Synthesis of Chiral 2-Aroyl-1-tetralols: Asymmetric Transfer Hydrgenation of 2-Aroyl-1-tetralones via Dynamic Kinetic Resolution

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The dynamic kinetic resolution of 2-aroyl-1-tetralones was achieved via asymmetric transfer hydrogenation using (*S*,*S*)-RuCl(*p*-cymene)TsDPEN (TsDPEN = *N*-(tosyl)-1,2-diphenylethylenediamine) in formic acid/triethylamine (5∶2, molar ratio), afforded the desired products in good yields (up to 85%) with diastereomeric ratio up to >99∶1 and high enantiomeric excesses (up to >99%). The absolute configuration of major the product was confirmed by X-ray crystal structure analysis.

Keywords dynamic kinetic resolution, asymmetric transfer hydrogenation, 2-aroyl-1-tetralones, enantioselectivity, chiral

Introduction

Dynamic kinetic resolution (DKR) has become a powerful method to prepare enantiomerically enriched compounds in high yields that overcomes the limitation of classic kinetic resolution.[1] Asymmetric transfer hydrogenation (ATH) is also proved to be a convenient tool for developing new chrial center by reduction of prochiral ketones or imines.

In 1999, Noyori and co-workers reported a highly enantio- and diastereoselective preparation of 1,2-diol by ATH of the benzil, in which the benzoin intermediate with a chirally labile stereogenic center is converted to one major stereoisomer, via dynamic kinetic resolution.[2] Since then, increasing attention has been paid to the DKR via ATH reaction using the classic Noyori's chiral catalyst [RuCl(*p*-cymene)]TsDPEN in the presence of formic acid and triethylamine. For example, Lassaletta and co-workers reported the first DKR process involving transfer hydrogenation of α-branched ketimines,[3] then they extended the scope of the methodology to cyclic β-ketoesters,[4] and cyclic α-branched ketones,[5] providing the corresponding chiral products in excellent stereoselectivities; Wills and co-workers reported transfer hydrogenation of 1-aryl-substituted cyclic ketones;[6] we also reported the DKR of α-sulfonylaldehydes[7] and β-keto sulfones.[8] In order to improve the performance of catalytic system, some research groups investigated the effects of the modification of the diamine ligand by introducing electron-withdrawing aryl sulfonyl groups and some interesting results were observed. Excellent examples include reduction of β-keto-α-amino esters[9] and β-ketoamides[10] using modified Noyori's chiral catalyst.

The enantiomerically pure chiral hydroxy carbonyl compounds and their derivatives are of very high importance as intermediates for the synthesis of many natural products and drugs.[11] Asymmetric catalytic aldol reactions[12] and Mukaiyama type-aldol reactions[13] are recognized as the most efficient and convenient methods to obtain the chiral β-hydroxy carbonyl compounds. Besides, Krische and Baba groups independently reported the synthesis of hydroxyl cyclic ketones by enone-selective reduction using $Co(dpm)_2$ (dpm = dipivaloylmethane) and di-*n*-butyliodotin hydride (*n*-Bu_2SnIH) catalytic system, whose substrates were limited to bearing both enone and formyl moieties.[14,15] Herein, we report a highly regio-, enantio- and diastereoselective synthesis of 2-aroyl-1-tetralols from the corresponding 2-aroyl-1-tetralones via asymmetric catalytic transfer hydrogenation. During the reaction cause, as one enantiomer of the substrate was reduced preferably, the excess of the other enantiomer of the substrate racemized rapidly, furnishing a DKR process, which could serve as an efficient approach to the chiral 2-aroyl-1-tetralols. To the best of our knowledge, no efficient and highly stereoselective synthesis of 2-aroyl-1-tetralols was reported before, although there are a few papers that are involved with the preparation of optically active 2-acetyl-1-tetralol or 2-benzoyl-1-tetralol.[16]

Results and discussion

The starting materials were synthesized in moderate

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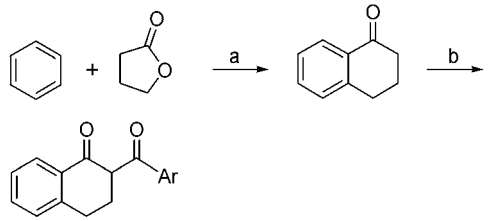
yields by the method shown in Scheme 1.[17]

