrous $CuBr_2$ (446 mg, 2 mmol) were added to a 25 mL oven-dried flask under N_2. Next, DCE (10 mL) was added via syringe. The reaction mixture was heated at 90 °C for 40 h. The precipitate was removed by filtration and the filtrate was concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE-EtOAc, 90:10) to afford the product (*S*)-**7a** as a colorless solid (306 mg, 86%).

4.2.5.2. Compound (*S*)-7b. Compound (*S*)-**7b** was prepared by the same procedure as that for (*S*)-**2f** (95% yield) and obtained as a colorless solid

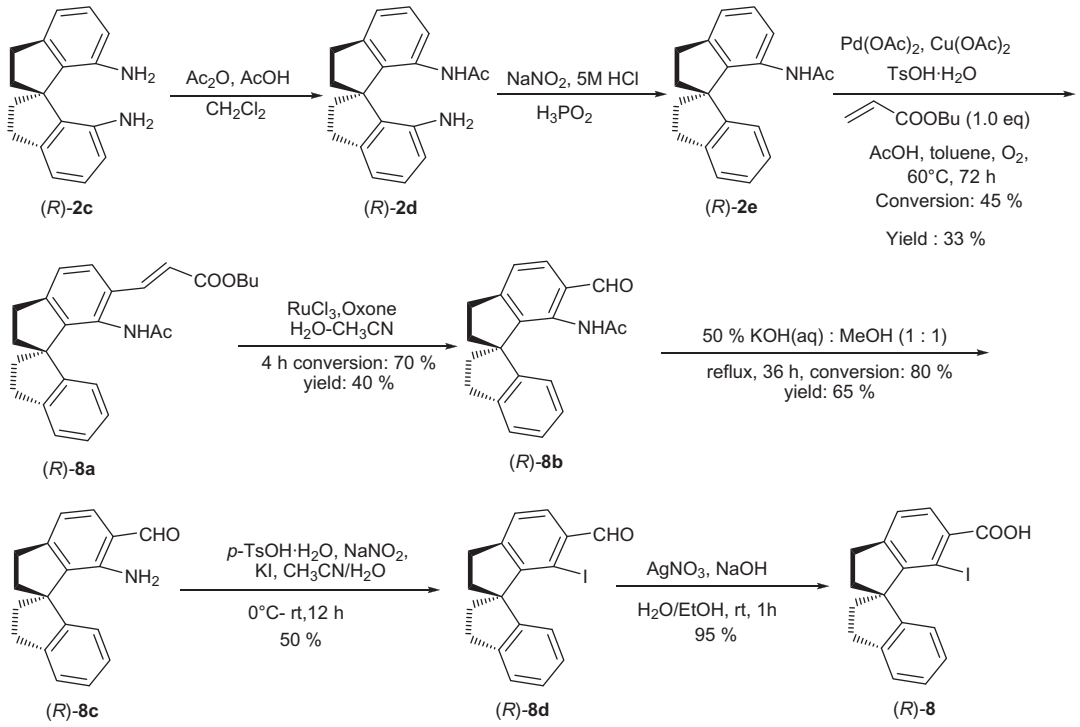
4.2.5.3. Compound (*S*)-7. Compound (*S*)-**7** was prepared by the same procedure as that for (*S*)-**2** (83% yield) as a colorless oil; $[\alpha]_D^{25} = -31.8$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.98–2.36 (m, 4H), 2.83–3.02 (m, 4H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 1H), 7.08–7.20 (m, 3H), 7.40 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.84, 32.27, 36.46, 40.87, 65.04, 91.00, 120.55, 124.29, 124.43, 126.70, 126.88, 131.68, 140.11, 143.92, 146.99, 148.61, 150.84; IR (KBr): 3018, 2927, 2846, 1618, 1478, 1436, 1379, 1308, 1270, 1222, 1150, 1101, 1186, 1056, 1022, 868, 801, 757, 725 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{18}NBrI$ $[M+NH_4]^+$: 441.9662, found: 441.9649.

4.2.6. Preparation of (*R*)-8

4.2.6.1. Compound (*R*)-8a. To a 25 mL one-neck flask were added (*R*)-**2e** (554 mg, 2 mmol), $Pd(OAc)_2$ (45 mg, 0.2 mmol), $Cu(OAc)_2$ (36 mg, 0.2 mmol), *p*-TsOH·H_2O (127 mg, 0.67 mmol) and 3 mL of AcOH at room temperature. Then a solution of butyl acrylate (431 μL, 3.0 mmol) in 2 mL of toluene was added to the mixture. A balloon of oxygen was then attached to the reaction flask. The flask was evacuated and refilled with oxygen three times. The reaction mixture was stirred for 72 h at 60 °C under oxygen. The resulting mixture was cooled to room temperature, diluted with CH_2Cl_2 (30 mL), and neutralized with a 2.0 M NaOH solution. After extraction of the aqueous phase with an additional 60 mL of CH_2Cl_2, the combined organic phases were washed with brine, dried over Na_2SO_4 and evaporated in vacuo to afford the crude product, which was purified by flash column chromatograpy (PE-EtOAc, 9:1) to give 266 mg of (*R*)-**8a** in a 33% yield as a colorless solid.

4.2.6.2. Compound (*R*)-8b. To a stirred mixture of (*R*)-**8a** (202 mg, 0.5 mmol) and $RuCl_3 \cdot 3H_2O$ (13 mg, 0.05 mol) in CH_3CN (7.5 mL) and water (4.5 mL) was added in portions a mixture of oxone (460 mg, 0.75 mmol) and $NaHCO_3$ (193 mg, 2.3 mmol) over a period of 10 min at room temperature. After 4 h, the reaction was quenched with a saturated aqueous solution of NaS_2O_3 and then extracted with CH_2Cl_2 twice (2 × 20 mL). The combined organic layer was washed with water and brine, dried over Na_2SO_4, and evaporated in vacuo to afford the crude product, which was purified by flash column chromatograpy (PE-EtOAc, 85:15) to give 61 mg of (*R*)-**8b** in a 40% yield as a colorless solid.

