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Rhodium-catalysed asymmetric ring opening of oxabicyclic alkenes with heteroatom nucleophiles

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Abstract

We describe a new rhodium catalysed asymmetric ring opening (ARO) reaction of oxabenzonorbornadienes. This reaction produces a new carbon–oxygen bond via an intermolecular allylic displacement of the bridgehead oxygen with a wide variety of alcohols and phenols. This reaction occurs under neutral reaction conditions, and no activation of the alcohol nucleophile is required. It proceeds with very high regio- and diastereoselectivity (> 99:1), and excellent enantioselectivity (up to 99%ee). Symmetrical substitution patterns on the aromatic ring of the oxabenzonorbornadienes had no effect on the course of the reaction nor the enantioselectivity. The reaction produces an unusual stereochemical outcome for oxabicyclic ring openings since the *trans* rather than the *cis* product is formed. Very low catalyst loadings can be used, typically 0.25 mol% of the catalytically active rhodium species.

Keywords: Asymmetric ring opening; Rhodium; Oxabenzonorbornadienes; Heteroatom nucleophiles

1. Introduction

Transition metal catalysed transformations at allylic positions have come to the forefront of synthetic organic chemistry. The mildness and selectivity of these reactions have allowed chemists easy access to structures, often in enantioenriched form, which were previously impossible or very difficult to obtain. Methods have been developed which enable a wide range of allylic leaving groups to react with a variety of nucleophile classes. Indeed, the application of π-allyl palladium chemistry to organic synthesis has made significant advancements and remains an area of intense research [1]. In addition to palladium catalysts, several other transition metals have been found to catalyse these transformations. By changing the metal, different, often complementary, selectivities can be obtained. For example, rhodium has recently been shown to react with allylic carbonates [2] and vinyl epoxides [3] to produce products complementary to the palladium 'benchmark.'

Among the myriad of molecular architectures present in pharmacological agents, we have noted that the hydronaphthalene skeleton is found in a wide range of compounds possessing diverse biological activities. Examples include sertraline **2** [4] (an antidepressant), diamine **3** [5] (an analgesic), **4** [6] (a dopamine agonist), homochelidonine **5** (a naturally occurring alkaloid), dihydrexidine **6** [7] (an antiparkinsonian agent), and etoposide **7** [8] (used in the treatment of various cancers). In addition, CNS agents [9], immunoregulatory agents [10], antibiotics [11] and antitumor agents [12] contain variations on this framework [13] (Scheme 1).

We sought to develop a new method which would permit access to this core structure in enantioenriched form and with the ability to introduce diversity at every position. In spite of the recent advances in the field of asymmetric ring opening (ARO) chemistry, no ARO reactions with oxabicyclic alkenes have been reported involving heteroatom nucleophiles. Thus our focus was to extend the scope of the ARO methodology such that heteroatoms would be incorporated into the molecule during the ring-opening step (Scheme 2).

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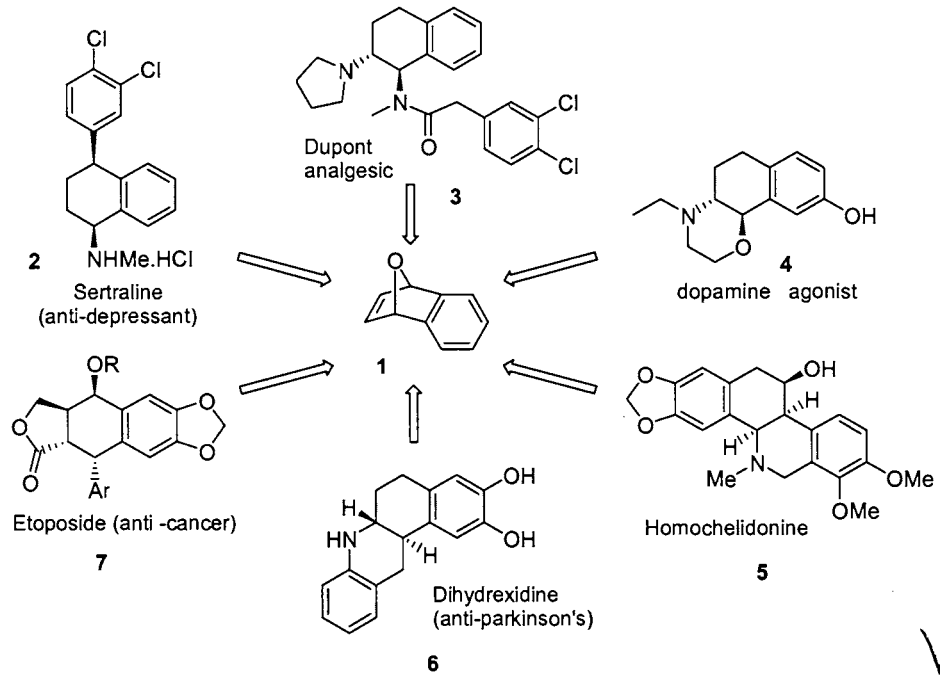


Scheme 1.

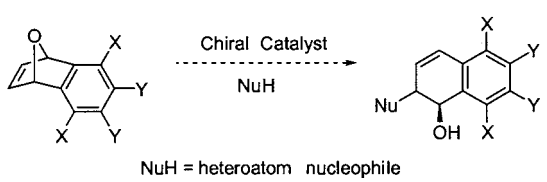
2. Synthetic precedent and adaptation to oxabenzonorbornadiene

In 1973, Hogeveen and Middelkoop reported that $[Rh(CO)_2Cl]_2$ catalysed the ring opening reaction of **8a** and **8b** with methanol to give methoxycyclohexandienol products **9a** and **9b**, respectively [14] (Scheme 3). Ashworth and Berchtold later showed that the stereochemistry of the incorporated methoxy substituent was *cis* to the resulting hydroxyl group by formation of the Diels–Alder adduct **10** [15]. In chloroform as the solvent, and in the absence of methanol, the oxabicycle rearranges to give the hydroxyfulvene product **11** [16].

Our initial experiments using the Hogeveen and Middelkoop conditions with oxabenzonorbornadiene **1** failed to induce any ring-opening reaction. Instead a red precipitate formed after a few minutes which did not dissolve even with heating. We reasoned that by using a more highly polarising solvent this problem could be avoided. Changing the solvent system to a 1:1 mixture of trifluoroethanol (TFE):methanol and increasing the reaction temperature to 60°C gave the desired product **12** in 70% yield (Scheme 4). To our surprise, the stereochemistry of **12** was proven to be *trans* by comparison to authentic samples of both stereoisomers of dimethoxytetrahydronaphthalene **13**. The authentic *cis* isomer of **12** was prepared by reaction of 1,2-dihydronaphthalene with OsO_4 followed by dimethylation with dimethylsulfate. *Trans*-**12** was prepared by epoxidation of 1,2-dihydronaphthalene followed by ring opening with sodium hydroxide and dimethylation with dimethylsulfoxide (DMS). Given that this stereochemical result is opposite to that proposed for the Hogeveen–Middelkoop substrate we verified the *cis* stereochemistry of **9a** by X-ray crystallography. This difference in stereochemical outcome implies that different mechanisms are operating in each case. These reaction conditions were found to be generally applicable for a variety of alcohol nucleophiles. EtOH, ^{i}PrOH, and 2-TMS ethanol can all be added in moderate yield (Table 1).

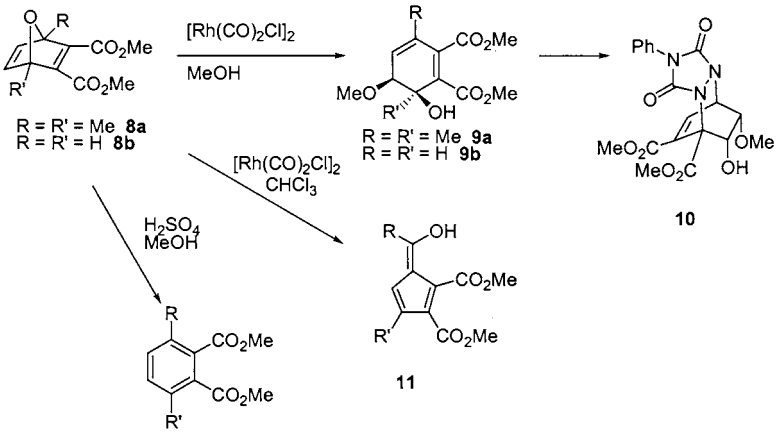
3. Development of an asymmetric variant

In order to establish an asymmetric variant of this ring opening reaction, the effect of added ligands was studied. Initial experiments using $[Rh(CO)_2Cl]_2$ as the rhodium source with a variety of phosphines[1] resulted in the formation of an insoluble red precipitate, and no ring opened product. This precipitate could not be dissolved by further heating nor prolonged stirring.