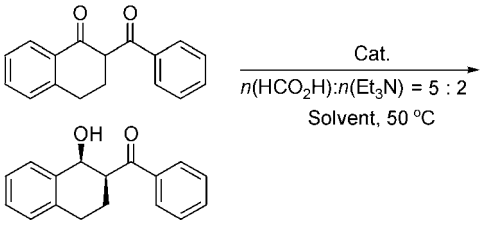
Scheme 1 Synthesis of substrates



Reagents and conditions: (a) $AlCl_3$, reflux; (b) NaH, THF, ArCOOMe, 50 ℃

Initially, classic Noyori's chiral catalyst [RuCl(*p*-cymene)]TsDPEN was chosen as the catalyst for the reaction in DMF, at 50 ℃, 2-benzoyl-3,4-dihydronaphthalen-1(2*H*)-one was chosen as the model substrate. Fortunately, the reaction completed within 12 h, and the product was obtained with 99∶1 *dr* and 98% *ee*. Encouraged by these excellent results, we continued to investigate the influence of solvents on the reaction (Table 1).

Table 1 Influence of the solvents on the DKR of **1a**[a]



Cat. = (*S*,*S*)-RuCl[*N*-(tosyl)-1,2-diphenylenediamine](*p*-cymene)

Entry	Solvent	S/C	Yield[b]/%	*dr*[c]	*ee*[c]/% (major)
1	DMF	40	67	99∶1	98
2	Toluene	40	70	98∶2	97
3	CH_3OH	40	50	94∶6	91
4	DMSO	40	73	95∶5	93
5	CH_3CN	40	65	96∶4	96
6	$CHCl_3$	40	75	98∶2	98
7	EtOAc	40	65	99∶1	99
8	Dioxane	40	78	99∶1	99

[a] All the reactions were processed under argon at 50 ℃ for 12 h. [b] Isolated yield. [c] The enantiomeric excess and diastereomeric ratio were determined by chiral HPLC analysis of the corresponding products on a chiralcel OD-H column.

As can be seen from Table 1, various solvents have little effect on the yield, diastereo- and enantioselectivity. Dioxane was the best solvent, and gave the product in up to 78% yield, 99∶1 *dr* and 99% *ee* (Table 1, Entry 8). So we chose dioxane as the solvent to investigate the influence of the catalyst/substrate ratio on the reaction. The results are listed in Table 2. The diastereo- and enantioselectivity of the transformation was only marginally influenced by the catalyst/substrate ratio. However, longer reaction time was necessary at lower catalyst loading (Table 2, Entries 3 and 4).

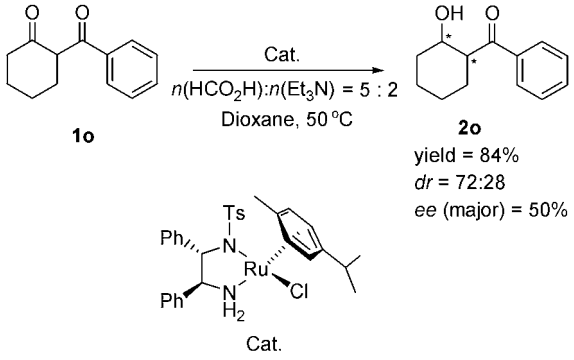
Table 2 Influence of the catalyst/substrate ratio on the DKR of **1a**

Entry	S/C	*t*/h	Yield[a]/%	*dr*[b]	*ee*[b]/% (major)
1	20	14	62	99∶1	99
2	40	12	78	99∶1	99
3	60	24	65	98∶2	98
4	80	24	63	98∶2	98

[a] Isolated yield. [b] The enantiomeric excess and diastereomeric ratio were determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column.

We decided to screen a series of substrates to evaluate the scope of the reaction. The reaction was performed at a scale of 0.5 mmol of substrate, using 0.0125 mmol of catalyst, in dioxane, at 50 ℃. As shown by the results summarized in Table 3, good yield and excellent *dr* and *ee* could be obtained with various Ar, except when Ar is an *ortho*-substituted phenyl group (Table 3, Entries 8 and 9). When Ar is a phenyl group substituted by an electron-donating group at *para*- or *meta*-position, the results were found slightly better than that of electron-withdrawing substituted Ar (Table 3, Entries 2, 3, 10, 11 and Entries 4—7). Moreover, when Ar is naphthalene-1- or 2-yl, or thiophen-2-yl, the reaction also gave the corresponding products with good to excellent diastereo- and enantioselectivities (Table 3, Entries 12—14).