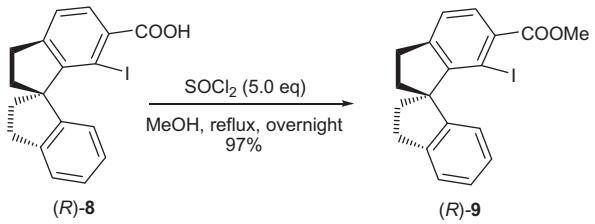
4.2.6.3. Compound (*R*)-8c. Compound (*R*)-**8b** (50 mg, 0.16 mmol) was dissolved in a mixture of 50% aqueous KOH (5 mL) and methanol (5 mL). The reaction mixture was stirred at reflux for 36 h. After cooling of the mixture to ambient temperature and removal of the methanol in vacuo, 4.0 M HCl was added until pH = 7. After extraction with dichloromethane (30 mL), the organic layers were dried over Na_2SO_4, and concentrated in vacuo to afford the product (*R*)-**8c** as a colorless oil (65% yield).



4.2.6.4. Compound (*R*)-8d. Compound (*R*)-**8d** was prepared by the same procedure as that for (*S*)-**2** (50% yield) and obtained as a colorless solid.

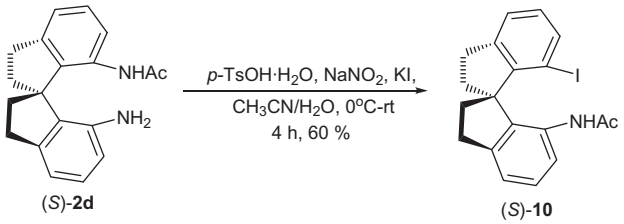
4.2.6.5. Compound (*R*)-8. To 2 mL of water were added $AgNO_3$ (37 mg, 0.214 mmol) and NaOH (17 mg, 0.428 mmol). The mixture was stirred at room temperature for 1 h. Then, a solution of (*R*)-**8d** (40 mg, 0.107 mmol) in 1.5 mL of EtOH was added to the resulting mixture. The reaction mixture was stirred at room temperature for another 12 h. Then, 4.0 M HCl was added to the mixture until pH = 7. After extraction with dichloromethane (30 mL), the organic layer was dried over Na_2SO_4, and concentrated in vacuo to afford 40 mg of product (*R*)-**8** as a colorless solid (95% yield); mp: 165–166 °C; $[\alpha]_D^{25} = +33.8$ (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.05–2.22 (m, 2H), 2.41–2. 48 (m, 2H), 3.01–3.14 (m, 4H), 6.93 (d, *J* = 7.6 Hz, 1H), 7.14–7.32 (m, 4H), 7.63 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.70, 30.83, 35.48, 42.21, 64.91, 92.61, 124.17, 124.30, 124.46, 126.73, 129.95, 135.20, 143.84, 149.10, 150.62, 151.30, 172.47; IR (KBr): 3446, 2961, 2917, 2849, 1669, 1581, 1551, 1473, 1428, 1382, 1261, 1235, 1202, 1100, 1085, 1053, 1022, 984, 825, 807, 776, 756, 720, 667 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{14}IO_2$ $[M - H]^+$: 389.0044, found: 389.0048.

4.2.7. Preparation of (*R*)-9



4.2.7.1. Compound (*R*)-9. To a solution of (*R*)-**8** (10 mg, 0.026 mmol) in MeOH (3 mL) was added $SOCl_2$ (18 mg, 0.15 mmol). The reaction mixture was then stirred at reflux for 12 h. After cooling of the mixture to ambient temperature, the solvent was removed in vacuo to afford a crude product which was purified by flash column chromatograpy (PE-EtOAc, 19:1) to give 10 mg of (*R*)-**9** as a colorless solid (97% yield); mp: 113–114 °C; $[\alpha]_D^{25} = +40.8$ (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01–2.14 (m, 2H), 2.34–2.38 (m, 2H), 2.91–3.06 (m, 4H), 3.81 (s, 3H), 6.86 (d, *J* = 7.2 Hz, 1H), 7.07–7.23 (m, 4H), 7.31 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (75 MHz): δ = 30.62, 30.86, 35.67, 42.23, 52.40, 64.74, 91.78, 124.15, 124.36, 124.45, 126.70, 126.75, 128.52, 137.86, 143.89, 149.11, 149.35, 150.77, 169.26; IR (KBr): 3440, 2952, 2917, 2849, 1738, 1473, 1449, 1423, 1386, 1287, 1262, 1207, 1125, 1088, 1063, 830, 808, 779, 718, 540 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{19}H_{18}IO_2$ $[M+H]^+$: 405.0346, found: 405.0347.

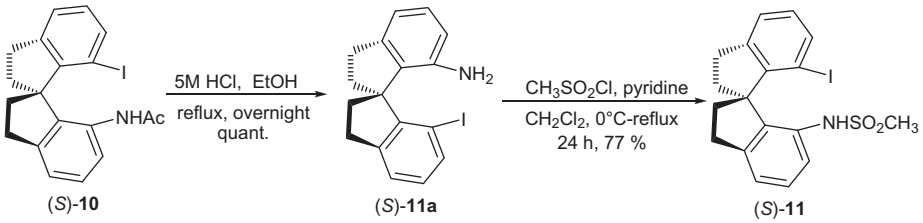
4.2.8. Preparation of (*S*)-10



4.2.8.1. Compound (*S*)-10. Compound (*S*)-**10** was prepared by the same procedure as that for (*S*)-**2** (60% yield) as a colorless solid; mp:76–78 °C; $[\alpha]_D^{25} = -111.9$ (*c* 0.93, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56 (s, 3H), 2.05–2.23 (m, 2H), 2.33–2.41 (m, 2H), 3.03–3.10 (m, 4H), 6.39 (s, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 7.06 (d,

J = 7.6 Hz, 1H), 7.24–7.28 (m, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz): δ = 24.00, 30.63, 30.78, 36.30, 37.73, 63.01, 92.46, 119.43, 121.01, 125.40, 128.27, 129.46, 134.20, 135.94, 138.83, 144.63, 146.42, 146.95, 167.74; IR (KBr): 3407, 3284, 3045, 3021, 2959, 2924, 2871, 2850, 1942, 1917, 1869, 1845, 1734, 1689, 1661, 1600, 1586, 1557, 1527, 1496, 1469, 1439, 1422, 1370, 1262, 1237, 1155, 1098, 1027, 924, 887, 860, 802, 785, 764, 755, 741, 680, 657, 633, 598, 580, 554 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{18}INONa$ [M+Na]$^+$: 426.0325, found: 426.0318.

