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ansa-Ruthenium(II) Complexes of R_2NSO_2DPEN-$(CH_2)_n(\eta^6$-Aryl) Conjugate Ligands for Asymmetric Transfer Hydrogenation of Aryl Ketones

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Abstract: New 3rd generation designer *ansa*-ruthenium(II) complexes featuring *N*,*C*-alkylene-tethered *N*,*N*-dialkylsulfamoyl-DPEN/η^6-arene ligands, exhibited good catalytic performance in the asymmetric transfer hydrogenation (ATH) of various classes of (het)aryl ketones in formic acid/triethylamine mixture. In particular, benzo-fused cyclic ketones furnished 98 to >99.9% *ee* using a low catalyst loading.

Keywords: alcohols; asymmetric catalysis; N ligands; reduction; ruthenium

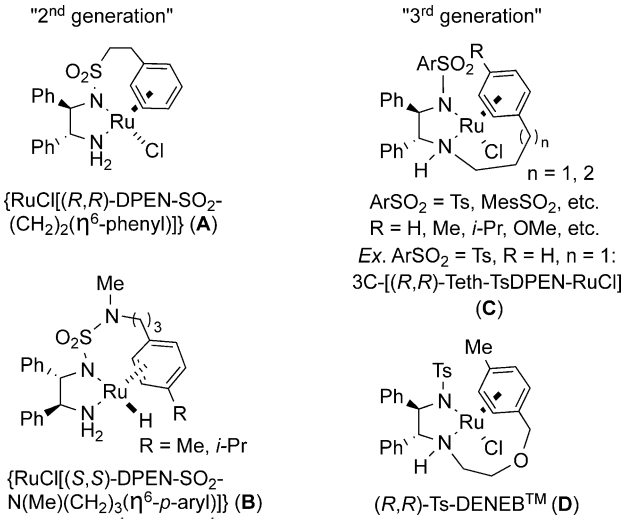


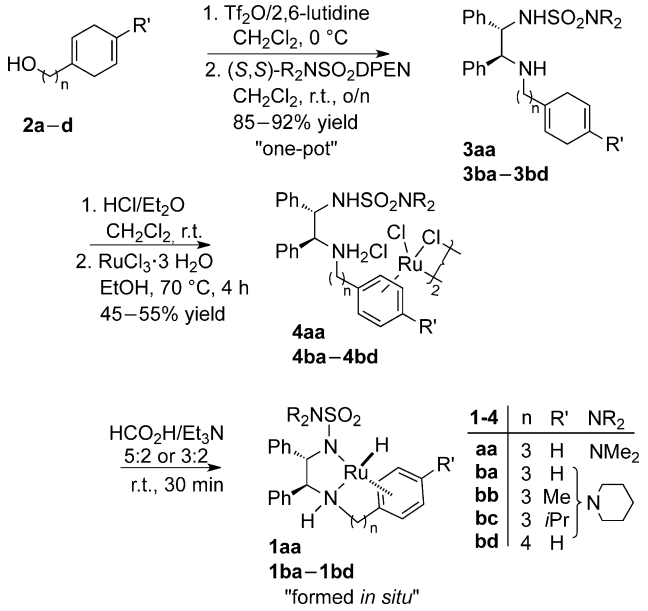
Figure 1. 2nd and 3rd generation DPEN-based Ru(II) complexes efficient in ATH.

In asymmetric transfer hydrogenation (ATH) of aryl ketones using HCO_2H/Et_3N mixture, *ansa*-ruthenium(II)-type complexes with intra-covalently tethered diamine and η^6-arene ligand units (complexes **A**–**D** of Figure 1) have displayed improved turnover rates over the untethered version.[1,2] In fact, 2nd and 3rd generation designed complexes wherein the η^6-arene ligand is linked to either SO_2DPEN terminal (available in both enantiomeric forms, DPEN = *trans*-1,2-diphenylethylenediamine) demonstrated enhanced longevity of the catalytic species. This aspect is economically attractive promoting their industrial implementation for the synthesis of enantioenriched α-substituted arylmethanols.[3]