We then examined the DKR of **1o** under the same reaction conditions (Eq. 1). The desired product was obtained in 84% yield. However, to our disappointment, only 72∶28 *dr* and 50% *ee* (major) were achieved. According to the results, we deduced that the steric effects and the rigidity of the fused ring system may play a very important role in this kind of reactions.



(1)

The absolute configuration of product **2e** (Table 3, Entry 5) was confirmed to be (1*S*, 2*S*) by X-ray analysis (Figure 1). The absolute configurations of products **2a**—**2d**, **2f**—**2g** and **2j**—**2n** were assigned as (1*S*, 2*S*) by analogy.

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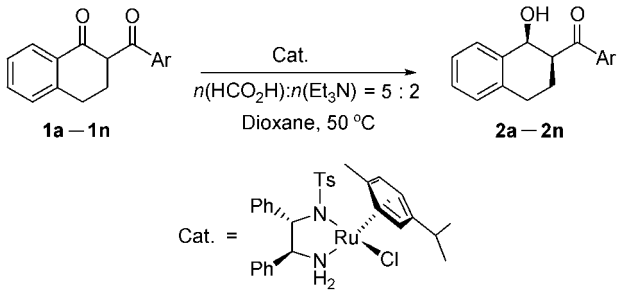
Table 3 Results of DKR of **1a**—**1n** at 50 ℃ in dioxane



a: Ar=C_6H_5; **b**: Ar=*p*-MeC_6H_4; **c**: Ar=*m*-MeC_6H_4; d: Ar=*p*-$ClCC_6H_4$; **e**: Ar=*p*-BrC_6H_4; **f**: Ar=*p*-IC_6H_4; **g**: Ar=*p*-FC_6H_4; **h**: Ar=*o*-ClC_6H_4; **i**: Ar=2,4-$Cl_2C_6H_3$; **j**: Ar=*p*-$MeOC_6H_4$; **k**: Ar=*m*-$MeOC_6H_4$; **l**: Ar=Naphthalen-1-yl; **m**: Ar=Naphthalen-2-yl; **n**: Ar=Thiophen-2-yl

Entry	Ar	Product	Yield[a]/%	*dr*[b]	*ee*[b]/% (major)	Abs config (major)
1	C_6H_5	**2a**	78	>99∶1	99	*S*,*S*
2	*p*-MeC_6H_4	**2b**	85	>99∶1	99	*S*,*S*
3	*m*-MeC_6H_4	**2c**	78	>99∶1	99	*S*,*S*
4	*p*-ClC_6H_4	**2d**	72	99∶1	93	*S*,*S*
5	*p*-BrC_6H_4	**2e**	70	95∶5	99	*S*,*S*
6	*p*-IC_6H_4	**2f**	72	98∶2	>99	*S*,*S*
7	*p*-FC_6H_4	**2g**	67	>99∶1	99	*S*,*S*
8	*o*-ClC_6H_4	**2h**	<5	nd[c]	nd[c]	—
9	2,4-$Cl_2C_6H_3$	**2i**	<5	nd[c]	nd[c]	—
10	*p*-$MeOC_6H_4$	**2j**	82	>99∶1	>99	*S*,*S*
11	*m*-$MeOC_6H_4$	**2k**	80	99∶1	99	*S*,*S*
12	Naphthalen-1-yl	**2l**	75	94∶6	>99	*S*,*S*
13	Naphthalen-2-yl	**2m**	85	99∶1	99	*S*,*S*
14	Thiophen-2-yl	**2n**	70	92∶8	99	*S*,*S*

[a] Isolated yield. [b] The enantiomeric excess and diastereomeric ratio were determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column or Chiralcel AD-H column. [c] Not determined.