4.2.9. Preparation of (*S*)-11

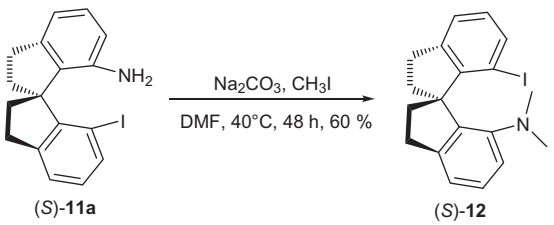


(*S*)-**10** (*S*)-**11a** (*S*)-**11**

4.2.9.1. Compound (*S*)-11a. (*S*)-**11a** was prepared by the same procedure as that for (*S*)-**2f** (quant.) and obtained as a colorless solid.

4.2.9.2. Compound (*S*)-11. To a solution of (*S*)-**11a** (235 mg, 0.65 mmol) in CH_2Cl_2 (20 mL) were added pyridine (205 mg, 2.6 mmol) and methanesulfonyl chloride (284 mg, 2.47 mmol) at 0 °C. The reaction mixture was then heated at reflux for 24 h. After the heating was finished, the mixture was diluted with CH_2Cl_2 (50 mL), and washed with saturated NH_4Cl (10 mL) and brine. The organic phase was then dried over Na_2SO_4, and concentrated in vacuo to afford the crude product, which was purified by flash column chromatograpy (PE-EtOAc, 95:5) to afford the product (*S*)-**11** as a colorless solid (220 mg, 77%); mp: 141–143 °C; $[\alpha]_D^{25} = -99.6$ (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.15–2.24 (m, 2H), 2.33–2.39 (m, 2H), 3.04 (s, 3H), 3.05–3.11 (m, 4H), 5.59 (s, 1H), 6.97–7.05 (m, 2H), 7.24–7.32 (m, 2H), 7.36 (d, J = 7.2 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.60, 30.89, 36.65, 37.30, 40.04, 62.78, 92.11, 114.29, 120.42, 126.02, 128.88, 130.15, 133.91, 134.45, 138.86, 145.95, 146.02, 146.56; IR (KBr): 3421, 3341, 2952, 2936, 2860, 1944, 1881, 1802, 1636, 1618, 1589, 1556, 1473, 1442, 1421, 1385, 1327, 1299, 1264, 1153, 1138, 1102, 1067, 1026, 965, 957, 984, 934, 873, 860, 778, 748, 707, 563, 535, 517, 544 cm^{-1}; HRMS (ESI): m/z calcd for $C_{18}H_{18}INO_2SNa$ [M+Na]$^+$: 461.9995, found: 461.9997.

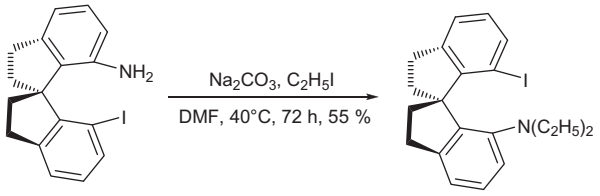
4.2.10. Preparation of (*S*)-12



(*S*)-**11a** (*S*)-**12**

4.2.10.1. Compound (*S*)-12. To a solution of (*S*)-**11a** (148 mg, 0.41 mmol) in DMF (3 ml) were added K_2CO_3 (170 mg, 1.23 mmol) and CH_3I (291 mg, 2.05 mmol). The mixture was stirred at 40 °C for 40 h. Then, water (10 mL) was added to the reaction mixture and the resulting mixture was extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE-EtOAc, 95:5) to afford the product (*S*)-**12** as a colorless solid (96 mg, 60% yield); mp: 50–52 °C; $[\alpha]_D^{25} = -14.2$ (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06–2.48 (m, 10 H), 2.98–3.02 (m, 4H), 6.75 (m, 1H), 6.94 (m, 2H), 7.15–7.16 (m, 2H), 7.48–7.50 (m, 1H); ^{13}C NMR (100 MHz): δ = 30.97, 31.49, 38.84, 39.26, 45.29, 63.58, 93.33, 120.07, 120.57, 124.21, 127.72, 128.11, 137.61, 143.87, 145.78, 146.12, 150.33, 151.54; IR (KBr): 3424, 3054, 2966, 2941, 2930, 2899, 2857, 2825, 2782, 1923, 1851, 1779, 1633, 1588, 1557, 1474, 1446, 1425, 1316, 1292, 1230, 1184, 1157, 1122, 1099, 1064, 1043, 1005, 981, 937, 953, 881, 856, 795, 764, 753, 732, 582, 567, 553 cm^{-1}; HRMS (ESI): m/z calcd for $C_{19}H_{21}IN$ [M+H]$^+$: 390.0713, found: 390.0715.