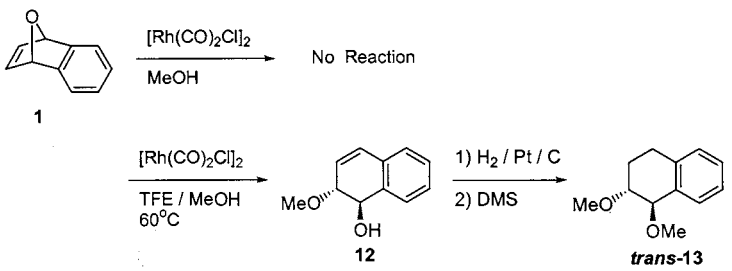


Scheme 2.

[1] Triphenylphosphine, dppe, dppf and dppb all resulted in insoluble complexes upon addition to a solution of $[Rh(CO)_2Cl]_2$.



Scheme 3.



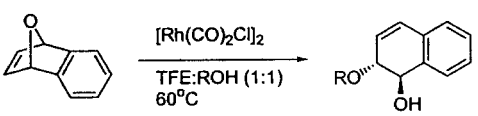
Scheme 4.

We next turned to $[Rh(COD)Cl]_2$ and phosphorous ligands which possess a greater degree of π-acid character, so as to mimic the CO ligands of the $[Rh(CO)_2Cl]_2$ catalyst. We noted that homogeneous solutions were produced on mixing the rhodium and phosphite ligands, and modest reactivity was observed (Table 2, entries 1–3). To determine if phosphine ligands were compatible, PPh_3 was also used and gave similar levels of reactivity (entry 4).

We next examined bidentate ligands. Indeed, not all ligands showed the same type or level of reactivity. For example, dppe did not produce any desired product; only the dimerisation of the oxabicycle was observed (entry 5). Dppb, which possesses a larger bite angle [17], showed improved reactivity (entry 6) and increasing the bite angle further through the use of dppf gave the best results (entry 7). The yield dropped significantly when the reaction was run at room temperature.

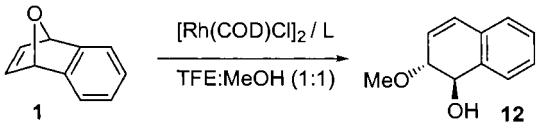
Chiral analogues of dppf are known, and of the ligands studied, PPF–P^{t}Bu$_2$ (**17**) gave the best results, producing **12** in 84% yield and 86%ee at 60°C (Table 3, entry 1). We therefore chose to focus our attention on ligands based on the Josiphos template. Varying the substituent on the phosphine moieties led to inferior results (entries 2–4), as did lowering the concentration of methanol (entry 5). Similarly, running the reaction in neat methanol also gave lower enantioselectivity. By increasing the oil bath temperature to 80°C and running the reaction at reflux, however, the ee was increased to 96% (entry 7). Under these conditions, the catalysed loading could be decreased to 0.5 mol% with no reduction in yield or enantioselectivity. A common by-product in all of these transformations is naphthol which accounts for the remainder of the mass balance. Further investigations into the effect of solvent choice revealed that THF gave similar levels of induction and quantitative conversion to the desired product by crude NMR. By allowing the reaction to run overnight, the catalyst loading could be lowered to 0.25 mol% (entry 11).

Table 1
Rhodium catalysed ring opening with various alcohols



Entry	Alcohol	Product	Yield (%)
1	MeOH	12	70
2	EtOH	14	61
3	^{i}PrOH	15	63
4	$TMSCH_2CH_2OH$	16	52

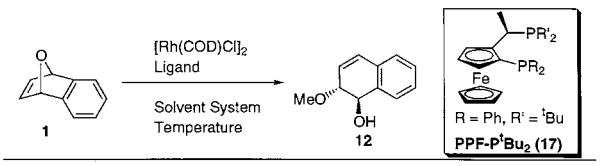
Table 2
Effect of ligands on reactivity with $[Rh(COD)Cl]_2$



Entry	Ligand	Bite Angle[a]	Temp.(°C)	Conv(%Yield)
1	$P(OEt)_3$	-	60	23(15)
2	$P(O^iPr)_3$	-	60	42(33)
3	$P(OCH_2CF_3)_3$	-	60	0[b]
4	PPh_3	-	60	22(18)
5	dppe	85	60	0[c]
6	dppb	97	60	31(24)
7	dppf	96	60	>98(88)
8	dppf	96	rt	40(37)

[a] ref. 17. [b] Only product was naphthol. [c] Only dimerisation of the oxabicycle was observed.

Table 3
Ligand and solvent studies



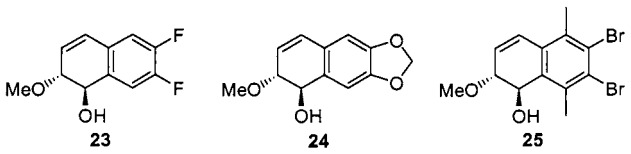
	Ligand						
Entry	R	R'	Mol% Cat.	Solvent System	Temp(°C)	Yield(%)	Ee(%)[a]
1	Ph	tBu	5.0	TFE:MeOH (1:1)	60	84	86
2	Ph	Cy	5.0	TFE:MeOH (1:1)	60	69	71
3	Cy	Ph	5.0	TFE:MeOH (1:1)	60	11	17
4	Cy	Cy	5.0	TFE:MeOH (1:1)	60	60	31
5	Ph	tBu	5.0	TFE/5eq.MeOH	60	32	30
6	Ph	tBu	5.0	neat MeOH	60	22	46
7	Ph	tBu	5.0	TFE:MeOH (1:1)	80	85	96
8	Ph	tBu	1.0	TFE:MeOH (1:1)	80	80	95
9	Ph	tBu	0.5	TFE:MeOH (1:1)	80	85	97
10	Ph	tBu	0.5	THF:MeOH (1:1)	reflux	95	97
11	Ph	tBu	0.25	THF:MeOH (1:1)	reflux	96	97

[a] Ee determind by chiral stationary phase chromatography with a Chiralcel OD column.

4. Scope of oxygen nucleophiles in the ARO of oxabenzonorbornadiene

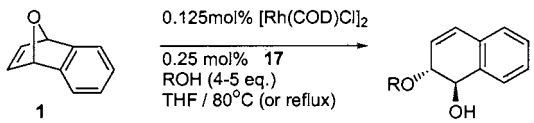
Many different alcohols are compatible with the reaction conditions providing the products in good yield and excellent enantioselectivity (Table 4). We were surprised to find that TFE was a good nucleophile for this transformation when THF was used as the solvent since no TFE-induced ring opening was detected when it was used as the solvent with MeOH as a nucleophile. Even the very weakly nucleophilic hexafluoroisopropanol (HFIP) added under these reaction conditions (entry 9). Once again, we were able to use very low catalyst loadings and still achieve excellent results.

In order to investigate the effects of substituents on the aromatic ring of **1**, difluoro, methylene dioxy, and dimethyldibromo substrates were prepared and reacted under the standard conditions. All gave the corresponding ring opened products **23**, **24** and **25** in good yields and excellent ee's indicating that this reaction is not sensitive to electronic effects on the aromatic ring.



We then examined the scope of this ARO reaction with substituted phenols. While phenol nucleophiles have been successfully been used in a few transition metal catalysed systems [18], rhodium had not previously been used as a catalyst with this class of nucleophile and we had no previous results indicating that phenols were sufficiently nucleophilic to participate in oxabicyclic ring opening reactions. Our initial experiments using ten equivalents of phenol gave the desired product **26** in near quantitative yield and outstanding

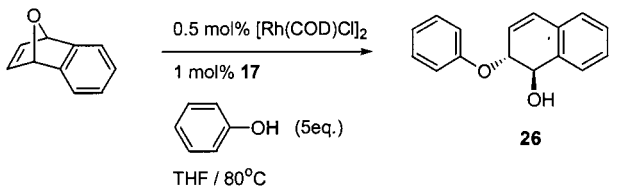
Table 4
Scope of the rhodium catalysed ARO with alcohols



Entry	ROH	Product	Rxn Time(h)	Yield(%)	ee(%)[b]
1	MeOH[a]	12	4	96	97
2	EtOH[a]	14	3	84	97
3	iPrOH[a]	15	3	94	93
4	Allyl Alcohol	18	9	92	>99
5	2-TMS Ethanol [a]	16	8	53	95
6	Benzyl Alcohol	19	24[d]	66	>98
7	PMB Alcohol [c]	20	24[d]	87	97
8	TFE	21	10	70	98
9	HFIP	22	9	90	93

[a] These reactions were performed under unoptimised conditions using 10 eq. ROH and 1mol% catalyst [b] ee determined by formation of Moshers ester or by CSP HPLC analysis with a Chiralcel OD column. [c] *p*-Methoxybenzyl alcohol. [d] Reaction was allowed to react ovemight.