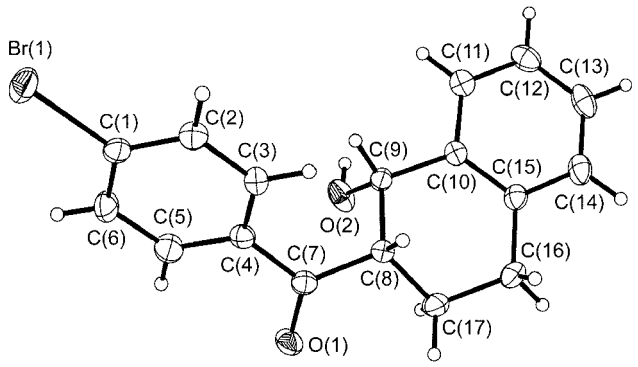


Figure 1 X-ray structure of the major diastereomer of **2e**.

In conclusion, a convenient and highly stereoselective approach to chiral 2-aroyl-1-tetralols has been developed. The ATH of the corresponding 2-aroyl-1-tetralone by using Noyori's RuCl(*p*-cymene)TsDPEN catalyst and HCOOH-Et_3N (*n*∶*n*=5∶2) as the hydrogen source proceeds via DKR to selectively afford the desired optically active 2-aroyl-1-tetralols in good yields (up to 85%) and the reaction is highly stereoselective (up to >99% *ee*, >99∶1 *dr*).

Experimental

All manipulations were carried out under argon. The reactions were monitored by TLC. NMR spectra were recorded in $CDCl_3$ on a Varian-Inova-400 or Varian System-300 NMR spectrometer. The enantiomeric excess (*ee*) and diastereomeric ratio (*dr*) were determined by HPLC analysis using a Chiralpak AD-H or a Chiralcel OD-H column with hexane-*i*-PrOH as the solvent. High resolution mass spectrometry (HRMS) was determided by Micromass TOF-MS or Micromass LC-MS; Optical rotations were measured on an Autopol IV automatic polarimeter. IR spectra were recorded by Varian 1000 FT-IR Spectrometer.

General procedure of asymmetric transfer hydrogenation

A suspension of $[RuCl_2(p\text{-cymene})]_2$ (3.83 mg, 0.00625 mmol) and (1*S*, 2*S*)-TsDPEN (4.58 mg, 0.0125 mmol) in dioxane (0.5 mL) was degassed three times, and then stirred at room temperature for 2 h. HCOOH-Et_3N (*n*∶*n*=5∶2, 0.2 mL) and substrate **1** (0.5 mmol) were added. The reaction was stirred at 50 ℃ until completion according to TLC detection. Water