We have recently introduced a 2nd generation-type {RuCl[(*S*,*S*)-DPEN-$SO_2N(Me)(CH_2)_n(\eta^6$-aryl)]} complex series (complex **B**)[4] wherein a *para*-substituted η^6-phenyl (e.g., *p*-Tol, *p*-*i*-Pr-C_6H_4) tethered to DPEN with -$SO_2N(Me)(CH_2)_n$- (n = 2 or 3) exhibited an exceptionally high efficiency in the ATH of aryl ketones.[2i,k] Thus, using substrate-to-catalyst ratios (S/Cs) of 200 to 1000, 1-naphthyl ketones, α-tetralone, α-chloroacetophenone, and 1,3-diaryl β-diketones furnished at 40–60 °C in reasonable times the corresponding alcohols in >98% to virtually perfect *ee*s with full conversion. Given the higher activity of the known 3rd generation *ansa*-Ru(II) complexes versus the 2nd generation, we were interested to explore this option using our R_2NSO_2DPEN[5] ligand.

Herein, we present an *ansa*-Ru(II) complex series **1** in which the η^6-arene is alkylene-tethered to R_2NSO_2DPEN from the *N*′-terminal (a "transshifted tether" compared to the 2nd generation version) (Scheme 1), and their ATH results against various types of prostereogenic aryl ketones.

The new homochiral (*S*,*S*)-R_2NSO_2DPEN-$(CH_2)_n(\eta^6$-*p*-aryl)-type combined preligands **3**, wherein the "$(CH_2)_n$" *ansa*-bridge length and the anchored "η^6-aryl" *para* end-substituent have been systematically varied, were prepared by us following an improved

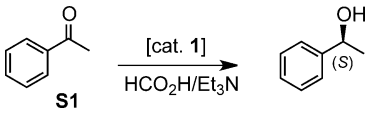


Scheme 1. Preparation of the active *ansa*-Ru(II)-type catalysts **1**.

procedure adapted from the general one introduced by Wills.[2e,6] Thus, the triflates of alcohols **2** were employed to selectively mono-*N*′-alkylate (*S*,*S*)-R_2NSO_2DPEN at room temperature leading to **3** in 85–92% isolated yield. Subsequently, the shelf-stable μ-chlorido Ru(II) dimers **4** were readily obtained in 45–55% yield by heating **3**·HCl with $RuCl_3{\cdot}3H_2O$ in EtOH at 70 °C. Finally, the ATH active *ansa*-Ru(II) catalysts **1** (wherein n = 3 or 4, and aryl = Ph, *p*-Tol, *p*-*i*-Pr-C_6H_4) were conveniently generated *in situ* at room temperature within 30 min from the corresponding dimers **4** in the HCO_2H/Et_3N medium.[7]

The ATH of the test substrate acetophenone (**S1**) using the *ansa*-Ru(II) catalysts **1** (S/C = 1000) was probed under nitrogen atmosphere (with continuous mild sweeping[8]) varying the HCO_2H/Et_3N ratio (5:2 or 3:2) and temperature (40–80 °C) (Table 1). From the start, the Me_2NSO_2-substituted catalyst **1aa** showed a slower reaction rate (an extra 1 h was required for 100% conversion) and afforded a slightly lower *ee* (~1%) compared to the $(CH_2)_5NSO_2$-substituted analogue **1ba**. Complete conversion was reached 8-fold faster with an increase of the temperature from 40 to 80 °C at the expense of a ~2% decrease in *ee*. Interestingly, the enantioselectivity increased marginally with systematic increase in the bulk of the *para*-R′ substituent (95.3% *ee* for H, to 95.5% *ee* for Me, to 96.2% *ee* for *i*-Pr), whereas the reduction rate markedly decreased (entries 5, 9 and 10). Reaction rates of **1ba** (3C tether) and **1bd** (4C tether) using an S/C = 30000 at 60 °C were of the same order (entries 8 and 13). Noteworthy, with prolonged reduction times during these latter tests, 1-phenylethanol (95.1% *ee*) was accompanied with 1-phenylethyl formate (95.1% *ee*, 30% yield by GC) and this was converted back to the alcohol upon $NaBH_4$ reduction. Importantly, employing a HCO_2H/Et_3N of 3:2 proved to be relatively advantageous compared to 5:2 as a modest, yet discernible ~1% increase in *ee* was observed in all runs. The induced *S*-enantioselectivity is in accord with the sense observed with complexes **A**–**D** of Figure 1 implying a similar stereochemical control by the elements of the structural stereoarray. Overall, complex **1ba** appeared to be the optimum choice in this screening.