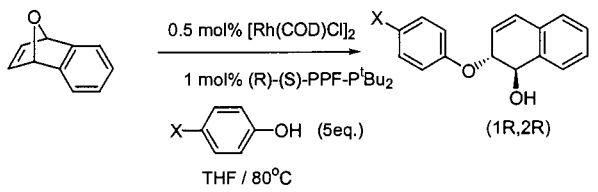
Table 5
Effects of number of equivalents of phenol



Phenol Equiv.	Reaction Time	Yield(%)[a]	Ee(%)[b]
10	6 h	89	>99
5	8 h	91	>99
2.5	5 d	35[c]	>99
1.5	5 d	10[c]	>99

[a] Isolated yield. [b] Ee determined by CSP HPLC. [c] Remainder is unreacted starting material.

Table 6
Scope of ARO with *p*-substituted phenols



Phenol (X)	Product	Rxn Time(h)	Yield(%)[a]	ee(%)[b]
F	**27**	5	92	97
Cl	**28**	6	89	92
Br	**29**	3	94	98
I	**30**	12[c]	92	98
$COCH_3$	**31**	2.5	91	>99
CF_3	**32**	8	87	95
CH_3	**33**	24[c]	60	91
-CN	**34**	5	88	97
OMe	**35**	6	85	95

[a] Isolated yields. [b] Ee determined by CSP HPLC or formation of the Mosher's Ester. [c] Reaction was allowed to react overnight.

enantioselectivity (> 99%ee). Subsequent experiments revealed that the amount of phenol could be lowered to five equivalents with no deleterious effects (Table 5). Below five equivalents, however, the reactions did not go to completion even after prolonged reaction times, although the enantioselectivity was not adversely affected.

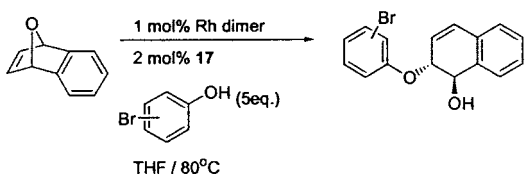
Various *para*-substituted phenols were shown to add in high yields and excellent enantioselectivity (Table 6). The reaction proceeded well even when aryl bromides and iodides were used indicating that the rhodium insertion into the aryl halide bond is slow compared to ring opening. This selectivity permits the preparation of various halo aryl ethers with which further coupling reactions could be envisaged. An X-ray crystal structure of **29** confirmed the regiochemistry, the relative stereochemistry, and provided the absolute configuration of the ring opened products.

We next examined the effect of other substitution patterns on the reactivity of the phenol. In the case of a bromo substituent, 3- and 4-bromophenol added in high yields and excellent enantioselectivity (Table 7, entries 1, 2), but 2-bromophenol did not give satisfactory results adding in only 17% yield after prolonged reaction times (entry 3). Despite the low conversion, the enantioselectivity was still very high, with **37** being produced in 97%ee. Changing the rhodium source to $[Rh(CO)_2Cl]_2$, increased the yield of the reaction with 2-bromophenol to 92% and had no detrimental effects on the enantioselectivity (entry 5). It is noteworthy that $[Rh(CO)_2Cl]_2$ forms an insoluble precipitate with dppf but no precipitate is formed with PPF–P^{t}Bu$_2$.

The enantioselectivity with $[Rh(COD)Cl]_2$/PPF–P^{t}Bu$_2$ with 2-bromophenol is similar to that observed for 3- and 4-bromophenol which suggests that the catalytically active complex is the same in each case. We reasoned that the poor yield with $[Rh(COD)Cl]_2$ might be due to the rhodium being sequestered from the catalytic cycle by reversible bidentate binding of the 2-halophenol through the oxygen and the bromine atoms. Such a binding pattern has been invoked by Noyori [19] for the ruthenium catalysed asymmetric hydrogenation of *o*-bromoacetophenone and by Wills [20] for the rhodium catalysed asymmetric hydrosilyation of *o*-chloroacetophenone and *o*-bromoacetophenone (Scheme 5).

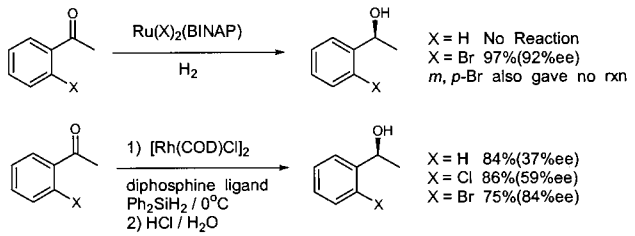
$[Rh(CO)_2Cl]_2$, upon mixing with certain classes of diphosphines, is known to produce complexes in which

Table 7
Effect of bromophenol substitution and rhodium source on reactivity

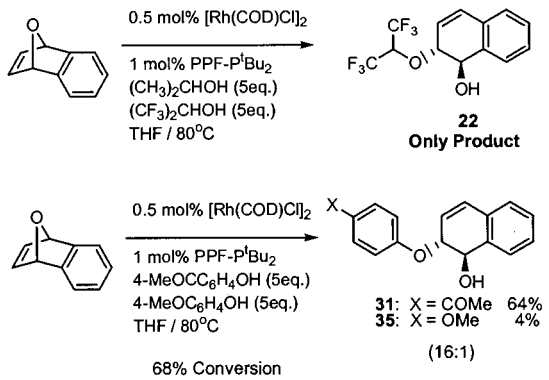


Entry	Phenol	Rh Source	Ligand	Product	Yield(%)[a](%ee[b])
1	4-Br	$[Rh(COD)Cl]_2$	PPF-P^{t}Bu$_2$	**29**	94(98)
2	3-Br	$[Rh(COD)Cl]_2$	PPF-P^{t}Bu$_2$	**36**	92(96)
3	2-Br	$[Rh(COD)Cl]_2$	PPF-P^{t}Bu$_2$	**37**	17[c](97)
4	2-Br	$[Rh(CO)_2Cl]_2$	DPPF	-	No Reaction[d]
5	2-Br	$[Rh(CO)_2Cl]_2$	PPF-P^{t}Bu$_2$	**37**	92(97)

[a] Isolated yield. [b] Ee determined by CSP HPLC. [c] Remainder is unreacted starting material. [d] An insoluble precipitate resulted upon mixing DPPF with the Rh source which did not disolve.



Scheme 5.



Scheme 6.

one of the carbonyls remains bound [21]. As a result, the $[Rh(CO)_2Cl]_2$/PPF–P^{t}Bu$_2$ catalyst system might have one less vacant coordination site compared to the $[Rh(COD)Cl]_2$ system. This difference could serve to disfavour bidentate phenol binding that occurs and thus increase the amount of the catalytically active species.

We observed significant differences in the relative rates of reaction, with the more acidic alcohols and phenols adding faster. Similar observations were made by Sinou of the reactivity of phenols in allylic etherification under palladium catalysis [22]. In order to quantify these observations, we conducted competition experiments using equimolar amounts of sterically similar nucleophiles possessing different acidities. The rate difference is best illustrated by the competition experiment between ^{i}PrOH and HFIP. In this case, the only product detected in the crude NMR was **22**. In another experiment, 4-hydroxyacetophenone and 4-hydroxyanisole were mixed. At 68% conversion we observed a 16:1 ratio of **31**:**35** (Scheme 6) confirming that the presence of an electron withdrawing group on the aromatic ring accelerates the rate of addition.

5. Conclusion

We have described an efficient new rhodium catalysed asymmetric ring opening (ARO) reaction of oxabenzonorbornadienes. This reaction produces a new carbon–oxygen bond via an intermolecular allylic displacement of the bridgehead oxygen with a wide variety of alcohols and phenols. While the optimal catalyst for the addition of alcohols and most phenols was determined to be $[Rh(COD)Cl]_2$/PPF–P^{t}Bu$_2$, the addition of *o*-halophenols required changing the rhodium source to $[Rh(CO)_2Cl]_2$. These reactions occur under neutral reaction conditions, and no activation of the nucleophile is required. It proceeds with very high regio- and diastereoselectivity (>99:1), and excellent enantioselectivity (up to 99%ee). Symmetrical substitution patterns on the aromatic ring of the oxabenzonorbornadienes were found to have no influence on the course of the reaction nor the enantioselectivity. The reaction also produces an unusual stereochemical outcome for oxabicyclic ring openings since the *trans* rather than the *cis* product is formed. Very low catalyst loadings can be used, typically 0.25 mol% of the catalytically active rhodium species. The hydronaphthalene products of this reaction belong to an important class of compound possessing a large range of biological activities. Efforts are underway to apply this methodology in the preparation of biologically active compounds and to elucidate the reaction mechanism.