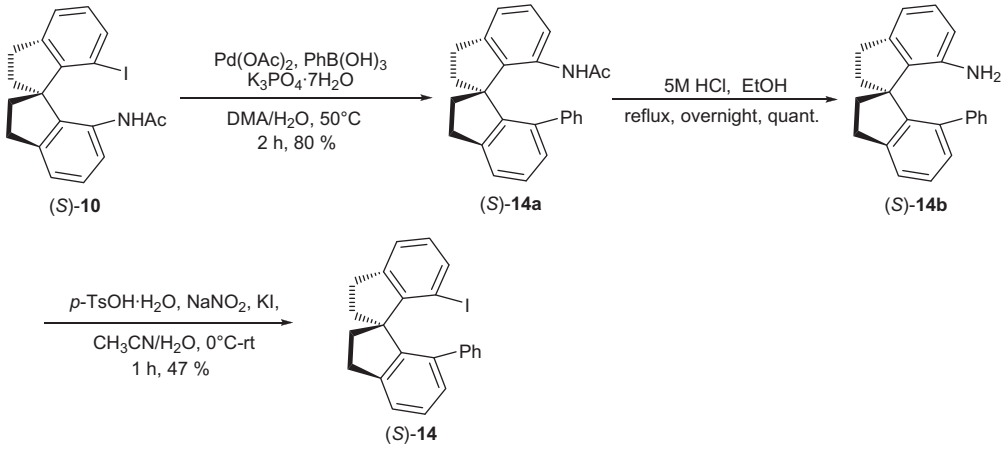
4.2.11. Preparation of (*S*)-13



(*S*)-**11a** (*S*)-**13**

4.2.11.1. Compound (*S*)-13. Compound (*S*)-**13** was prepared by a similar procedure as that for (*S*)-**12** (55% yield) as a colorless solid; mp: 64–65 °C; $[\alpha]_D^{25} = -42.9$ (c 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.56 (t, J = 7.2 Hz, 6H), 2.02–2.19 (m, 2H), 2.36–2.70 (m, 6H), 2.94–3.05 (m, 4H), 6.73 (t, J = 7.2 Hz, 1H), 6.87 (d, J = 7.2 Hz, 1H), 6.94 (d, J = 7.2 Hz, 1H), 7.11–7.16 (m, 2H), 7.48 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz): δ = 12.22, 31.02, 31.53, 39.06, 39.34, 47.37, 63.75, 93.85, 120.44, 122.04, 124.27, 127.70, 137.80, 144.25, 146.05, 146.43, 149.94, 150.75; IR (KBr): 3424, 3057, 2971, 2936, 2918, 2867, 2840, 2801, 2726, 1915, 1846, 1783, 1661, 1631, 1585, 1556, 1470, 1462, 1423, 1378, 1354, 1315, 1262, 1238, 1164, 1118, 1099, 1066, 1041, 958, 890, 861, 788, 769, 746, 735, 688, 575, 557 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{25}IN$ [M+H]$^+$: 418.1026, found: 418.1029.

4.2.12. Preparation of (*S*)-14

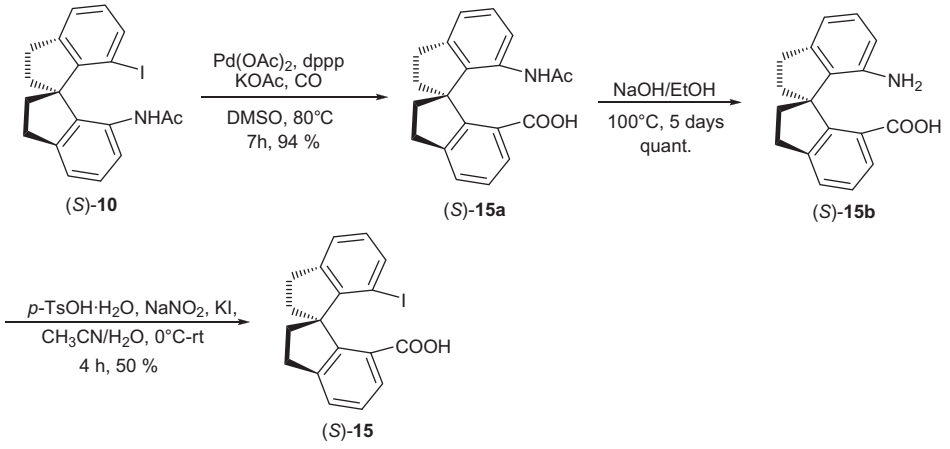


4.2.12.1. Compound (*S*)-14a. To a solution of (*S*)-**10** (100 mg, 0.25 mmol), phenylboronic acid (46 mg, 0.375 mmol) and $K_3PO_4·7H_2O$ (169 mg, 0.5 mmol) in 2 mL of DMA/H_2O (1: 1) was added $Pd(OAc)_2$ (5.6 mg, 10%). The reaction was stirred at 50 °C and monitored by TLC. After 2 h, 1 M NaOH (10 mL) was added and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE-EtOAc, 95:5) to afford the product (*S*)-**14a** as a colorless solid (71 mg, 80% yield).

4.2.12.2. Compound (*S*)-14b. Compound (*S*)-**14b** was prepared by the same procedure as that for (*S*)-**2f** (quant.) and obtained as a colorless solid.

4.2.12.3. Compound (*S*)-14. Compound (*S*)-**14** was prepared by the same procedure as that for (*S*)-**2** (47% yield) as a colorless solid; mp:77 °C; $[\alpha]_D^{25} = -72.6$ (*c* 0.73, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.98–2.06 (m, 1H), 2.29–2.33 (m, 2H), 2.47–2.63 (m, 2H), 2.76–2.85 (m, 1H), 3.07–3.11 (m, 2H), 6.54 (t, *J* = 7.6 Hz, 1H), 6.82–6.98 (m, 7H), 7.18–7.25 (m, 2H), 7.30 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.29, 30.93, 39.30, 39.91, 64.04, 94.14, 123.57, 123.99, 126.05, 126.59, 126.80, 127.93, 128.86, 129.04, 137.82, 139.41, 140.45, 144.78, 145.88, 146.15, 149.02; IR (KBr): 3418, 3053, 3024, 2956, 2921, 2870, 2850, 1929, 1856, 1737, 1633, 1573, 1560, 1494, 1460, 1442, 1427, 1378, 1310, 1261, 1179, 1155, 1103, 1083, 1027, 881, 856, 790, 759, 700, 559 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}NI$ $[M+NH_4]^+$: 440.0870, found: 440.0877.

4.2.13. Preparation of (*S*)-15

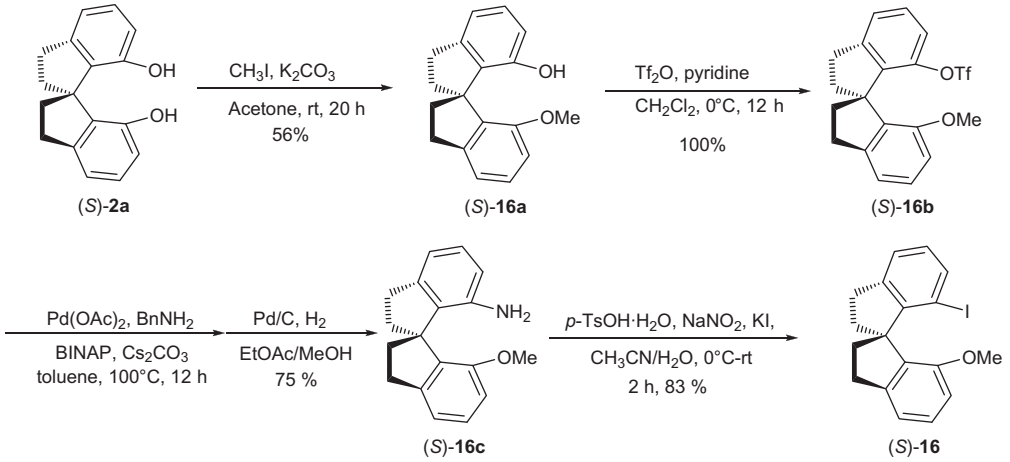


4.2.13.1. Compound (*S*)-15a. A mixture of (*S*)-**10** (202 mg, 0.5 mmol), $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), dppp (82 mg, 0.2 mmol) and KOAc (196 mg, 2 mmol) was dissolved in 4 mL of DMSO under a CO atmosphere. The reaction mixture was stirred at 80 °C for 7 h. After the heating was finished, the mixture was diluted with EtOAc (50 mL). The organic layer was washed with water (3 × 5 mL) and brine, dried over Na_2SO_4, and concentrated in vacuo to afford the crude product which was purified by flash column chromatograpy (PE-EtOAc-AcOH, 90:7:3) to afford the product (*S*)-**15a** as a colorless solid.