Table 1. *ansa*-Ru(II) complexes **1** catalyzed ATH of acetophenone (**S1**).[a]



Entry	Cat. **1**	S/C	HCO_2H/Et_3N	*T* [°C]	*t* [h]	Conv. [%]	*ee* [%]
1	**1aa**	1000	5:2	60	5	100	93.4
2	**1aa**	1000	3:2	60	5	100	94.6
3	**1ba**	1000	5:2	60	3.5	100	94.5
4	**1ba**	1000	3:2	40	8	100	96.1
5	**1ba**	1000	3:2	60	3.5	100	95.3
6	**1ba**	1000	3:2	70	1.5	100	94.7
7	**1ba**	1000	3:2	80	1	100	94.3
8	**1ba**	30000	3:2	60	96	83[b]	95.0
9	**1bb**	1000	3:2	60	7	100	95.5
10	**1bc**	1000	3:2	60	8.5	100	96.2
11	**1bd**	1000	5:2	60	3	100	93.6
12	**1bd**	1000	3:2	60	3	100	95.0
13	**1bd**	30000	3:2	60	96	80[b]	94.5

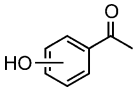
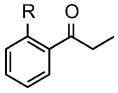
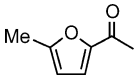
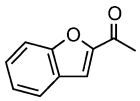
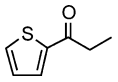
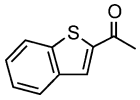
[a] Runs were carried out with acetophenone (1 mmol) in neat HCO_2H/Et_3N (0.5 mL). The *ee*s were determined by chiral GC, for details see the Supporting Information.

[b] 1-Phenylethyl formate (95.1% *ee*, 30% yield) accompanied with 1-phenylethanol.

Based on this initial exploration on acetophenone, the results obtained with complex **1ba** parallel closely those of the 3rd generation-type Ru(II) complexes of the Wills 3C-[Teth-TsDPEN-RuCl] (complex **C**) and the Ikariya Ts-DENEB (complex **D**).[9] Also, an increased activity was noticeable compared to the 2nd generation (complex **B**).

Next, screening at 60 °C on a representative array of acetophenones in HCO_2H/Et_3N 3:2 revealed a useful activity of **1ba** against *o*-, *m*-, or *p*-HO-substituted derivatives (**S2**–**S4**, **S6**) leading from 93.8 to 95.7% *ee* (Table 2).[10] A facile upgrading to 99% *ee* by simple crystallization of the **S4** reduction product was also feasible. In addition, **1bb** catalyzed the reduction of 2-acetylpyridine (**S7**) at 40 °C with 96.9% *ee* within 2 h using an S/C = 100, while a steady decrease in *ee* and longer reaction times resulted from lowering the catalyst loading.

Table 2. *ansa*-Ru(II) complexes **1** catalyzed ATH of various het(aryl) ketones.[a]

Ketone		Cat. **1**	HCO_2H/Et_3N	*T* [°C]	*t* [h]	*ee* [%]
	**S2**: *o*-	**1ba**	3:2	60	2	94.5
	S3: *m*-	**1ba**	3:2	60	5	95.7
	S4: *p*-	**1ba**	3:2	60	10	93.8
	**S5**: R = H	**1ba**	3:2	60	6	93.6
	S6: R = OH	**1ba**	3:2	60	2	93.6
		1bb	3:2	60	3	94.7
	**S7**	**1bb**[b]	3:2	40	2	96.9
		1bb[c]	3:2	40	6	94.2
		1bb	3:2	40	15	93.0
	**S8**	**1aa**	5:2	60	3.5	92.1
		1ba	5:2	40	15	98.3
		1ba	3:2	40	15	97.3
		1ba	5:2	60	3	97.4
		1bb	5:2	60	5	94.1
		1bc	5:2	60	5	97.0
		1bd	5:2	60	3.5	96.9
	**S9**	**1ba**	5:2	40	15	94.0
		1ba	5:2	60	4	91.4
	**S10**	**1ba**	3:2	60	2	95.1
		1bb	5:2	60	3	85.6
		1bb	3:2	60	3	96.9
	**S11**	**1ba**	3:2	40	15	96.8
		1ba	3:2	60	5.5	95.9
		1bb	3:2	60	7	95.2
		1bc	3:2	60	12	95.7
	**S12**	**1ba**	3:2	60	7	95.0
		1bd	3:2	60	9	94.1
	**S13**	**1ba**	3:2	60	3	95.5

[a] Runs were carried out on 1 mmol scale of ketone in neat HCO_2H/Et_3N (0.5 mL) with an S/C = 1000 for the time indicated (100% conversion). Isolated yields after work-up were 1–4% lower. The *ee*s were determined by chiral GC or HPLC. (*S*)-Configured corresponding alcohols were obtained. For details, see the Supporting Information.