(15.0 mL) was added to the reaction, the mixture was then extracted with EtOAc (10 mL×3), dried over anhydrous sodium sulfate and concentrated under vacuum. After removal of the solvent, the residue was purified by column chromatography on silica gel (eluent: petroleum ether/AcOEt = 20/1) to give the desired product, which was then analysed by IR, ^{1}H NMR, ^{13}C NMR, HRMS, and HPLC spectroscopy.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](phenyl)methanone (2a) White solid, 78% yield; m.p. 76—78 ℃; $[\alpha]_D^{25}$ −161.4 (*c* 1.01, acetone); *dr* > 99 ∶ 1, *ee* = 99% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (10 ∶ 90); t_1=10.949 min, t_2=11.930 min, t_3=13.536 min]; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 7.97 (d, *J*=7.4 Hz, 2H), 7.62 (t, *J*=7.3 Hz, 1H), 7.51 (t, *J*=7.5 Hz, 2H), 7.43—7.35 (m, 1H), 7.31—7.15 (m, 3H), 5.11 (s, 1H), 3.76—3.62 (m, 2H), 3.08—2.87 (m, 2H), 2.48—2.30 (m, 1H), 2.14—2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 204.35, 137.13, 136.20, 136.03, 133.73, 130.11, 129.21, 129.06, 128.55, 128.45, 126.56, 68.63, 47.00, 28.78, 21.07; IR (KBr) *v*: 3464, 2938, 2873, 1681, 1597, 1487, 1450 cm^{-1}. HRMS (EI) calcd for $[C_{17}H_{16}O_2]^+$ 252.1150, found 252.1149.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](*p*-tolyl)methanone (2b) White solid, 85% yield; m.p. 131—133 ℃; $[\alpha]_D^{25}$ −148.7 (*c* 1.02, acetone); *dr*>99∶1, *ee*=99% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (10∶90); t_1=11.461 min, t_2=12.104 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.88 (d, *J*=8.1 Hz, 2H), 7.39 (d, *J*=7.1 Hz, 1H), 7.30 (d, *J*=8.0 Hz, 2H), 7.28—7.20 (m, 2H), 7.18 (d, *J*=7.4 Hz, 1H), 5.10 (s, 1H), 3.83 (d, *J*=3.7 Hz, 1H), 3.71—3.65 (m, 1H), 3.05—2.90 (m, 2H), 2.47—2.32 (m, 4H), 2.10—2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 204.07, 144.66, 137.18, 136.19, 133.46, 130.09, 129.71, 129.16, 128.66, 128.36, 126.48, 68.66, 46.72, 28.77, 21.88, 21.20; IR (KBr) *v*: 3457, 2946, 2887, 1672, 1605, 1493, 1450, 1397 cm^{-1}. HRMS (ESI) calcd for $C_{18}H_{18}O_2Na$ $[M+Na]^+$ 289.1204, found 289.1208.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](*m*-tolyl)methanone (2c) Colorless oil, 78% yield; $[\alpha]_D^{25}$ −153.7 (*c* 1.00, acetone); *dr* > 99 ∶ 1, *ee* = 99% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (5 ∶ 95); t_1=19.732 min, t_2=23.604 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.82—7.72 (m, 2H), 7.46—7.35 (m, 3H), 7.31—7.15 (m, 3H), 5.10 (s, 1H), 3.74—3.65 (m, 2H), 3.06—2.89 (m, 2H), 2.48—2.31 (m, 4H), 2.12—2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 204.49, 138.84, 137.12, 136.19, 136.07, 134.42, 130.06, 129.14, 128.98, 128.82, 128.35, 126.45, 125.68, 68.59, 46.95, 28.70, 21.57, 20.93; IR (KBr) *v*: 3479, 2922, 1682, 1602, 1585, 1491, 1381 cm^{-1}. HRMS (ESI) calcd for $C_{18}H_{18}O_2Na$ $[M+Na]^+$ 289.1204, found 289.1208.

(4-Chlorophenyl)((1*S*,2*S*)-1-hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanone (2d) White solid, 72% yield; m.p. 142—144 ℃; $[\alpha]_D^{25}$ −168.8 (*c* 1.02, acetone); *dr*=99∶1, *ee*=93% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (5∶95); t_1=27.041 min, t_2=35.092 min, t_3=40.695 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.91 (d, *J*=8.4 Hz, 2H), 7.48 (d, *J*=8.3 Hz, 2H), 7.42—7.36 (m, 1H), 7.31—7.21 (m, 2H), 7.18 (d, *J*=7.1 Hz, 1H), 5.09 (s, 1H), 3.65 (dt, *J*=11.8, 2.7 Hz, 1H), 3.47 (d, *J*=4.2 Hz, 1H), 3.05—2.89 (m, 2H), 2.43—2.31 (m, 1H), 2.11—2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 202.79, 140.13, 136.99, 136.13, 134.40, 130.06, 129.95, 129.39, 129.22, 128.54, 126.63, 68.62, 47.22, 28.68, 20.88; IR (KBr) *v*: 3453, 2933, 2875, 1668, 1584, 1486, 1455 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{15}{}^{35}ClO_2Na$ $[M+Na]^+$ 309.0658, found 309.0665.

(4-Bromophenyl)((1*S*,2*S*)-1-hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl)methanone (2e) White solid, 70% yield; m.p. 144—146 ℃; $[\alpha]_D^{25}$ −159.0 (*c* 1.05, acetone); *dr*=95∶5, *ee*=99% [HPLC; Chiralpak OD-H, *i*-PrOH–hexane (10∶90); t_1=12.800 min, t_2=13.460 min, t_3=18.164 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.83 (d, *J*=8.5 Hz, 2H), 7.65 (d, *J*=8.6 Hz, 2H), 7.38 (d, *J*=7.3 Hz, 1H), 7.31—7.09 (m, 3H), 5.09 (s, 1H), 3.64 (dt, *J*=11.8, 2.7 Hz, 1H), 3.44 (d, *J*=4.3 Hz, 1H), 3.05—2.85 (m, 2H), 2.44—2.29 (m, 1H), 2.11—1.98 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 202.82, 136.97, 136.10, 134.81, 132.31, 130.01, 129.99, 129.16, 128.76, 128.47, 126.56, 68.56, 47.23, 28.61, 20.74; IR (KBr) *v*: 3450, 2968, 2932, 2874, 1668, 1582, 1491, 1455 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{15}{}^{79}BrO_2Na$ $[M+Na]^+$ 353.0153, found 353.0168.