4.2.13.2. Compound (*S*)-15b. A mixture of (*S*)-**15a** (151 mg, 0.47 mmol) and NaOH (200 mg, 5 mmol) was dissolved in 2 mL of EtOH. The reaction mixture was heated at 100 °C for 5 days. After cooling of the mixture to ambient temperature and removal of the ethanol in vacuo, 4.0 M HCl was added until pH = 7. After extraction with dichloromethane, the combined organic layers were dried over Na_2SO_4, and concentrated in vacuo to afford the product (*S*)-**15b** as a colorless solid (quant.).

4.2.13.3. Compound (*S*)-15. Compound (*S*)-**15** was prepared by the same procedure as that for (*S*)-**2** (50% yield) as a colorless solid; mp:156 °C; $[\alpha]_D^{25} = -43.1$ (*c* 0.37, EtOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.17–2.39 (m, 3H), 2.50–2.53 (m, 1H), 3.04–3.10 (m, 4H), 6.80 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.46–7.52 (m, 2H), 7.74 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.39, 30.94, 37.21, 37.90, 64.74, 90.56, 124.02, 126.93, 127.27, 128.08, 129.08, 129.18, 137.79, 145.90, 146.04, 149.43, 149.61, 171.54; IR (KBr): 3429, 3049, 2940, 2856, 2659, 2595, 2540, 1693, 1586, 1559, 1472, 1446, 1408, 1310, 1281, 1197, 1167, 1151,1099, 1072, 1054, 930, 858, 799, 764, 737, 673, 611, 562 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{14}IO_2$ [M - H]$^+$: 389.0044, found: 389.0047.

4.2.14. Preparation of (*S*)-16



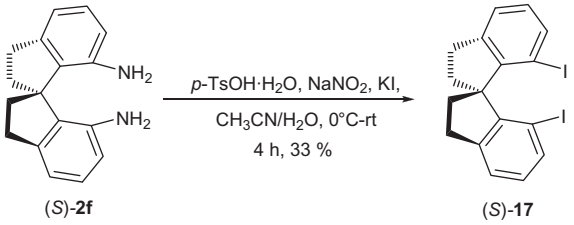
4.2.14.1. Compound (*S*)-16a. To a solution of (*S*)-**2a** (1.26 g, 5 mmol) in acetone (6 mL) was added K_2CO_3 (828 mg, 6 mmol). The mixture was stirred at room temperature for 1 h. Then CH_3I (5.5 mmol, 0.35 mL) was added. After 20 h, the reaction mixture was filtered and the filtrate was concentrated in vacuo to give the crude product which was purified by flash column chromatograpy (PE-EtOAc, 95:5) to afford the product (*S*)-**16a** as a colorless solid (56% yield).

4.2.14.2. Compound (*S*)-16b. To a solution of (*S*)-**16a** (266 mg, 1 mmol) in 10 mL of CH_2Cl_2 was added pyridine (175 μL, 2.19 mmol), and followed by the dropwise addition of triflic anhydride (410 μL, 1.1 mmol). The mixture was stirred at room temperature for 12 h. After removal of the solvent, the residue was diluted with EtOAc (40 mL) and then washed with 5% aqueous HCl, saturated $NaHCO_3$, and brine. The organic layers were dried over Na_2SO_4, and concentrated in vacuo to afford the product (*S*)-**16b** as a colorless solid (quant.).

4.2.14.3. Compound (*S*)-16c. Compound (*S*)-**16c** was prepared by the same procedure as that for compound (*S*)-**2c** as a colorless solid (75%).

4.2.14.4. Compound (*S*)-16. (*S*)-**16** was prepared by the same procedure as that for (*S*)-**2** (83% yield) as a colorless solid; mp:65–68 °C; $[\alpha]_D^{25} = -134.8$ (*c* 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.17–2.30 (m, 4H), 2.95–3.06 (m, 4H), 3.56 (s, 3H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.81–6.89 (m, 2H), 7.21–7.26 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.65, 31.22, 36.71, 37.59, 55.26, 62.88, 91.99, 108.45, 117.08, 124.39, 127.76, 128.50, 134.91, 137.68, 145.20, 145.95, 149.65, 156.53; IR (KBr): 3418, 3051, 2997, 2935, 2899, 2856, 2831, 1905, 1602, 1588, 1558, 1478, 1466, 1439, 1423, 1302, 1262, 1224, 1211, 1084, 1068, 1054, 959, 920, 858, 829, 801, 769, 738, 729, 693, 642, 577, 555 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{18}IO$ [M+H]$^+$: 377.0397, found: 377.0395.

4.2.15. Preparation of (*S*)-17



4.2.15.1. Compound (*S*)-17. Compound (*S*)-**17** was prepared by the same procedure as that for (*S*)-**2** (33% yield) as a colorless solid[1]; mp:106–107 °C; $[\alpha]_D^{25} = -58.2$ (*c* 0.55, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.20–2.38 (m, 4H), 3.00–3.13 (m, 4H), 6.92 (t, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz): δ = 30.65, 36.92, 66.24, 93.70, 124.66, 128.57, 137.93, 146.78, 148.21.