[b] S/C = 100.

[c] S/C = 500.

Further on, a set of 2-acetylfurans and 2-acetylthiophenes (**S8**–**S13**) underwent ATH with the catalyst series **1** at 40–60 °C affording *ee*s in the range of 94–98%. Reduction at 60 °C was several times faster than at 40 °C, and the absence of a *p*-substituent on the η^6-aryl of **1** (catalyst **1ba**) was also favorable in these cases.

Finally, the ATH catalyzed by **1** (S/C = 1000) of benzo-fused 5–7-membered cyclic ketones such as 1-indanones (**S14–S19**), α-tetralones (**S20–S24**) and oxygen-, sulfur- or SO_2-containing analogues (4-chromanones **S25**–**S28**, thiochroman-4-one (**S29**) and its 1,1-dioxide **S30**), and 1-benzosuberone (**S31**) was particularly efficient (Table 3; a comprehensive testing was carried out with catalysts **1** but only selected results are presented). These data emphasize the catalyst–substrate structure dependence as a specific catalyst **1** constitutes the optimum match for a given substrate of interest. On top of that, the reaction conditions set needed to be adjusted on a case-by-case basis for a maximized catalysis effect by incremental improvement of enantioselectivity and kinetics. Importantly, operating at 60 °C, the corresponding (*S*)-alcohols were readily formed in excellent *ee*s within few hours.

To the best of our knowledge, these results represent one of the highest enantioselectivities obtained for such ketones *via* reduction and advantageously applying a low catalyst loading.[11,12] In particular, various catalyst systems have been employed for the reduction of α-tetralones with a varying degree of success. Most notably, under ATH conditions in HCO_2H/Et_3N 5:2, Ts-DENEB (complex **D**) and 3C-[Teth-TsDPEN-RuCl] (complex **C**) complexes afforded α-tetralol in >99% *ee* (S/C = 1000, 60 °C, 5 h, 100% conversion)[2g] and 99.8% *ee* (S/C = 500, 40 °C, 5 h, 100% conversion),[2l] respectively. Also, $RuCl_2$[(*S*)-XylBINAP][(*R*)-IPHAN] catalyst (S/C = 3000, 25 °C) led to 99% *ee* (>99% conversion) under 9 atm of H_2.[13]

Notably, post-reduction selective functionalization of the free phenolic OH group (e.g., etherification of the reduction product of **S16**; see Table 3, footnote [b]) further extends the scope of applicability of this transformation.

Demonstrating the practical applicability of this new catalyst system, the ATH of 4-chromanone (**S25**) using **1bd** with an S/C = 30000 and affording (*S*)-4-chromanol in 99.5% *ee* and full conversion within 30 h, is highlighted in Scheme 2.

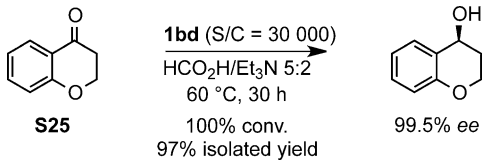
Moreover, ATH at 60 °C of benzil (**S33**) and 1,3-diphenyl-1,3-propanedione (**S34**) in the presence of HCO_2H/Et_3N (3.4:2 for **S33**[14] and 3:2 for **S34**) using **1ba** led respectively to (*R*,*R*)-hydrobenzoin with *dl*:*meso* 96:4 and 99% *ee*, and (*S*,*S*)-1,3-diphenyl-1,3-propanediol with *dl*:*meso* >99.9 and >99.9% *ee* (Scheme 3; ATH conditions for **S34**: 1 mmol substrate, 500 μL HCO_2H/Et_3N 3:2, 1.5 mL PhCl).