X-ray crystal data for product 2e

Careful evaporation of a solution of **2e** in EtOAc-hexane (1∶5) gave a single crystal suitable for crystallographic analysis. Selective crystal structure data: Empirical formula $C_{17}H_{15}BrO_2$; formula weight 331.20; temperature 223(2) K; wavelength 0.71075 Å; crystal system, orthorhombic; space group, $P2_12_12_1$; unit cell dimensions, a=9.8770(11) Å, b=12.0136(14) Å, c=12.1370(13) Å, $\alpha=\beta=\gamma=90°$; V=1440.2(3) Å^3; Z=4; D_c=1.528 Mg/m^3; absorption coefficient 2.852 mm^{-1}; $F(000)$=672; crystal size 0.70 mm×0.55 mm×0.40 mm. θ range, 3.15° to 27.49°; limiting indices, $-12\leqslant h\leqslant 12$, $-10\leqslant k\leqslant 15$, $-14\leqslant l\leqslant 14$; reflections collected/unique, 8247/3131; (R_{int}=0.0320). Final R indices [$I>2\sigma(I)$], R_1=0.0258, wR_2=0.0614; R indices (all data), R_1=0.0363, wR_2=0.0640; absolute structure parameter −0.007(9); largest diff. peak and hole 0.243 and −0.430 e•Å^{-3}.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](4-iodophenyl)methanone (2f) Yield 72%; m.p. 105—107 ℃; $[\alpha]_D^{25}$ −144.3 (*c* 1.03, acetone); *dr* = 98 ∶ 2, *ee* > 99% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (10 ∶ 90); t_1=15.454 min, t_2=24.920 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.87 (d, *J*=8.6 Hz, 2H), 7.67 (d, *J*=8.6 Hz, 2H), 7.41—7.35 (m, 1H), 7.29—7.22 (m, 2H), 7.17 (d, *J*=7.6 Hz, 1H), 5.09 (s, 1H), 3.63 (dt, *J*=11.8, 2.8 Hz, 1H), 3.43 (d, *J*=4.2 Hz, 1H), 3.05—2.87 (m, 2H), 2.43—2.28 (m, 1H), 2.11—2.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 203.23,

138.36, 136.99, 136.12, 135.36, 130.04, 129.87, 129.20, 128.52, 126.62, 101.66, 68.59, 47.19, 28.66, 20.81; IR (KBr) *v*: 3447, 2929, 2872, 1668, 1578, 1490 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{15}IO_2Na$ $[M + Na]^+$ 401.0014, found 401.0034.