6. Experimental

The following general experimental details apply to all following reactions.

All flasks were flame-dried under a stream of nitrogen or argon and cooled before use. Solvents and solutions were transferred with syringes and cannulae using standard inert atmosphere techniques.

^{1}H-NMR spectra were recorded at 200 MHz using a Varian Gemini NMR spectrometer or at 400 MHz using a Varian XL400 spectrometer with $CDCl_3$ as reference standard (*d* 7.24 ppm) or some other suitable solvent. Spectral features are tabulated in the following order: chemical shift (*d*, ppm); number of protons; multiplicity (s — singlet, d — doublet, t — triplet, q — quartet, m — complex multiplet, br — broad); coupling constants (*J*, Hz). ^{13}C-NMR spectra were recorded at 400 MHz with $CDCl_3$ as reference standard ($d = 77.0$ ppm) or some other suitable solvent.

IR spectra were obtained using a Nicolet DX FT-JR spectrometer as a KBr pellet or neat film between KBr plates. High resolution mass spectra were obtained from a VG 70-250S (double focusing) mass spectrometer at 70 eV. Combustion analyses were submitted to Canadian Microanalytical Service Ltd., BC. Optical rotations were measured on a Perkin Elmer model 243 polarimeter using the sodium D line with spectro-grade $CHCl_3$ in a 1 dm cell. Melting points were taken on a Fisher–Johns melting point apparatus and are uncorrected.

Gas chromatography was performed on a Hewlett Packard 5890 gas chromatograph using an Advanced Separation Technologies G-TA or B-TA chiral columns. HPLC analysis was performed on a Waters 600E with Chiralcel OD or OJ columns. Analytical TLC was performed using EM Separations precoated silica gel 0.2 mm layer UV 254 fluorescent sheets. Column chromatography was performed as 'flash chromatography' as reported by Still [23] using (200–400 mesh) Merck grade silica gel.

Diethyl ether, THF, benzene and toluene were distilled from sodium benzophenone ketyl immediately prior to use. CH_2Cl_2 was distilled from calcium hydride. DME was distilled from sodium benzophenone ketyl and stored. DMF was dried and stored over activated molecular sieves. Furan was distilled prior to use. 4,5-dibromobenzodioxole was prepared by bromination of benzodioxole in acetic acid in the presence of NaOAc. Mosher's acid chloride was prepared by refluxing Mosher's acid (MTPA, obtained from Aldrich) in thionyl chloride in the presence of a catalytic amount of NaCl for 60 h and purified by bulb to bulb distillation. The PPF–P^{t}Bu$_2$ ligand was donated by Solvias. The oxabenzonorbornadienes were prepared according to literature procedure [24]. All other reagents were obtained from Aldrich and used as received unless otherwise stated.

6.1. General procedure for the ARO reactions with alcohol nucleophiles

[Rh(COD)Cl]$_2$ (**1**) was added to a flame dried round bottom flask, (*S*,*R*)-PPF–P^{t}Bu$_2$ (unless otherwise indicated) followed by addition of THF and nucleophile (THF:nucleophile 1:1) The mixture was heated until the reaction was complete as judged by thin layer chromatography. The solvents were removed in vacuo and the crude mixture was purified by flash chromatography.

6.1.1. (1R,2R)-2-Methoxy-1,2-dihydro-naphthalen-1-ol (12)

Following the general procedure using (*R*,*S*)-PPF-P^{t}Bu$_2$, **12** was obtained as a white crystalline solid (586 mg, 96%). The ee was determined to be 97% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 10.1 min (major) and 11.1 min. $R_f = 0.29$ on silica gel (10% ethyl acetate:hexanes); m.p. 86–87°C (Et_2O); $[\alpha]_D^{25} = -208$ (c = 10.1, $CHCl_3$); $R_f = 0.39$ on silica (20% ethyl acetate:hexanes). IR (KBr, cm^{-1}) 3277 (br), 2971 (m), 1466 (m), 1285 (m), 1114 (s), 1048 (m), 979 (m), 775 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60–7.62 (1H, m), 7.30–7.21 (2H, m), 7.13–7.11 (1H, m), 6.50 (1H, dd, $J = 9.9$,1.8 Hz), 6.04 (1H, dd, $J = 9.9$, 2.2 Hz), 4.85 (1H, dd, $J = 9.9$, 6.2 Hz), 3.50 (3H, s), 2.89 (1H, d, $J = 12.8$ Hz); ^{13}C-NMR (400 MHz, acetone-*d*) δ 138.5, 133.2, 129.1, 128.4, 128.3, 128.2, 126.8, 126.3, 83.1, 73.0, 57.1. HRMS Calc. for $C_{11}H_{12}O_2$ [M$^+$]: 176.0837. Found: 176.0835.

6.1.2. (1S,2S)-2-(Ethoxy)-1,2-dihydro-naphthalen-1-ol (14)

Following the general procedure, **14** was obtained as a white crystalline solid (553 mg, 84%). The ee was determined to be 97% using HPLC analysis on a Chiralcel OD column, $\lambda = 254$ nm. Retention times in 1.5% isopropanol in hexanes were 13.6 min and 14.2 min (major). $R_f = 0.26$ on silica gel (20% ethyl acetate:hexanes); m.p. 33°C (Et_2O); $[\alpha]_D^{25} = 185.9$ (c = 9.6, $CHCl_3$); IR (KBr, cm^{-1}) 3601 (br), 3040 (m), 2977 (s), 1454 (s), 1396 (m), 1185 (s), 1104 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59–7.57 (1H, m), 7.27–7.20 (2H, m), 7.07–7.05 (1H, m), 6.43 (1H, dd, $J = 9.9$, 2.2 Hz), 6.01 (1H, dd, $J = 9.9$, 2.2 Hz), 4.90 (1H, d, $J = 10.6$ Hz), 4.18 (1H, ddd, $J = 10.6$, 2.2, 2.2 Hz), 3.79 (1H, AB, dq, $J = 9.4$, 6.9 Hz),), 3.58 (1H, AB, dq, $J = 9.4$, 6.9 Hz), 2.65 (1H, s), 1.27 (3H, t, $J = 6.9$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 135.9, 131.9, 128.0, 127.8, 127.8, 126.1, 124.9, 80.7, 72.5, 64.6, 15.5. HRMS Calc. for $C_{12}H_{14}O_2$ [M$^+$]: 190.0994. Found: 190.0993.

6.1.3. (1S,2S)-2-(Isopropoxy)-1,2-dihydro-naphthalen-1-ol (15)

Following the general procedure, **15** was obtained as a colourless oil (666 mg, 94%). The ee was determined to be 92% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 9.7 min (major) and 10.7 min. $R_f = 0.42$ on silica gel (10% ethyl acetate:hexanes); $[\alpha]_D^{25} = +154.0$ ($c = 12.6$, $CHCl_3$); IR (KBr, cm^{-1}) 3435 (br), 3038 (w), 2952 (s), 1454 (m), 1249 (s), 1087 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61–7.58 (1H, m), 7.27–7.19 (2H, m), 7.06–7.04 (1H, m), 6.40 (1H, dd, $J = 9.9$, 2.0 Hz), 5.95 (1H, dd, $J = 9.9$, 2.2 Hz), 4.87 (1 H, d, $J = 10.8$ Hz), 4.24 (1H, ddd, $J = 10.8$, 2.2, 2.2 Hz), 3.85 (1H, h, $J = 6.2$ Hz), 2.98 (1H, s), 1.25 (6H, dd, $J = 8.8$, 6.2 Hz); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 136.2, 132.3, 129.6, 128.0, 127.9, 127.8, 126.3, 125.0, 78.9, 73.0, 71.1, 23.5, 22.4. HRMS Calc. for $C_{13}H_{16}O_2$ [M$^+$]: 204.1150. Found: 204.1150.