In conclusion, we have presented a new ATH 3rd generation *ansa*-Ru(II) complex series **1** wherein the η^6-arene is 1,3-propylene- or 1,4-butylene-tethered to

Table 3. *ansa*-Ru(II) complexes **1** catalyzed ATH of benzo-fused cyclic ketones.[a]

Ketone		Cat. **1**	HCO_2H/Et_3N	*T* [°C]	*t* [h]	*ee* [%]
	S14: R = H	**1ba**	3:2	60	4	98.9
		1bd	3:2	60	3	99.1
	S15: R = 6-OH	**1ba**	5:2	60	6	98.8
	S16: R = 7-OH	**1ba**	3:2	60	6	94.6[b]
		1bb	3:2	60	7	95.0[b]
	S17: R = 5-Br[c]	**1bb**	3:2	60	5	97.3
		1bd	3:2	60	2	98.1
	S18[c]	**1ba**	5:2	60	4	86.8
		1bb	5:2	40	24	91.6
	S19	**1ba**	3:2	60	9	99.4[d]
		1bd	3:2	60	8	99.6[d]
	S20: R = H	**1ba**	5:2	60	6	98.7
		1bd	5:2	60	3	>99.9
	S21: R = 6-OMe	**1bd**	5:2	60	8	99.4
	S22: R = 7-OMe	**1bd**	5:2	60	4	99.2
	S23	**1ba**	3:2	60	20[e]	99.6[f]
		1bd	3:2	60	20[e]	99.5[f]
	S24	**1ba**	5:2	60	48[g]	97.6
	S25: R = H	**1ba**	5:2	60	2	99.4
		1bd	5:2	60	2	99.7
	S26: R = Cl	**1ba**	5:2	60	2	99.5
	S27	**1ba**	3:2	60	10	99.1
		1bd	3:2	60	5	99.5
	S28	**1ba**	3:2	60	4	99.4
		1bd	3:2	60	2	99.7
	S29	**1ba**	5:2	60	2	99.7
	S30[h]	**1bd**	3:2	60	2	98.7
	S31	**1ba**	5:2	60	7	97.6
		1bd	5:2	60	7	98.4
	S32	**1ba**	5:2	60	2	82.1
		1bb	5:2	40	15	91.8
		1bb	5:2	60	2	87.6

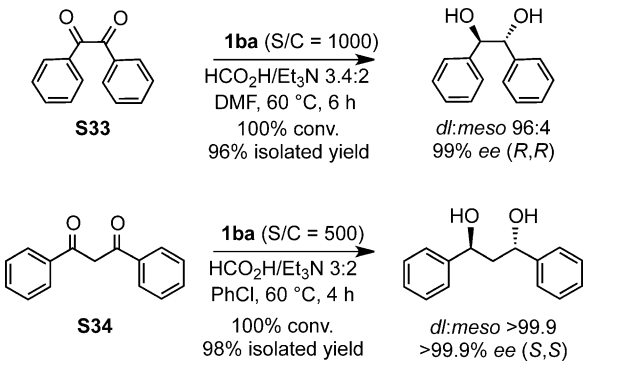
[a] ATH conditions as in Table 2 (S/C = 1000). Isolated yields after work-up were 1–4% lower. (*S*)-Configured corresponding alcohols were obtained.
[b] The *ee* was determined after conversion to 7-methoxy-1-indanol (*conditions*: MeI/K_2CO_3/Me_2CO, 50 °C).
[c] EtOAc (2 mL) used as co-solvent.
[d] *cis*:*trans* > 99.9.
[e] 87% conversion with **1ba**; 98% conversion with **1bd**.
[f] *cis*:*trans* = 93:7 with **1ba** and 90:10 with **1bd**.
[g] S/C = 100 and 95% conversion.
[h] 1,2-Dichloroethane (1.5 mL) used as co-solvent.



Scheme 2. *ansa*-Ru(II) complex **1bd** catalyzed ATH of 4-chromanone (**S25**).

R_2NSO_2DPEN from the *N*′-terminal. Employing an S/C = 1000, enantioselectivities up to >99.9% coupled with 100% conversion were attained in HCO_2H/Et_3N mixture for a variety of (het)aryl ketones and benzo-fused cyclic ketones. In particular, excellent enantioselectivities were obtained for α-tetralone, 4-chromanone, thiochroman-4-one, and 1,3-diphenyl-1,3-propanedione.