4.2.16. Preparation of (*S*)-18

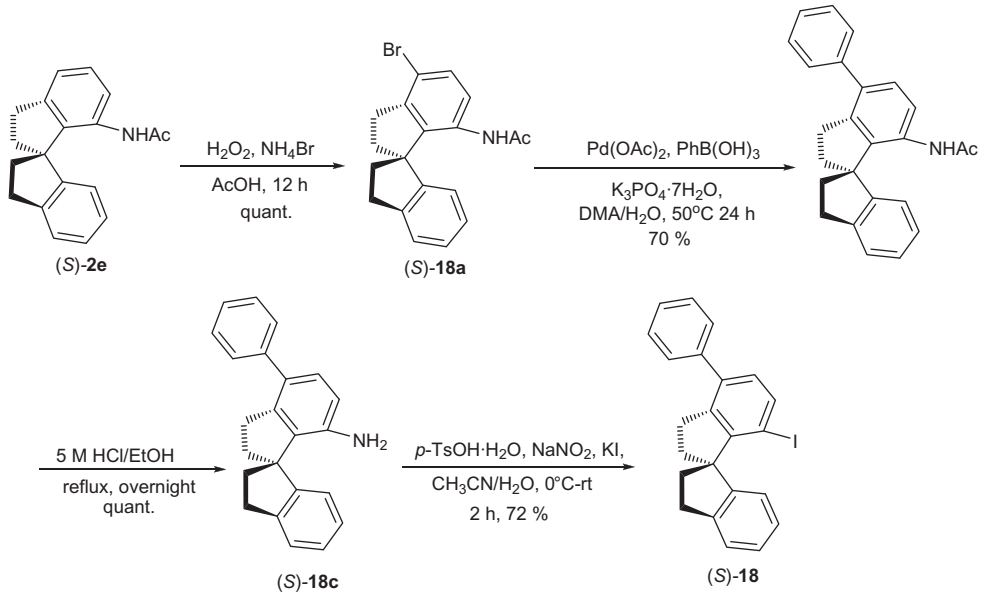
4.2.16.1. Compound (*S*)-18a. To a mixture of (*S*)-**2e** (111 mg, 0.4 mmol) and ammonium bromide (43 mg, 0.44 mmol) in 2 mL of AcOH was added dropwise 30% H_2O_2 (0.5 mL, 1.6 mmol). The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction, saturated aqueous $NaHCO_3$ (3 mL) was added and the resulting mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, and concentrated in vacuo to afford the product (*S*)-**18a** as a colorless solid (quant.).

4.2.16.2. Compound (*S*)-18b. Compound (*S*)-**18b** was prepared by the same procedure as that for (*S*)-**14a** (70% yield) and obtained as a colorless solid.

4.2.16.3. Compound (*S*)-18c. Compound (*S*)-**18c** was prepared by the same procedure as that for (*S*)-**2f** (quant.) and obtained as a colorless solid.

4.2.16.4. Compound (*S*)-18. Compound (*S*)-**18** was prepared by the same procedure as that for (*S*)-**2** (72%.) as a colorless solid; mp:114 °C; $[\alpha]_D^{25} = -30.6$ (*c* 0.53, $CHCl_3$); ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 1.99–2.07 (m, 1H), 2.25–2.31 (m, 1H), 2.37–2.46 (m, 2H), 2.92–2.98 (m, 1H), 3.05–3.13 (m, 3H), 6.92–6.98 (m, 2H), 7.17–7.29 (m, 4H), 7.34–7.38 (m, 1H), 7.42–7.47 (m, 3H), 7.72 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz): δ = 30.62, 30.92, 35.96, 42.06, 63.90, 91.59, 124.39, 124.47, 126.61, 126.69, 127.19, 128.35, 128.50, 129.26, 138.37, 139.13, 140.37, 144.08, 144.66, 149.25, 149.56; IR (KBr): 3417, 3058, 3039, 3017, 2955, 2920, 2871, 2849, 1946, 1892, 1735, 1639, 1596, 1568, 1449, 1433, 1374, 1309, 1259, 1183, 1149, 1107, 1177, 1025, 820, 765, 730, 699, 599 cm^{-1}; HRMS (ESI): m/z calcd for $C_{23}H_{23}NI$ $[M+NH_4]^+$: 440.0870, found: 440.0878.



4.3. α-Tosyloxylation of ketones

4.3.1. 1-Oxo-1-(3-(trifluoromethyl)phenyl)propan-2-yl 4-methylbenzenesulfonate 19

Colorless solid, mp: 91–93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (d, J = 6.8 Hz, 3H), 2.34 (s, 3H), 5.64 (q, J = 6.8 Hz, 1H), 7.18–7.20 (m, 2H), 7.54 (t, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 1H), 8.02–8.05 (m, 2H); ^{13}C NMR (100 MHz): δ = 18.45, 21.51, 77.52, 125.56 (q, J = 3.8 Hz), 127.85, 129.38, 129.80, 130.07 (q, J = 3.4 Hz), 131.91, 133.00, 134.14, 145.33, 194.03; ^{19}F NMR (376 MHz): δ = -62.90; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 240 nm. t_R = 15.9 min (minor), 17.0 min (major).

4.3.2. 1-(3-Nitrophenyl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 20

Colorless solid, mp: 79–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.56 (d, J = 6.8 Hz, 3H), 2.35 (s, 3H), 5.61 (q, J = 6.8 Hz, 1H), 7.20–7.23 (m, 2H), 7.60–7.67 (m, 3H), 8.20 (d, J = 7.6 Hz, 1H), 8.36 (d, J = 8.4 Hz, 1H), 8.60 (s, 1H); ^{13}C NMR (100 MHz): δ = 18.34, 21.61, 77.59, 123.70, 127.84, 127.90, 129.91, 130.01, 133.02, 134.35, 135.00, 145.49, 148.36, 193.46; IR (KBr): 3386, 3095, 2926, 1709, 1614, 1397, 1534, 1350, 1191, 1177, 1095, 1074, 1019, 919, 816, 775, 714, 665, 554 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{15}NO_6SNa$ $[M+Na]^+$: 372.0512, found: 372.0517; HPLC conditions: Chiracel AD column, hexane/2-propanol, 80:20, 0.6 mL/min, 254 nm. t_R = 31.3 min (minor), 38.1 min (major).

4.3.3. 1-(4-Nitrophenyl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 21

Colorless solid, mp: 145–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (d, J = 7.2 Hz, 3H), 2.37 (s, 3H), 5.60 (q, J = 7.2 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 8.8 Hz, 2H), 8.23 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz): δ = 18.21, 21.67, 77.69, 123.83, 127.89, 129.93, 129.95, 133.01, 138.35, 145.50, 150.46, 194.13; HPLC conditions: Chiracel AD column, hexane/2-propanol, 85:15, 0.8 mL/min, 220 nm. t_R = 34.9 min (minor), 76.8 min (major).