6.1.4. (1S,2S)-3-(1-propenyloxy)-1,2-dihydro-naphthalen-1-ol (18)

Following the general procedure, **18** was obtained as a colourless oil (898 mg, 60%) which solidified on sitting. The ee was determined to be >99% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 15.2 and 16.3 min (major). $R_f = 0.17$ on silica gel (10% ethyl acetate:hexanes); m.p. 25–26°C (Et_2O); $[\alpha]_D^{25} = +195.1°$ ($c = 11.5$, $CHCl_3$); IR (KBr, cm^{-1}) 3435 (br),

3037 (m), 2857 (s), 1454 (s), 1165 (s), 1083 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61–7.58 (1H, m), 7.27–7.20 (2H, m), 7.08–7.05 (1H, m), 6.44 (1H, dd, $J = 9.9$, 2.0 Hz), 6.00 (1H, dd, $J = 9.9$, 2.4 Hz), 6.00–5.92 (1H,m), 5.32 (1 H, ddd, $J = 17.2$, 3.3, 1.6 Hz), 5.21 (1H, ddd, $J = 10.4$, 2.9, 1.3 Hz), 4.94 (1H, d, $J = 10.2$ Hz), 4.27 (1H, ddd, $J = 10.3$, 2.2, 2.2 Hz),), 4.23 (1H, dddd, $J = 12.8$, 5.5, 1.5, 1.5 Hz), 4.12 (1H, dddd, $J = 12.8$, 5.9, 1.5, 1.5 Hz), 3.09 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$) δ135.8, 134.5, 131.8, 128.1, 127.7, 127.6, 127.4, 126.1, 125.0, 117.5, 80.1, 76.7, 72.4, 70.2. HRMS Calc. for $C_{14}H_{14}O_2$ [M^+]: 202.0994. Found: 202.0994.

6.1.5. (1S,2S)-2-(2-Trimethylsilyl-ethoxy)-1,2-dihydro-naphthalen-1-ol (**16**)

Following the general procedure, **16** was obtained as a colourless oil (482 mg, 53%). The ee was determined to be 95% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 0.5% isopropanol in hexanes were 17.9 and 18.5 min (major). $R_f = 0.25$ on silica gel (10% ethyl acetate:hexanes); $[\alpha]_D^{25} = +119.2$ ($c = 13.0$, $CHCl_3$); IR (KBr, $cm^{-1)}$ 3447 (br), 3037 (m), 2972 (s), 1454 (m), 1381 (m), 1118 (s), 1078 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59–7.57 (1H, m), 7.28–7.21 (2H, m), 7.08–7.06 (1H, m), 6.43 (1H, dd, $J = 9.9$, 2.0 Hz), 6.03 (1H, dd, $J = 9.9$, 2.2 Hz), 4.89 (1 H, d, $J = 10.6$ Hz), 4.18 (1H, ddd, $J = 10.6$, 2.2, 2.2 Hz), 3.85–3.78 (2H, m), 3.63–3.56 (2H, m), 2.79 (1H, s), 1.05–0.97 (2H, m), 0.36 (9H, m); ^{13}C-NMR (400 MHz, $CDCl_3$) δ. 135.9, 132.0, 127.9, 127.9, 127.8, 127.6, 126.1, 124.9, 80.4, 72.6, 66.5, 18.6, −1.4. HRMS Calc. for $C_{15}H_{22}O_2Si$ [M^+]: 262.1389. Found: 262.1388.

6.1.6. (1S,2S)-2-Benzyloxy-1,2-dihydro-naphthalen-1-ol (**19**)

Following the general procedure, **19** was obtained as a crystalline solid (1.22 g, 70%). The ee was determined to be $>98\%$ using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 29.0 and 32.5 min (major). $R_f = 0.34$ on silica gel (20% ethyl acetate:hexanes); m.p. 52–54°C (Et_2O); $[\alpha]_D^{25} = +167.3$ ($c = 10.0$, $CHCl_3$); IR (KBr, cm^{-1}) 3305 (br), 3020 (w), 2876 (w), 1496 (m), 1352 (m), 1281 (m), 1169 (m), 1050 (s), 777 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.58–7.56 (1H, m), 7.41–7.22 (7H, m), 7.22–7.07 (1H, m), 6.46 (1H, dd, $J = 9.9$, 2.1 Hz), 6.05 (1H, dd, $J = 9.9$, 2.1 Hz), 4.98 (1H, d, $J = 10.4$ Hz), 4.78 (1H, d, $J = 11.7$ Hz), 4.63 (1H, d, $J = 11.7$ Hz), 4.33 (1H, ddd, $J = 10.4$, 2.2, 2.2 Hz), 2.61 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 138.0, 135.9, 131.9, 128.5, 128.3, 128.1, 127.9, 127.9, 127.8, 127.4, 126.2, 125.1, 80.4, 72.6, 71.3. HRMS Calc. for $C_{17}H_{16}O_2$ [M^+]: 252.1150. Found: 252.1148.

6.1.7. (1S,2S)-2-(4-methoxybenzyloxy-1,2-dihydro-naphthalen-1-ol (**20**)

Following the general procedure, 20 was obtained as a crystalline solid (1.18 g, 87%). The ee was determined to be 97% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 37.1 and 42.1 min (major). $R_f = 0.53$ on silica gel (30% ethyl acetate:hexanes); m.p. 63–64°C (Et_2O); $[\alpha]_D^{25} = +138.5$ ($c = 10.5$, $CHCl_3$); IR (KBr, cm^{-1}) 3435 (br), 3035 (m), 2836 (s), 1612 (s), 1513 (s), 1454 (m), 1249 (s), 1082 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59–7.57 (1H, m), 7.32 (2H, ddd, $J = 8.7$, 2.8, 1.9 Hz), 7.28–7.22 (1H, m), 6.90 (2H, ddd, $J = 8.7$, 2.8, 1.9 Hz), 6.46 (1H, dd, $J = 9.9$, 2.1 Hz), 6.04 (1H, dd, $J = 9.9$, 2.4 Hz), 4.96 (1H, d, $J = 10.1$ Hz), 4.64 (1H, dd, $J = 57.1$, 11.4 Hz), 4.32 (1H, ddd, $J = 10.2$, 2.2, 2.2 Hz), 3.80 (1H, s), 2.96 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 159.2, 135.9, 131.9, 129.9, 129.5, 128.1, 127.8, 127.6, 127.5, 126.1, 125.0, 113.8, 80.0, 72.5, 70.9, 55.1. HRMS Calc. for $C_{17}H_{16}O_2$ [M^+]: 252.1150. Found: 252.1148.

6.1.8. (1S,2S)-2-(2,2,2-Trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-ol (**21**)

Following the general procedure, **21** was obtained as a white crystalline solid (594 mg, 70%). The ee was determined to be 98% using HPLC analysis on a Chiralcel OD column, $\lambda = 254$ nm. Retention times in 4% isopropanol in hexanes were 11.3 (major) and 13.3 min. $R_f = 0.41$ on silica gel (20% ethyl acetate:hexanes); m.p. 79–80°C (Et_2O); $[\alpha]_D^{25} = 145.4$ ($c = 12.6$, $CHCl_3$); IR (KBr, cm^{-1}) 3354 (br), 3036 (w), 2939 (w), 1455 (w), 1275 (s), 1169 (s), 1050(m), 977 (m); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57–7.55 (1H, m), 7.30–7.23 (2H, m), 7.10–7.08 (1H, m), 6.48 (1H, dd, $J = 9.9$, 2.0 Hz), 5.94 (1H, dd, $J = 9.9$, 2.4 Hz), 4.96 (1 H, d, $J = 2.2$ Hz), 4.38 (1H, ddd, $J = 9.9$, 2.4, 2.2 Hz), 4.03 (2H, q, $J^{H-F} = 8.6$ Hz), 2.55 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 135.5, 131.7, 129.2, 128.3, 128.1, 126.6, 125.9, 125.2, 122.4, 83.0, 72.8, 67.0 (q, $J^{C-F} = 34.4$ Hz). HRMS Calc. for $C_{12}H_{11}O_2F_3$ [M^+]: 244.0711. Found: 244.0720.

6.1.9. (1S,2S)-2-(2,2,2-Trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-ol (**22**)

Following the general procedure, **22** was obtained as a white solid (974 mg, 90%). The ee was determined to be 93% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 11.3 and 17.6 min (major); $R_f = 0.28$ on silica gel (10% ethyl acetate:hexanes); m.p. 88.5–90°C (Et_2O); $[\alpha]_D^{25} = +101.8$ ($c = 10.9$, $CHCl_3$); IR (KBr, cm^{-1}) 3191 (br), 2937 (m), 1379 (s), 1280 (s), 1247 (s), 1194 (s), 1100 (s), 954 (s), 753 (m); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.55–7.53 (1H, m),

7.31–7.26 (2H, m), 7.11–7.09 (1H, m), 6.49 (1H, dd, $J = 9.9$, 2.1 Hz), 5.92 (1H, dd, $J = 9.9$, 2.4 Hz), 5.07 (1H, dd, $J = 9.7$, 5.0 Hz), 4.63 (1H, ddd, $J = 9.9$, 1.5, 1.5 Hz), 4.58 (1H, h, $J^{H-F} = 6.1$ Hz), 2.50 (1H, d, $J = 4.2$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 135.2, 131.5, 129.7, 128.5, 128.3, 126.7, 125.2, 122.9, 120.1, 85.4, 75.4 (h, $J^{C-F} = 32.2$ Hz), 73.5. HRMS Calc. for $C_{13}H_{10}O_2F_6$ [M^+]: 312.0585 Found: 312.0574.