(4-Fluorophenyl)[(1*S*,2*S*)-1-hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl]methanone (2g) Colorless oil, yield 67%; $[\alpha]_D^{25}$ −157.5 (*c* 0.57, acetone); *dr*＞99∶1, *ee* = 99% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (5∶95); t_1=29.352 min, t_2=35.228 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 8.04—7.97 (m, 2H), 7.42—7.36 (m, 1H), 7.31—7.13 (m, 5H), 5.09 (s, 1H), 3.66 (dt, *J*= 11.9, 2.8 Hz, 1H), 3.58 (d, *J*=3.8 Hz, 1H), 3.06—2.87 (m, 2H), 2.45—2.30 (m, 1H), 2.10—2.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 202.41, 166.07 (d, $^1J_{CF}$= 256.2 Hz), 137.02, 136.11, 132.44 (d, $^4J_{CF}$=3.3 Hz), 131.19 (d, $^3J_{CF}$ = 10.0 Hz), 130.04, 129.16, 128.45, 126.55, 116.15 (d, $^2J_{CF}$=22.3 Hz), 68.62, 47.06, 28.65, 20.91; IR (KBr) *v*: 3469, 2926, 1679, 1597, 1501, 1456 cm^{-1}. HRMS (ESI) calcd for $C_{17}H_{15}FO_2Na$ $[M+Na]^+$ 293.0954; found 293.0973.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](4-methoxyphenyl)methanone (2j) Colorless oil, yield 82%; $[\alpha]_D^{25}$ −130.9 (*c* 1.02, acetone); *dr*＞99∶1, *ee*＞99% [HPLC; Chiralpak AD-H, *i*-PrOH-hexane (10∶90); t_1=45.293 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.97 (d, *J*=8.3 Hz, 2H), 7.40 (d, *J*=7.0 Hz, 1H), 7.27—7.20 (m, 2H), 7.18 (d, *J*=7.5 Hz, 1H), 6.98 (d, *J*=8.2 Hz, 2H), 5.09 (s, 1H), 4.01 (d, *J*= 2.6 Hz, 1H), 3.89 (s, 3H), 3.66 (d, *J*=12.0 Hz, 1H), 3.07—2.90 (m, 2H), 2.48—2.35 (m, 1H), 2.09—2.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 202.76, 163.85, 137.08, 136.06, 130.74, 129.97, 128.99, 128.67, 128.15, 126.25, 114.02, 68.54, 55.55, 46.22, 28.63, 21.11; IR (KBr) *v*: 3472, 2935, 2840, 1673, 1600, 1510, 1457 cm^{-1}. HRMS (ESI) calcd for $C_{18}H_{18}O_3Na$ $[M+Na]^+$ 305.1154, found 305.1180.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](3-methoxyphenyl)methanone (2k) Colorless oil, yield 80%; $[\alpha]_D^{25}$ −135.4 (*c* 1.0, acetone); *dr*= 99∶1, *ee*=99% [HPLC; Chiralpak AD-H, *i*-PrOH-hexane (10∶90); t_1=22.550 min, t_2=25.462 min, t_3= 33.684 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.57—7.46 (m, 2H), 7.44—7.35 (m, 2H), 7.30—7.20 (m, 2H), 7.20—7.11 (m, 2H), 5.10 (s, 1H), 3.87 (s, 3H), 3.68 (dt, *J* = 11.9, 2.8 Hz, 1H), 3.61 (d, *J* = 3.9 Hz, 1H), 3.05—2.88 (m, 2H), 2.45—2.31 (m, 1H), 2.12—2.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 203.84, 160.11, 137.40, 137.10, 136.14, 130.00, 129.88, 129.09, 128.31, 126.42, 120.92, 119.92, 112.83, 68.60, 55.54, 47.18, 28.64, 20.88; IR (KBr) *v*: 3482, 2938, 2836, 1581, 1488, 1455, 1377 cm^{-1}. HRMS (EI) calcd for $[C_{18}H_{18}O_3]^+$ 282.1256, found 282.1259.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](naphthalen-1-yl)methanone (2l) Brown oil, yield 75%; $[\alpha]_D^{25}$ −99.5 (*c* 1.05, acetone); *dr*=94∶6, *ee*＞99% [HPLC; Chiralpak AD-H, *i*-PrOH-hexane (10∶90); t_1=19.106 min, t_2=23.410 min, t_3=34.918 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 8.40 (d, *J*=8.3 Hz, 1H), 8.01 (d, *J*=8.2 Hz, 1H), 7.90 (d, *J*=7.5 Hz, 1H), 7.80 (d, *J*=7.1 Hz, 1H), 7.65—7.46 (m, 3H), 7.41—7.13 (m, 4H), 5.11 (d, *J*=2.0 Hz, 1H), 3.71 (dt, *J*=11.8, 2.7 Hz, 1H), 3.16 (s, 1H), 3.06—2.95 (m, 1H), 2.95—2.80 (m, 1H), 2.43—2.27 (m, 1H), 2.19—2.06 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 207.61, 137.24, 136.31, 135.94, 134.15, 132.43, 130.52, 129.91, 129.10, 128.51, 128.32, 127.93, 126.71, 126.47, 126.42, 125.81, 124.43, 68.68, 50.60, 28.69, 19.95; IR (KBr) *v*: 3480, 3060, 2930, 1689, 1508, 1456 cm^{-1}. HRMS (EI) calcd for $[C_{21}H_{18}O_2]^+$ 302.1307, found 302.1311.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](naphthalen-2-yl)methanone (2m) White solid, 85% yield; m.p. 124—126 ℃; $[\alpha]_D^{25}$ −220.2 (*c* 1.01, acetone); *dr*=99∶1, *ee*=99% [HPLC; Chiralpak AD-H, *i*-PrOH-hexane (10∶90); t_1=26.777 min, t_2= 33.584 min t_3=45.837 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 8.49 (s, 1H), 8.03 (dd, *J*=8.6, 1.5 Hz, 1H), 8.00— 7.88 (m, 3H), 7.68—7.53 (m, 2H), 7.41 (d, *J*= 6.7 Hz, 1H), 7.33—7.18 (m, 3H), 5.17 (s, 1H), 3.88 (dt, *J* = 11.7, 2.7 Hz, 1H), 3.70 (d, *J* = 4.0 Hz, 1H), 3.10—2.96 (m, 2H), 2.53—2.39 (m, 1H), 2.19—2.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 204.24, 137.19, 136.26, 135.92, 133.38, 132.68, 130.23, 130.12, 129.81, 129.24, 129.00, 128.93, 128.47, 128.00, 127.14, 126.56, 124.18, 68.78, 47.06, 28.78, 21.13; IR (KBr) *v*: 3456, 2956, 2873, 1672, 1626, 1493, 1454 cm^{-1}. HRMS (EI) calcd for $[C_{21}H_{18}O_2]^+$ 302.1307, found 302.1305.