4.3.4. 1-(2-Fluorophenyl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 22

Colorless solid, mp: 63–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (d, J = 6.8 Hz, 3H), 2.35 (s, 3H), 6.68 (q, J = 6.8 Hz, 1H), 7.03–7.08 (m, 1H), 7.15–7.23 (m, 3H), 7.45–7.52 (m, 1H), 7.71–7.73 (m, 3H); ^{13}C NMR (100 MHz): δ = 17.73, 21.62, 79.53 (d, J = 8.4 Hz), 116.53 (d, J = 23.4 Hz), 122.77 (d, J = 13.7 Hz), 124.84 (d, J = 3 Hz), 127.90, 129.72, 131.20 (d, J = 2.6 Hz), 133.62, 135.41 (d, J = 9.1 Hz), 144.86, 161.14 (d, J = 252.3 Hz), 193.32 (d, J = 3.9 Hz); ^{19}F NMR (376 MHz): δ = -108.53; IR (KBr): 2992, 2927, 1702, 1610, 1599, 1481, 1454, 1366, 1293, 1271, 1211, 1190, 1178, 1097, 1076, 1020, 973, 924, 818, 776, 756, 666, 555 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{15}FO_4SNa$ $[M+Na]^+$: 345.0567, found: 345.0569; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm, t_R = 28.8 min (major), 30.6 min (minor).

4.3.5. 1-Oxo-1-*p*-tolylpropan-2-yl 4-methylbenzenesulfonate 23

Colorless solid, mp: 87–88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 7.2 Hz, 3H), 2.33 (s, 3H), 2.34 (s, 3H), 5.70 (q, J = 7.2, 1H), 7.16–7.20 (m, 4H), 7.67–7.72 (m, 4H); ^{13}C NMR (100 MHz): δ = 18.78, 21.60, 21.70, 77.31, 127.89, 128.82, 129.42, 129.71, 131.06, 133.44, 144.93, 194.26; HPLC conditions: Chiracel AD column, hexane/2-propanol, 88:12, 0.7 mL/min, 220 nm, t_R = 25.0 min (minor), 29.6 min (major).

4.3.6. 1-(4-Methoxyphenyl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 24

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, J = 6.8 Hz, 3H), 2.33 (s, 3H), 3.80 (s, 3H), 5.66 (q, J = 6.8 Hz, 1H), 6.85 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz): 18.83, 21.60, 55.52, 77.32, 113.94, 126.43, 127.89, 129.70, 131.15, 133.45, 144.92, 164.04, 193.04; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.8 mL/min, 220 nm, t_R = 43.2 min (minor), 49.9 min (major).

4.3.7. 1-Oxo-1-phenylbutan-2-yl 4-methylbenzenesulfonate 25

Colorless solid, mp: 80–82 °C; $[\alpha]_D^{25} = -8.2$ (*c* 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.2 Hz, 3H), 1.84–1.90 (m, 2H), 2.31 (s, 3H), 5.49 (dd, *J* = 5.4, 7.8 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 7. 2 Hz, 2H); ^{13}C NMR (75 MHz): δ = 9.49, 21.56, 26.18, 82.47, 127.96, 128.58, 128.67, 129.65, 133.22, 133.71, 133.76, 144.92, 194.85; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.7 mL/min, 220 nm, t_R = 20.7 min (minor), 23.9 min (major).

4.3.8. 1-Oxo-1-phenylpentan-2-yl 4-methylbenzenesulfonate 26

Colorless solid, mp: 62–63 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7.2 Hz, 3H), 1.31–1.44 (m, 2H), 1.75–1.85 (m, 2H), 2.32 (s, 3H), 5.52–5.56 (dd, *J* = 4.5, 8.4 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz): δ = 13.30, 18.38, 21.57, 34.67, 81.13, 128.00, 128.61, 128.68, 129.65, 133.26, 133.68, 134.11, 144.90, 195.00; IR (KBr): 2962, 2931, 2875, 1701, 1597, 1449, 1363, 1190, 1176, 1095, 941, 891, 815, 776, 697, 666, 578 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{20}O_4SNa$ $[M+Na]^+$: 355.0975, found: 355.0978; HPLC conditions: Chiracel AD column, hexane/2-propanol, 88:12, 0.8 mL/min, 220 nm, t_R = 14.7 min (minor), 16.6 min (major).

4.3.9. 2-Oxo-1,2-diphenylethyl 4-methylbenzenesulfonate 27

Colorless solid, mp: 104–105 °C; $[\alpha]_D^{25} = -33.0$ (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 3H), 6.60 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.21–7.22 (m, 3H), 7.28–7.32 (m, 4H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz): δ = 21.60, 82.23, 127.96, 128.11, 128.62, 128.93, 129.06, 129.60, 132.59, 133.46, 133.70, 133.92, 144.87, 191.97; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm, t_R = 55.7 min (minor), 68.3 min (major).

4.3.10. 1-(Naphthalen-2-yl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 28

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.49 (d, *J* = 6.9 Hz, 3H), 2.19 (s, 3H), 5.73 (q, *J* = 6.9 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 7.32–7.43 (m, 3H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.66–7.75 (m, 2H), 7.86 (d, *J* = 8.1 Hz, 1H), 8.11–8.14 (m, 1H); ^{13}C NMR (75 MHz): δ = 18.33, 21.43, 78.72, 124.08, 125.07, 126.59, 127.51, 127.63, 127.98, 128.35, 129.60, 130.21, 132.42, 133.06, 133.35, 133.73, 144.79, 198.23; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm; t_R = 32.2 min (major), 33.9 min (minor).

4.3.11. 1-(Furan-2-yl)-1-oxopropan-2-yl 4-methylbenzenesulfonate 29

Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.49 (d, *J* = 6.8 Hz, 3H), 2.36 (s, 3H), 5.45 (q, *J* = 6.8 Hz, 1H), 6.50–6.51 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.55 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz): δ = 18.43, 21.65, 77.35, 112.66, 120.08, 127.97, 129.80, 133.25, 145.12, 147.44, 149.51, 183.37; IR (KBr): 3367, 3137, 3068, 2990, 2925, 1794, 1742, 1688, 1590, 1569, 1464, 1367, 1190, 1178, 1122, 1015, 933, 892, 880, 816, 784, 752, 667, 574, 554 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{14}O_5SNa$ $[M+Na]^+$: 317.0454, found: 317.0462; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm; t_R = 34.2 min (minor), 36.3 min (major).