6.1.10. (1S,2S)-6,7-Difluoro-2-methoxy-1,2-dihydro-naphthalen-1-ol (23)

Following the general procedure, **23** was obtained as a white crystalline solid (74.9 mg, 88%). The ee was determined to be 96.4% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 8.9 and 10.1 min (major). $R_f = 0.27$ on silica gel (30% ethyl acetate:hexanes); m.p. 129–131°C (Et_2O); $[\alpha]_D^{25} = +134.4$ ($c = 9.3$, $CHCl_3$); IR (KBr, cm^{-1}) 3269 (br), 2937 (w), 1597 (m), 1503 (s), 1306 (s), 1103 (s), 893 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (1H, ddd, $J^{H-F} = 10.8$, 7.8 Hz, $J^{H-H} = 0.6$ Hz), 6.85 (1H, dd, $J^{H-F} = 10.9$, 7.8 Hz), 6.31 (1H, dd, $J = 10.0$, 2.0 Hz), 6.05 (1H, dd, $J = 10.0$, 2.0 Hz), 4.79 (1H, d, $J = 11.0$ Hz), 4.05 (1H, ddd, $J = 11.0$, 2.0, 2.0 Hz), 3.49 (3H, s), 2.94 (1H, d, $J = 2.2$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 151.0 (d, $J^{H-F} = 12.5$ Hz), 148.5 (dd, $J^{H-F} = 12.5$,2.9 Hz), 133.2 (dd, $J^{H-F} = 5.2$, 3.6 Hz), 128.9 (dd, $J^{H-F} = 6.6$, 4.4 Hz), 128.0 (d, $J^{H-F} = 2.2$ Hz), 126.5 (dd, $J^{H-F} = 2.2$, 1.5 Hz), 115.1 (d, $J^{H-F} = 18.3$ Hz), 114.8 (d, $J^{H-F} = 19.8$ Hz), 82.3, 72.0, 57.0. HRMS Calc. for $C_{11}H_{10}O_2F_2$ [M^+]: 212.0649. Found: 212.0658.

6.1.11. (1S,2S)-6-Methoxy-5,6-dihydro-naphtho-[2,3-d][1,3]dioxol-5-ol (24)

Following the general procedure, **24** was obtained as a white crystalline solid (127.5 mg, 90%). The ee was determined to be 95% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 19.2 min (major) and 22.6 min. $R_f = 0.24$ on silica (30% ethyl acetate:hexanes); m.p. 117–119°C (Et_2O); $[\alpha]_D^{25} = +298.7$ ($c = 11.1$, $CHCl_3$); IR (KBr, cm^{-1}) 3248 (br), 2926 (s), 1600 (m), 1483 (s), 1260 (s), 1113 (s), 941 (s), 876 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.10 (1H, s), 6.59 (1H, s), 6.34 (1H, d, $J = 9.9$ Hz), 5.92–5.99 (3H, m), 4.77 (1H, d, $J = 9.9$ Hz), 4.04 (1H, d, $J = 10.1$ Hz), 3.49 (3H, s), 2.2 (1Hs); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 147.2, 146.9, 130.4, 128.1, 126.0, 124.8, 107.1, 106.7, 101.0, 82.0, 72.3, 56.7. HRMS Calc. for $C_{12}H_{12}O_4$ [M^+]: 220.0736. Found: 220.0684.

6.1.12. (1S,2S)-6,7-Dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol (25)

Following the general procedure, **25** was obtained as a white crystalline solid (171.6 mg, 79%). The ee was determined to be 97% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 16.8 (major) and 19.3 min. $R_f = 0.39$ on silica gel (50% ethyl acetate:hexanes); m.p. 114–116°C (Et_2O); $[\alpha]_D^{25} = -197.1$ ($c = 10.0$, $CHCl_3$); IR (KBr, cm^{-1}) 3349 (s), 2901 (m), 1700 (w), 1532 (w), 1404 (m), 1258 (m), 1081 (s), 936 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.96–6.93 (1H, m), 6.23–6.19 (1H, m), 4.89 (1H, s), 3.96–3.90 (1H, m), 3.38–3.35 (3H, m), 2.61–2.57 (3H, m), 2.54 (3H, s), 1.82–1.54 (1H, m); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 137.3, 134.4, 133.2, 129.7, 129.5, 129.0, 128.1, 125.3, 75.3, 66.6, 56.6, 21.0, 20.6. HRMS Calc. for $C_{13}H_{16}O_2Br_2$ [M^+]: 361.9518. Found: 361.9335.

6.2. General procedure for the ARO reactions with phenol nucleophiles

To a flame dried round bottom flask, $[Rh(COD)Cl]_2$, (*S*,*R*)-PPF–P^{t}Bu$_2$ (unless otherwise indicated) and **1** were added. THF (2 ml) and the phenol nucleophile were then added followed by heating to 80°C for 1.5 h. The reaction mixture was then poured in to ether and washed three times with 5% aqueous NaOH. The aqueous layers were combined and back extracted three times with ether. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting crude product was purified by flash chromatography.

6.2.1. (1S,2S)-2-Phenoxy-1,2-dihydro-naphthalen-1-ol (26)

Following the general procedure, **26** was obtained as a white crystalline solid (130.7 mg, 83%). The ee was determined to be 99.2% using HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 15.2 (major) and 17.8 min. $R_f = 0.26$ on silica gel (10% ethyl acetate:hexanes); m.p. 109–110°C (Et_2O); $[\alpha]_D^{25} = +204.7$ ($c = 10.1$, $CHCl_3$); IR (KBr, cm^{-1}) 3337 (br), 3029 (w), 2866 (w), 1600 (m), 1496 (s), 1249 (s), 1062 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (1H, m), 7.33–7.25 (4H, m), 7.13–7.11 (1H, m), 7.01–6.95 (3H, m), 6.51 (1H, dd, $J = 9.9$, 1.6 Hz), 6.02 (1H, dd, $J = 9.9$, 2.2 Hz), 5.19 (1H, d, $J = 10.4$ Hz), 5.11 (1H, ddd, $J = 10.4$, 2.0, 2.0 Hz), 2.66 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 157.4, 135.5, 131.9, 129.7, 129.0, 128.2, 128.0, 126.4, 126.1, 125.2, 121.5, 115.9, 79.1, 72.4. HRMS Calc. for $C_{16}H_{14}O_2$ [M^+]: 238.0994. Found: 238.0984.

6.2.2. (1S,2S)-2-(4-Fluorophenoxy)-1,2,-dihydro-naphthalen-1-ol (27)

Following the general procedure, **27** was obtained as a white crystalline solid (163 mg, 92%). The ee was determined to be 97% by HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm). Retention times in 1.5% isopropanol in hexanes were 28.1 (major) and 29.5 min.

$R_f = 0.39$ on silica (20% ethyl acetate in hexanes); m.p. 127–129°C (Et_2O); $[\alpha]_D^{25} = +216$ ($c = 9.5$, $CHCl_3$). IR (KBr, cm^{-1}) 3309 (b), 3071 (w), 2864 (w), 1504 (s), 1284 (m), 1052 (s), 781 (s), 692 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.63–7.61 (1H, m), 7.31–7.26 (2H, m), 7.12–7.10 (1H, m), 7.00–6.95 (2H, m), 6.92–6.88 (2H, m), 6.51 (1H, dd, $J = 2.1$, 9.9 Hz), 5.98 (1H, dd, $J = 2.2$, 9.9 Hz), 5.15 (1H, dd, $J = 3.6$, 10.0 Hz), 5.01 (1H, ddd, $J = 2.1$, 2.1, 10.1 Hz), 2.54 (1H, d, $J = 3.8$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 157.6 (d, $J^{C-F} = 239$ Hz), 156.4, 153.4, 135.4, 131.8, 129.1, 128.2, 126.5, 125.7, 125.2, 117.5 (d, $J^{C-F} = 8$ Hz), 116.1 (d, $J^{C-F} = 23.5$ Hz);. HRMS Calc. for $[M^+]$ ($C_{16}H_{13}O_2F$): 256.0810. Found: 256.0911.