Such a conformationally rigid catalyst structure **1** having embedded diversity-oriented ligands with varied electronic and steric features, offers an inter-



Scheme 3. *ansa*-Ru(II) complex **1ba** catalyzed ATH of benzil (**S33**) and 1,3-diphenyl-1,3-propanedione (**S34**).

esting opportunity to improve catalysis outcome through cooperative interactions.

Experimental Section

Preparation of *ansa*-Ruthenium(II) Catalysts 1

A round-bottom flask equipped with a magnetic stir bar was charged successively with the (*S,S*)-DPEN-derived Ru(II) dimer **4** and HCO_2H/Et_3N (5:2 or 3:2 depending on the ketone) then the mixture was stirred at room temperature for 30 min. The green-colored solution was used directly in catalysis.

Tests with S/C = 100: Ru(II) dimer **4** (0.005 mmol based on Ru atom), HCO_2H/Et_3N (250 μL), ketone (0.5 mmol).

Tests with S/C = 500: Ru(II) dimer **4** (0.001 mmol based on Ru atom), HCO_2H/Et_3N (250 μL), ketone (0.5 mmol).

Tests with S/C = 1000: Ru(II) dimer **4** (0.002 mmol based on Ru atom), HCO_2H/Et_3N (1.0 mL), ketone (2.0 mmol).

Tests with S/C = 30000: Ru(II) dimer **4** (0.667 μmol based on Ru atom), HCO_2H/Et_3N (10 mL), ketone (20.0 mmol).

ATH Procedure

The above HCO_2H/Et_3N solution of Ru(II) catalyst **1** was added to the ketone and the mixture was stirred at the temperature and time as indicated in the Tables.

Work-up: the reaction mixture was partitioned between EtOAc (10 mL) and H_2O (5 mL). The organic layer was successively washed with H_2O (5 mL) and brine (5 mL), filtered through a bed of silica gel/Na_2SO_4 then concentrated. In the case of hydroxy-substituted ketones, the reaction mixtures were acidified with 1 M HCl (pH 4–5) then extracted with EtOAc. In the case of 6-methoxy-1-tetralone, 7-methoxy-1-tetralone, 2-benzofuryl methyl ketone, 2-acetylpyridine and 2-tetralone, the reaction mixtures were basified with 1 M NaOH (pH 8–9) then extracted with EtOAc. The residue was analyzed by ^{1}H NMR (for determination of conversion and *dr*) and chiral GC or HPLC (for *ee*). Absolute configurations were assigned by comparison of optical rotations of the isolated products and/or of the t_R of chiral GC or HPLC analysis with the literature data (see the Supporting Information).

(*S*)-4-Chromanol

A solution of Ru(II) dimer **4bd** (0.93 mg, 1.33 μmol Ru atom) in HCO_2H/Et_3N 5:2 (20 mL) was stirred at room temperature for 30 min under an N_2 atmosphere then 4-chromanone (5.926 g, 40.0 mmol) was added. After stirring at 60 °C for 30 h with continuous mild N_2 sweeping, the mixture was partitioned between EtOAc (80 mL) and H_2O (50 mL), the organic layer washed successively with H_2O (50 mL) and brine (50 mL), filtered through a bed of silica gel/Na_2SO_4, and concentrated. An almost colorless oil was obtained which solidified upon standing; yield: 5.826 g (97%). ^{1}H NMR: $\delta = 1.72$ (br s, 1H), 1.95–2.22 (m, 2H), 4.19–4.40 (m, 2H), 4.80 (t, $J = 4.0$ Hz, 1H), 6.77–7.02 (m, 2H), 7.17–7.24 (m, 1H), 7.31 (dd, $J = 7.6$ and 1.4 Hz, 1H); $[\alpha]_D^{23}$: −78 (*c* 1.0, EtOH), 99.5% *ee* {*R*-isomer:[2g] $[\alpha]_D^{20}$: +70.2 (*c* 1.0, EtOH), 99.0% *ee*}. The *ee* was determined by chiral HPLC [Chiralcel OD-H column (25 cm); eluent hexane/2-PrOH = 95/5, flow rate 1.0 mL min^{-1}, $\lambda = 220$ nm]: t_R: 10.0 min (*S*), 11.7 min (*R*).