4.3.12. 1-Oxo-1-(thiophen-2-yl)propan-2-yl 4-methylbenzenesulfonate 30

Colorless solid, mp: 106–107 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 6.8 Hz, 3H), 2.34 (s, 3H), 5.38 (q, *J* = 6.8 Hz, 1H), 7.07 (t, *J* = 4.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 4.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.80 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (100 MHz): δ = 19.03, 21.60, 78.43, 127.98, 128.38, 129.78, 133.13, 133.75, 135.19, 139.83, 145.17, 187.90; IR (KBr): 3094, 2921, 2850, 1702, 1684, 1597, 1575, 1437, 1413, 1370, 1306, 1263, 1245, 1190, 1177, 1073, 1018, 945, 892, 852, 809, 748, 666 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{14}O_4S_2Na$ $[M+Na]^+$: 333.0226, found: 333.0231; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 210 nm, t_R = 29.0 min (minor), 33.4 min (major).

4.3.13. 1-Oxo-1,2,3,4-tetrahydronaphthalen-2-yl 4-methylbenzenesulfonate 31

Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.33–2.40 (m, 4H), 2.47–2.52 (m, 1H), 3.04–3.08 (m, 2H), 5.10 (dd, *J* = 4.8, 10.4 Hz, 1H), 7.17–7.30 (m, 4H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.84–7.90 (m, 3H); ^{13}C NMR (100 MHz): δ = 21.69, 27.34, 30.56, 80.09, 127.08, 128.01, 128.08, 128.64, 129.72, 131.14, 133.59, 134.23, 142.86, 144.89, 190.48; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm. t_R = 37.0 min (major), 39.2 min (minor).

4.3.14. 2-Oxocyclohexyl 4-methylbenzenesulfonate 32

Colorless solid, mp: 72–74 °C; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.64–1.73 (m, 2H), 1.85–1.98 (m, 3H), 2.30–2.34 (m, 2H), 2.44 (s, 3H), 2.52–2.56 (m, 1H), 4.88–4.92 (dd, *J* = 6.0, 10.8 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 2H), 7.83 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz): δ = 21.62, 23.08, 26.83, 34.52, 40.53, 81.79, 127.83, 129.67, 133.52, 144.86, 202.74; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 220 nm, t_R = 35.0 min (minor), 43.1 min (major).

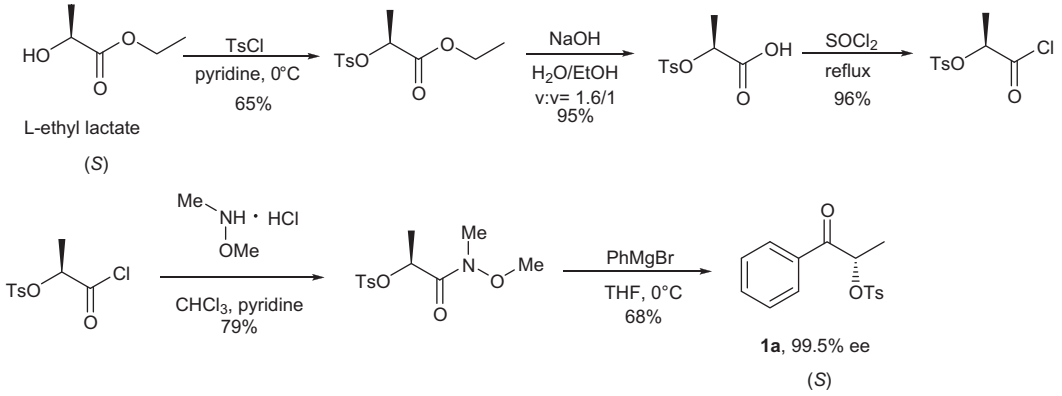
4.3.15. 1-Cyclohexyl-1-oxopropan-2-yl 4-methylbenzenesulfonate 33

Colorless solid, mp: 74–75 °C; $[\alpha]_D^{25} = -7.75$ (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 1.15–1.31 (m, 8H), 1.56–1.68 (m, 5H), 2.38 (s, 3H), 2.59–2.60 (m, 1H), 4.85–4.90 (m, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.72–7.75 (m, 2H); ^{13}C NMR (100 MHz): δ = 17.70, 21.66, 25.30, 25.52, 25.60, 27.86, 28.64, 46.03, 79.57, 127.85, 129.91, 133.51, 145.16, 209.09; IR (KBr): 2932, 2856, 1718, 1598, 1450, 1368, 1190, 1178, 1097, 1015, 935, 914, 865, 826, 817, 790, 666, 567, 554 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{16}H_{22}O_4SNa$ $[M+Na]^+$: 333.1131, found: 333.1132; HPLC conditions: Chiracel AD column, hexane/2-propanol, 90:10, 0.6 mL/min, 254 nm, t_R = 13.9 min (minor), 14.7 min (major).

4.3.16. 4,4-Dimethyl-3-oxopentan-2-yl 4-methylbenzenesulfonate 34

Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 9H), 1.40 (d, *J* = 6.6 Hz, 3H), 2.44 (s, 3H), 5.42 (q, *J* = 6.6 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz): δ = 18.75, 21.62, 26.36, 43.74, 75.05, 127.84, 129.76, 133.86, 144.93, 209.36; IR (KBr): 2987, 2961, 2937, 1928, 1727, 1656, 1482, 1455, 1380, 1353, 1308, 1291, 1189, 1176, 1152, 989, 922, 819, 740, 665, 553, 528 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{24}O_4SN$ $[M+NH_4]^+$: 302.1421, found: 302.1421; HPLC conditions: Chiracel AD column, hexane/2-propanol, 97:3, 0.5 mL/min, 220 nm; t_R = 24.4 min (minor), 25.4 min (major).

4.4. Determination of the absolute configuration of 1a



The absolute configuration of **1a** was determined by an independent synthesis from (*S*)-L-lactic acid. After five steps, (*S*)-**1a** was obtained with 99.5% ee, determined by HPLC. According to the retention time in HPLC, it was confirmed that in our system the excess enantiomer of **1a** had an (*S*)-configuration.

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