6.2.3. (1S,2S)-2-(4-Chlorophenoxy)-1,2,-dihydro-naphthalen-1-ol (**28**)

Following the general procedure, **28** was obtained as a white crystalline solid (169 mg, 89%). The ee was determined to be 92% by formation of Mosher's ester. $R_f = 0.47$ on silica (20% ethyl acetate in hexanes); m.p. 125–125.5°C (Et_2O); $[\alpha]_D^{25} = +150$ ($c = 10.6$, $CHCl_3$). IR (KBr, cm^{-1}) 3302 (br), 3064 (w), 2874 (w), 1590 (m), 1489 (s), 1362 (w), 1230 (s), 1052 (m), 890 (w), 846 (m), 778 (s), 663 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.65–7.64 (1H, m), 7.33–7.26 (4H, m), 7.16–7.13 (1H, m), 6.91(1H, ddd, $J = 2.0$, 2.0, 8.9 Hz), 6.55 (1H, dd, $J = 1.8$, 9.9 Hz), 5.99 (1H, dd, $J = 2.2$, 9.9 Hz), 5.19 (1H, dd, $J = 3.8$, 10.0 Hz), 5.07 (1H, ddd, $J = 2.0$, 2.0, 10.1 Hz), 2.56 (1H, d, $J = 4.0$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 155.8, 135.2, 131.7, 129.5, 129.3, 128.2, 128.1, 126.5, 126.2, 125.3, 125.2, 116.9, 79.2, 72.1. HRMS Calc. for $[M - H_2O]^+$ ($C_{16}H_{11}OCl$): 254.0498. Found: 254.0499.

6.2.4. (1R,2R)-2-(4-Bromophenoxy)-1,2-dihydro-naphthalen-1-ol (**29**)

Following the general procedure using (*R*,*S*)-PPF-P^{t}Bu$_2$, **29** was obtained as a white crystalline solid (239.7 mg, 90%). The ee was determined by debrominating **29** (40 mg, 0.11 mmol) by reaction with ^{t}BuLi (0.32 ml, 1.7 M) in diethyl ether (2 ml) at -78°C followed by quenching with isopropanol. Extraction with ether from water, washing with brine, drying over anhydrous sodium sulfate and removal of the solvents in vacuo gave a white crystalline solid **26** (24 mg, 92%). The ee was determined to be 96.8% by HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 15.2 and 17.5 min (major). $R_f = 0.26$ on silica gel (10% ethyl acetate:hexanes); m.p. 145–146°C (Et_2O); $[\alpha]_D^{25} = -135.7$ ($c = 10.2$, $CHCl_3$); IR (KBr, cm^{-1}) 3290 (br), 3060 (m), 2870 (w), 1583 (m), 1484 (s), 1227 (s), 1052 (m), 980 (s), 776 (s); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70–7.65 (1H, m), 7.44–7.42 (2H, m), 7.35–7.32 (2H, m), 7.18 – 7.16 (1H, m), 6.88–6.86 (2H, m), 6.56 (1H, dd, $J = 10.0$, 2.0 Hz), 6.00 (1H, dd, $J = 9.7$, 2.2 Hz), 5.20 (1H, dd, $J = 9.7$, 3.6 Hz), 5.09 (1H, ddd, $J = 10.0$, 2.0, 2.0 Hz), 2.70 (1H, d, $J = 3.9$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$) δ 156.5, 135.3, 132.5, 131.7, 129.3, 128.3, 128.1, 126.5, 125.3, 117.6, 113.7, 79.4, 72.2. HRMS Calc. for $C_{16}H_{11}OBr$ $[M - H_2O]^+$ 297.9994. Found: 297.9995.

6.2.5. (1S,2S)-2-(4-Iodophenoxy)-1,2,-dihydro-naphthalen-1-ol (**30**)

Following the general procedure, **30** was obtained as a white crystalline solid (193 mg, 73%). The ee was determined by deiodinating **30** (40 mg, 0.11 mmol) by reaction with t-BuLi (0.32 ml, 1.7M) in diethyl ether (2 ml) at -78°C followed by quenching with isopropanol. Extraction with ether from water, washing with brine, drying over anhydrous sodium sulfate and removal of the solvents in vacuo gave a white crystalline solid **26** (24 mg, 92%). The ee was determined to be 98% by HPLC analysis on a Chiralcel OD column, $\lambda = 256$ nm. Retention times in 4% isopropanol in hexanes were 15.2 (major) and 17.9 min; $R_f = 0.44$ on silica (20% ethyl acetate in hexanes); m.p. 160–162°C (Et_2O); $[\alpha]_D^{25} = +107$ ($c = 9.7$, $CHCl_3$). IR (KBr, cm^{-1}) 3264 (br), 3050 (w), 2926 (w), 2843 (w), 1581 (m), 1485 (s), 1388 (w), 1279 (m), 1246 (s), 1046 (m), 824 (m), 780 (m), 571 (w); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.63–7.61 (1H, m), 7.58–7.55 (2H, m), 7.30–7.27 (2H, m), 7.13–7.11 (1H, m), 6.73 (2H, ddd, $J = 2.2$, 2.2, 9.0 Hz), 6.52 (1H, dd, $J = 1.8$, 9.8 Hz), 5.96 (1H, dd, $J = 2.2$, 9.8 Hz), 5.16 (1H, d, $J = 10.0$ Hz), 5.05 (1H, ddd, $J = 2.0$, 2.0, 10.0 Hz), 2.54 (1H, s); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 157.3, 138.5, 135.3, 131.7, 129.4, 128.3, 128.1, 126.6, 125.3, 125.3, 118.1, 83.6, 79.2, 72.2. HRMS Calc. for $[M - H_2O]^+$ ($C_{16}H_{11}OI$): 345.9855. Found: 345.9849.

6.2.6. (1S,2S)-2-(4-Acylphenoxy)-1,2,-dihydro-naphthalen-1-ol (**31**)

Following the general procedure, **31** was obtained as a white crystalline solid (177 mg, 91%). The ee was determined to be >99% by formation of Mosher's ester; $R_f = 0.28$ on silica (30% ethyl acetate in hexanes); m.p. 124–126°C (Et_2O); $[\alpha]_D^{25} = +153$ ($c = 9.8$, $CHCl_3$). IR (KBr, cm^{-1}) 3367 (b), 3069 (w), 2916 (w), 1668 (s), 1601 (s), 1265 (s), 1053 (m), 835 (m), 779 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.94 (2H, d, $J = 8.8$ Hz), 7.66–7.64 (1H, m), 7.34–7.27 (2H, m), 7.16–7.14 (1H, m), 6.98 (2H, d, $J = 8.8$ Hz), 6.57 (1H, d, $J = 9.9$ Hz), 5.99 (1H, d, $J = 9.9$ Hz), 5.21 (2H, s), 2.85 (1H, s), 2.56 (3H, s); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 196.8, 161.4, 135.3, 131.7, 130.7, 130.6, 129.6, 128.3, 128.1, 126.6, 125.4, 125.0, 115.2, 79.0, 72.0, 26.3. HRMS Calc. for $[M - H_2O]^+$ ($C_{18}H_{14}O_2$): 262.0994. Found: 262.0989.

*6.2.7. (1S,2S)-2-(α,α,α)-Trifluoro-4-methylphenoxy)-1,2,-dihydro-naphthalen-1-ol (**32**)*

Following the general procedure, **32** was obtained as a white crystalline solid (184 mg, 87%). The ee was determined to be 95% by HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 4% isopropanol in hexanes were 14.8 and 17.3 min (major). $R_f = 0.46$ on silica (20% ethyl acetate in hexanes); m.p. 118–119°C (Et_2O); $[\alpha]_D^{25} = +178$ ($c = 9.6$, $CHCl_3$). IR (KBr, cm^{-1}) 3360 (br), 3061 (w), 2874 (w), 1617 (m), 1518 (m), 1326 (s), 1103 (s), 1051 (m), 839 (m), 782 (m), 745 (w); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.63–7.54 (1H, m), 7.55 (2H, d, $J = 8.6$ Hz), 7.33–7.24 (2H, m), 7.14–7.12 (1H, m), 7.01 (2H, d, $J = 8.6$ Hz), 6.55 (1H, dd, $J = 1.6$, 9.9 Hz), 5.97 (1H, dd, $J = 2.0$, 9.9 Hz), 5.21–5.13 (2H, m), 2.47 (1H, d, $J = 3.6$ Hz); ^{13}C-NMR (400 MHz, $CDCl_3$): δ 159.9, 135.2, 131.7, 129.6, 128.4, 128.2, 127.1 (q, $J^{C-F} = 3.6$ Hz), 126.6, 125.4, 124.9, 123.4 (d, $J^{C-F} = 33.0$ Hz), 122.9 (d, $J^{C-F} = 271.6$ Hz), 115.6, 79.1, 72.1; HRMS Calc. for [M^+] ($C_{17}H_{13}O_2F_3$): 306.0868. Found: 306.0852.