(*R,R*)-Hydrobenzoin

A solution of Ru(II) dimer **4ba** (6.87 mg, 10 μmol Ru atom) in HCO_2H/Et_3N 3.4:2 (4.60 g) was stirred at room temperature for 30 min under an N_2 atmosphere then DMF (10 mL) and benzil (2.100 g, 10.0 mmol) were sequentially added. After stirring at 60 °C for 4 h with continuous mild N_2 sweeping, the mixture was partitioned between Et_2O (60 mL) and H_2O (30 mL), the organic layer washed successively with H_2O (3 × 30 mL) and brine (30 mL), filtered through a bed of silica gel/Na_2SO_4, and concentrated. An off-white solid was obtained; yield: 2.035 g (96%). ^{1}H NMR: $\delta = 2.79$ (s, 2H), 4.73 (s, 2H) [4.48 (s, 2 × CH, *meso*)], 7.13–7.25 (m, 10H); $[\alpha]_D^{23}$: +83 (*c* 1.0, EtOH), 99% *ee*, {*S,S*-enantiomer:[2g] $[\alpha]_D^{20}$: −91.4 (*c* 1.0, EtOH), 99% *ee*}; *dl*:*meso* 96:4 (by ^{1}H NMR). The *ee* was determined by chiral HPLC analysis [Chiralcel OJ-H column (25 cm); eluent hexane/2-PrOH = 90/10, flow rate 0.5 mL min^{-1}, $\lambda = 220$ nm]: t_R: 27.9 min (*S,S*), 31.4 min (*R,R*), 38.5 min (*meso*).

(*S,S*)-1,3-Diphenyl-1,3-propanediol

A solution of Ru(II) dimer **4ba** (13.7 mg, 20 μmol Ru atom) in HCO_2H/Et_3N 3:2 (5.0 mL) was stirred at room temperature for 30 min under an N_2 atmosphere then chlorobenzene (15 mL) and 1,3-diphenyl-1,3-propanedione (2.243 g, 10.0 mmol) were sequentially added. After stirring at 60 °C for 6 h with continuous mild N_2 sweeping, the mixture was partitioned between EtOAc (60 mL) and H_2O (30 mL), the organic layer successively washed with H_2O (30 mL) and brine (30 mL), filtered through a bed of silica gel/Na_2SO_4, and concentrated. Off-white crystals were obtained; yield: 2.214 g (98%). ^{1}H NMR: $\delta = 2.19$ (t, $J = 5.8$ Hz, 2H), 2.80 (br s, 2H), 4.99 (t, $J = 4.7$ Hz, 2H), 7.23–7.42 (m, 10H); $[\alpha]_D^{23}$: −71 (*c* 1.0, CH_3OH), >99.9% *ee*; {*S,S*-enantiomer:[15] $[\alpha]_D^{28}$: −68.2 (*c* 1.12, CH_3OH), 99% *ee*}; *dl*:*meso* >99 (by ^{1}H NMR). The *ee* was determined by chiral HPLC analysis [Chiralcel OD-H column (25 cm); eluent hexane/2-PrOH = 95/5, flow rate 1.0 mL min^{-1}, $\lambda = 220$ nm]: t_R: 24.9 min (*S,S*), 29.9 min (*R,R*), 37.4 min (*meso*).

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[4] The structure **B** depicted in Figure 1 is suggested based on the X-ray-characterized analogous complex **A** of Wills et al.[2a]

[5] For a preparation of (*S*,*S*)-R_2NSO_2DPEN, see: D. Šterk, M. Stephan, B. Mohar, *Tetrahedron: Asymmetry* **2002**, *13*, 2605–2608.

[6] The following improved adapted protocol uses less amounts of reagents and obviates the need for Et_3N resulting in higher yields: To a cold (0 °C) solution of **2** (1.19 equiv.) and 2,6-lutidine (1.44 equiv.) in CH_2Cl_2 is added a solution of triflic anhydride (1.22 equiv.) in CH_2Cl_2 at a such a rate that the temperature does not rise above 0 °C. After stirring for 30 min at such a temperature and for 1 h at room temperature, a cold (0 °C) solution of (*S*,*S*)-*N*-(1-piperidylsulfonyl)DPEN (1.00 equiv.) in CH_2Cl_2 is added and stirred overnight at room temperature. After a standard CH_2Cl_2-extractive work-up, 85–92% of pure **3** is obtained. See also the Supporting Information.