[(1*S*,2*S*)-1-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl](thiophen-2-yl)methanone (2n) Brown oil, 70% yield; $[\alpha]_D^{25}$ −131.6 (*c* 1.05, acetone); *dr*=92∶8, *ee* = 99% [HPLC; Chiralpak AD-H, *i*-PrOH-hexane (15∶85); t_1=16.446 min, t_2=23.168 min, t_3=24.404 min]; ^{1}H NMR ($CDCl_3$, 400 MHz) *δ*: 7.78 (d, *J*=3.8 Hz, 1H), 7.71 (d, *J*=4.9 Hz, 1H), 7.43—7.35 (m, 1H), 7.32—7.10 (m, 4H), 5.12 (d, *J*=1.9 Hz, 1H), 3.76 (s, 1H), 3.55 (dt, *J*=12.1, 2.7 Hz, 1H), 3.10—2.85 (m, 2H), 2.56—2.41 (m, 1H), 2.15—2.04 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) *δ*: 196.83, 143.11, 136.78, 136.02, 134.64, 132.56, 130.04, 129.10, 128.50, 128.36, 126.41, 68.70, 48.36, 28.62, 21.28; IR (KBr) *v*: 3482, 2944, 2888, 1656, 1515, 1490, 1454 cm^{-1}. HRMS (EI) calcd for $[C_{15}H_{14}O_2S]^+$ 258.0715, found 258.0705.

(2-Hydroxycyclohexyl)(phenyl)methanone (2o) White solid, 84% yield; m.p. 74—76 ℃; $[\alpha]_D^{25}$ +43.6 (*c* 1.00, acetone); *dr* = 72 ∶ 28, *ee* (major) = 50% [HPLC; Chiralpak OD-H, *i*-PrOH-hexane (5∶95); t_1= 6.816 min, t_2=8.360 min, t_3=9.467 min, t_4=10.217 min]; ^{1}H NMR (major) ($CDCl_3$, 400 MHz) *δ*: 7.97 (d, *J*=7.3 Hz, 2H), 7.57 (t, *J*=7.4 Hz, 1H), 7.48 (t, *J*=7.7 Hz, 2H), 4.09 (td, *J*=10.1, 4.2 Hz, 1H), 3.31—3.24 (m, 1H), 2.38 (s, 1H), 2.14—1.69 (m, 4H), 1.50—1.24 (m, 4H); ^{13}C NMR (major) ($CDCl_3$, 101 MHz) *δ*: 203.95, 136.73, 133.32, 128.81, 128.60, 70.94, 53.98, 33.76, 29.85, 25.69, 24.77; IR (major) (KBr) *v*: 3388, 2929, 2857, 1673, 1597, 1446 cm^{-1}; HRMS (major) (EI) calcd for $[C_{13}H_{16}O_2]^+$ 204.1150, found 204.1158.

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