*6.2.8. (1S,2S)-2-(4-Methylphenoxy)-1,2,-dihydro-naphthalen-1-ol (**33**)*

Following the general procedure, **33** was obtained as a white crystalline solid (57 mg, 65%). The ee was determined to be 91% by HPLC analysis on a Chiralcel OD column, $\lambda = 256$ nm. Retention times in 1% isopropanol in hexanes were 33.8 (major) and 37.1 min. $R_f = 0.49$ on silica (20% ethyl acetate in hexanes); m.p. 80–81°C (Et_2O); $[\alpha]_D^{25} = +145$ ($c = 12.1$, $CHCl_3$). IR (KBr, cm^{-1}) 3303 (br), 3050 (w), 2210 (m), 1598 (s), 1503 (s), 1238 (s), 1025 (m), 859 (m), 778 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.67–7.65 (1H, m), 7.33–7.28 (2H, m), 7.14–7.11 (3H, m), 6.88 (2H, d, $J = 8.4$ Hz), 6.51 (1H, dd, $J = 1.8$, 9.9 Hz), 6.04 (1H, dd, $J = 2.0$, 9.9 Hz), 5.20 (1H, dd, $J = 1.6$, 10.2 Hz), 5.09 (1H, ddd, $J = 1.8$, 1.8, 10.2 Hz), 2.87 (1H, d, $J = 2.7$ Hz), 2.33 (3H, s). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 155.0, 135.4, 131.8, 130.7, 130.1, 128.8, 128.1, 127.9, 126.4, 126.2, 125.1, 115.6, 79.0, 72.3, 20.5. HRMS Calc. for [M^+] ($C_{17}H_{16}O_2$): 252.1150. Found: 252.1140.

*6.2.9. (1S,2S)-2-(4-Cyanophenoxy)-1,2,-dihydro-naphthalen-1-ol (**34**)*

Following the general procedure, **34** was obtained as a white crystalline solid (160 mg, 88%). The ee was determined to be 97% by HPLC analysis on a Chiralcel OD column, $\lambda = 256$ nm. Retention times in 3% isopropanol in hexanes were 35.3 and 37.7 min (major). $R_f = 0.40$ on silica (30% ethyl acetate in hexanes); m.p. 140–141°C (Et_2O); $[\alpha]_D^{25} = +182.3$ ($c = 11.2$, $CHCl_3$) IR (KBr, cm^{-1}) 3303 (b) 3050 (w) 2210 (m) 1598 (s) 1503 (s) 1238 (s) 1025 (m) 859 (m) 778 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.62–7.57 (3H, m), 7.33–7.27 (3H, m), 7.14–7.12 (1H, m), 6.56 (1H, dd, $J = 1.4$, 9.7 Hz), 5.93 (1H, dd, $J = 1.4$, 9.7 Hz), 5.20–5.13 (2H, m), 2.25 (1H, s). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 160.8, 135.0, 134.2, 131.5, 130.0, 128.5, 128.3, 126.7, 125.4, 124.4, 119.0, 116.2, 104.6, 79.2, 72.0. HRMS Calc. for $[M - H_2O]^+$ ($C_{17}H_{11}ON$): 245.0841. Found: 245.0845.

*6.2.10. (1S,2S)-2-(4-Methoxyphenoxy)-1,2,-dihydro-naphthalen-1-ol (**35**)*

Following the general procedure, **35** was obtained as a white crystalline solid (159 mg, 85%). The ee was determined to be 95% by HPLC analysis on a Chiralcel OD column, $\lambda = 256$ nm. Retention times in 4% isopropanol in hexanes were 22.1 (major) and 25.9 min. $R_f = 0.33$ on silica (20% ethyl acetate in hexanes); m.p. 91–92°C (Et_2O); $[\alpha]_D^{25} = +129$ ($c = 9.9$, $CHCl_3$); IR (KBr, cm^{-1}) 3349 (br), 3050 (w), 2822 (w), 1508 (s), 1233 (s), 1046 (m), 825 (m), 751 (m), 695 (w); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66–7.64 (1H, m), 7.30–7.27 (2H, m), 7.12–7.10 (1H, m), 6.91 (2H, ddd, $J = 2.3$, 2.3, 9.1 Hz), 6.84 (2H, ddd, $J = 2.4$, 2.4, 9.2 Hz), 6.49 (1H, dd, $J = 2.0$, 9.9 Hz), 6.02 (1H, dd, $J = 2.4$, 9.9 Hz), 5.17 (1H, dd, $J = 3.3$, 10.1 Hz), 5.02 (1H, ddd, $J = 2.0$, 2.0, 10.3 Hz), 3.77 (3H, s), 3.12 (1H, d, $J = 3.4$ Hz). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 154.3, 151.2,135.5, 131.9, 128.7, 128.1, 127.9, 126.4, 126.3, 125.2, 117.2, 114.8, 80.0, 72.4, 55.7. HRMS Calc. for [M^+] ($C_{17}H_{14}O_2$): 250.0994. Found: 250.1006.

*6.2.11. (1S,2S)-2-(3-Bromophenoxy)-1,2,-dihydro-naphthalen-1-ol (**36**)*

Following the general procedure, **36** was obtained as a white crystalline solid (200 mg, 92%). The ee was determined to be 96% by HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5% isopropanol in hexanes were 22.8 and 32.1 min (major). $R_f = 0.44$ on silica (20% ethyl acetate in hexanes); m.p. 120–122°C (Et_2O); $[\alpha]_D^{25} = +254°$ ($c = 9.2$, $CHCl_3$). IR (KBr, cm^{-1}) 3341 (br), 3071 (w), 2884 (w), 1581 (m), 1472 (s), 1358 (m), 1237 (s), 1028 (s), 987 (s), 780 (s), 689 (m), 569 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.57–7.62 (1H, m), 7.22–7.30 (2H, m), 7.14–7.08 (4H, m), 6.82–6.88 (1H, m), 6.49 (1H, dd, $J = 1.4$, 9.9 Hz), 5.94 (1H, dd, $J = 2.1$, 9.9 Hz), 5.13 (1H, dd, $J = 2.9$, 9.9 Hz), 5.03 (1H, ddd, $J = 1.9$, 1.9, 9.9 Hz), 2.76 (1H, d, $J = 3.6$ Hz). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 158.1, 135.3, 131.7, 130.7, 129.6, 128.3, 128.1, 126.5, 125.3, 125.3, 124.5, 122.9, 119.2, 114.5, 79.3, 72.1. HRMS calculated for $[M - H_2O]^+$ ($C_{16}H_{11}OBr$): 297.9993. Found: 297.9976.

*6.2.12. (1S,2S)–2-(2-Bromophenoxy)-1,2,-dihydro-naphthalen-1-ol (**37**)*

Following the general procedure, **37** was obtained as a white crystalline solid (206 mg, 94%). The ee was determined to be 97% by HPLC analysis on a Chiralcel OD column, $\lambda = 486$ nm. Retention times in 1.5%

isopropanol in hexanes were 22.8 and 32.1 min (major). $R_f = 0.44$ on silica (20% ethyl acetate in hexanes); m.p. 120–122°C (Et_2O); $[\alpha]_D^{25} = +254$ ($c = 9.2$, $CHCl_3$). IR (KBr, cm^{-1}) 3341 (br), 3071 (w), 2884 (w), 1581 (m), 1472 (s), 1358 (m), 1237 (s), 1028 (s), 987 (s), 780 (s), 689 (m), 569 (m); ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, d $J = 6.8$ Hz), 7.58 (1H, dd, $J = 1.5$, 7.9 Hz), 7.33–7.23 (3H, m), 7.14–7.12 (1H, m), 6.95(1H, dd, $J = 1.1$, 8.2 Hz), 6.92–6.87 (1H, m), 6.52 (1H, dd, $J = 2.0$, 9.9 Hz), 6.06 (1H, dd, $J = 1.8$, 9.9 Hz), 5.32 (1H, d, $J = 11.0$ Hz), 5.10 (1H, ddd, $J = 2.0$, 2.0, 11.0 Hz), 2.85 (1H, d, $J = 3.2$ Hz). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 154.3, 135.4, 133.6, 131.8, 129.1, 128.6, 128.3, 128.0, 126.4, 126.0, 124.9, 122.9, 115.6, 113.5, 82.2, 72.5. HRMS Calc. for $[M - H_2O]^+$ ($C_{16}H_{11}OBr$): 297.9993. Found: 297.9976.

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