[7] Although we failed to isolate any monomeric Ru(II) structure **1**, their formation as such is evidenced by the resulting high catalyst activity and enantioselectivity. In addition, a coordination-induced proximity effect should favor the formation of such monomeric structures in this case by analogy to the Wills et al. C3-[(*R*,*R*)-Teth-TsDPEN-RuCl] (complex **C**) and the Ikariya et al. (*R*,*R*)-Ts-DENEB (complex **D**) complexes.

[8] Operating in an open flask (i.e., in the absence of N_2 sweeping) and with an S/C = 1000, the reduction stagnated at < 50% conversion without affecting the *ee*.

[9] C3-[(*R*,*R*)-Teth-TsDPEN-RuCl] (complex **C**) and (*R*,*R*)-Ts-DENEB (complex **D**) (S/C = 1000) afforded 95% *ee* (5 h for 100% conversion at 40 °C) and 97% *ee* (3 h for > 99% conversion at 60 °C), respectively. In our hands, testing the commercially available C3-[(*R*,*R*)-Teth-TsDPEN-RuCl] (complex **C**) and (*R*,*R*)-Ts-DENEB (complex **D**) at 60 °C gave 94.4% *ee* (3 h for 100% conversion) and 96.3% *ee* (4 h for > 99% conversion), respectively.

[10] a) For additional ATH results of substituted acetophenones, see the Supporting Information (Table S1). b) For asymmetric hydrogenation of *m*-hydroxyacetophenone (**S3**) catalyzed by Ir-(*S*)-SpiroPAP-3-Me and affording 97% *ee*, see: P.-C. Yan, G.-L. Zhu, J.-H. Xie, X.-D. Zhang, Q.-L. Zhou, Y.-Q. Li, W.-H. Shen, D.-Q. Che, *Org. Process Res. Dev.* **2013**, *17*, 307–312. c) For comparative literature ATH results of hetaryl ketones, see the Supporting Information (Table S2).

[11] For indicative literature results on metal-catalyzed ATH or asymmetric hydrogenation of benzo-fused cyclic ketones of Table 3, see the Supporting Information (Table S3). For example, (*R*,*R*)-Ts-DENEB (complex **D**)-catalyzed ATH (S/C = 1000, HCO_2H/Et_3N 5:2, 60 °C) of 1-indanone (**S14**) afforded 98% *ee* with 97% conversion (5 h), and 4-chromanone led to > 99% *ee* with > 99% conversion (5 h).[2g]

[12] For relevant articles to the work presented in Table 3 regarding α-tetralone and analogues (**S20**–**S26**, **S29**), see: a) A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 2521–2522; b) P. N. Liu, P. M. Gu, F. Wang, Y. Q. Tu, *Org. Lett.* **2004**, *6*, 169–172; c) D. S. Matharu, D. J. Morris, G. J. Clarkson, M. Wills, *Chem. Commun.* **2006**, 3232–3234; d) J. Wettergren, A. Bøgevig, M. Portier, H. Adolfsson, *Adv. Synth. Catal.* **2006**, *348*, 1277–1282; e) D. S. Matharu, J. E. D. Martins, M. Wills, *Chem. Asian J.* **2008**, *3*, 1374–1383; f) C. V. Manville, G. Docherty, R. Padda, M. Wills, *Eur. J. Org. Chem.* **2011**, 6893–6901; g) B. Zhang, H. Wang, G.-Q. Lin, M.-H. Xu, *Eur. J. Org. Chem.* **2011**, 4205–4211; h) L. Tang, Z. Lin, Q. Wang, X. Wang, L. Cun, W. Yuan, J. Zhu, J. Deng, *Tetrahedron Lett.* **2012**, *53*, 3828–3830; i) K. E. Jolley, A. Zanotti-Gerosa, F. Hancock, A. Dyke, D. M. Grainger, J. A. Medlock, H. G. Nedden, J. J. M. Le Paih, S. J.

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[14] We have noticed that substrate concentration in addition to the co-solvent nature affects markedly the diastereoselectivity. The ATH conditions were adopted from: K. Murata, K. Okano, M. Miyagi, H. Iwane, R. Noyori, T. Ikariya, *Org. Lett.* **1999**, *1*, 1119–1121. ATH using Ts-DENEB (complex **D**) leading to *dl*:*meso* 97.2:2.8 (>99% *ee*) is mentioned in ref.[2g]
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