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Asymmetric transfer hydrogenation of unsaturated ketones; factors influencing 1,4- vs 1,2- regio- and enantioselectivity, and alkene vs alkyne directing effects

Thomas H. Hall, Hannah Adams, Vijyesh K. Vyas, K.L. Michael Chu, Martin Wills*

Department of Chemistry, The University of Warwick, Coventry, CV4 7AL, UK

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Dedicated to the memory of Professor Jonathan M. J. Williams, a brilliant scientist and a friend since our PhD years. Jon once said to me at a conference some time ago that he was trying to introduce the term "hydrogen borrowing" to synthetic chemistry, and hoped it would catch on. It certainly did.

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Reduction
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Alkyne
Enantioselective
Regioselective

ABSTRACT

A detailed study has been completed on the asymmetric transfer hydrogenation (ATH) of a series of enones using Ru(II) catalysts. Electron-rich rings adjacent to the C=O group reduce the level of C=O reduction compared to C=C. The ATH reaction can readily discriminate between double and triple bonds adjacent to ketones, reducing the double bond but leaving a triple bond intact in the major product.

1. Introduction

Asymmetric transfer hydrogenation (ATH) of ketones using Ru(II)/arene/TsDPEN complexes such as **1**–**7** (Fig. 1) is a well-established process that generates alcohols in high enantioselectivities [1-6]. The catalysts are well-suited to the reductions of acetophenone derivatives and alkynyl(acetylenic) ketones, which are reduced in high ee through relatively well-understood transition states (Fig. 2) [2]. Complex **1** was first reported by Noyori et al. in 1995 [3] and in 2005, we reported tethered complexes of type **2** [4], which have subsequently seen widespread application [5]. Related complexes, **3** [4], **4** [5], **5** [5], **6** [4] and **7** [4] have been reported and widely studied in ATH applications [6].

ATH, using the Ru(II) catalysts **1**–**5**, of α,β-unsaturated ketones reveals a rather more complex pattern of selectivities. Deng et al. [7] described the reductions of ketones with catalyst **1** to the corresponding allylic alcohols, using a combination of formic acid and trimethylamine (FA/TEA) as solvent and reducing agent, in high yield; enantioselectivities depended on the substitution pattern on the alkene (Fig. 3a). Using chalcone as the substrate for TH with the achiral ligand N-tosylethyenediamine (TsEN), the reduction product was a ca. 3:1 mixture of saturated ketone and saturated alcohol [7].

Increasing the steric bulk of the alkyl substituent on benzylidineacetones has a complicated effect on the reduction selectivity using catalyst **1** (Fig. 3b) [8]. The ethyl substituent increased the 1,2

* Corresponding author.
E-mail address: m.wills@warwick.ac.uk (M. Wills).

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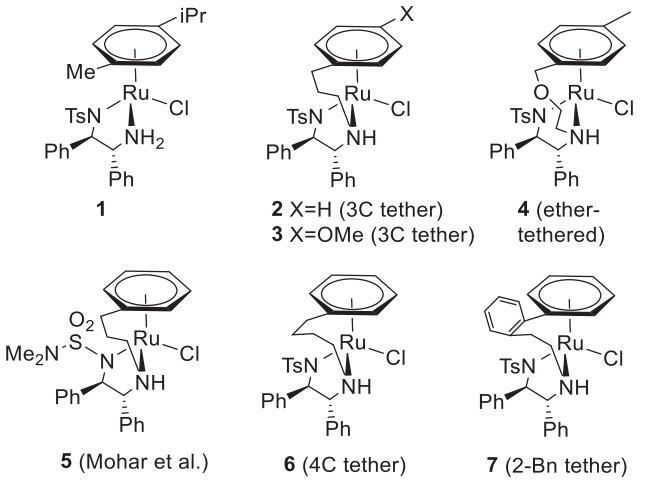


Fig. 1. Ru(II)/arene/TsDPEN complexes reported for the ATH of ketones and imines.

selectivity whilst the larger isopropyl group gave equal proportions of 1,2- and 1,4-reduction products in lower conversion. The *tert*-butyl substituent strongly disfavoured all ketone reduction. Noyori catalyst **1** was applied to the ATH of β-alkyl β-trifluoromethyl α,β-unsaturated ketones to yield 1,2-reduction products selectively [9]. Aryl-ketone substrates were reduced in high ee as expected, while a methyl ketone gave a product in poor enantioselectivity (Fig. 3c).

The (non-asymmetric) TH of C=C bonds in enones, using TsEN as a ligand in the Ru(II) complex, can be promoted by incorporating an electron withdrawing groups into the substrate [7], including nitro, ester, nitrile and carboxylic acids. Some asymmetric examples of C=C reduction have been reported [7]. A series of α-substituted cyclic α,β-unsaturated ketones were reduced selectively with the Noyori-Ikariya complex **1** to the corresponding cycloalkenols **8**–**10**, although the carbamate substrate also yielded a small amount of the 1,4-reduction product **11** (Fig. 4) [10]. The acyclic analogue of **10** in contrast was reduced with complete 1,4-alkene selectivity, yielding a mixture of 33% saturated ketone and 67% saturated alcohol.

In some cases an enone can be formed *in situ* and directly reduced. Adolfsson's α-amino acid hydroxyamide ligand **12** has been applied to ATH of allylic alcohols by oxidation to the corresponding enone, followed by complete reduction of alkene and carbonyl functionalities (Fig. 5) [11]. Use of the stronger base potassium *tert*-butoxide was important for the success of this reduction.

Kosmalski applied the Noyori catalyst **1** to the reduction of β-dimethylamino-acetophenone and found that the main product was the partially reduced elimination product [12]. Therefore there is still scope for increased understanding of the subtle effects of substrate structure on the regioselectivity of enone ATH. In this paper, we report our results from our investigation into this area.

2. Results and discussion

We first examined the ATH of β-chloropropiophenone **13** [13]. Reduction using catalyst *(S,S)*-**2** in FA/TEA at 60 °C gave complete conversion to 1-phenylpropan-1-ol **14**, in high enantioselectivity (Fig. 6).

Subjecting **15** to the same ATH conditions gave **14**, in identical ee as obtained previously, as did the reduction of **16**, indicating that both were likely to be common intermediates in the formation of **14**. Vinyl alcohol **17** was inert under the same conditions in contrast to the result in Fig. 5 [11] and no **17** was observed in the reduction of **15** or **16**. Initial 1,4-reduction of **15** is expected to be favourable due to the high reactivity of the unhindered mono-substituted vinyl group. *trans*-Benzylideneacetophenone **18** (chalcone) was reduced using both catalyst (*S,S*)-**2** and the methoxy analogue **3** under a variety of conditions (Table 1).

With both catalysts, 1,4-reduction was favoured. The substrate was fully consumed but some saturated ketone **20** was observed. Alcohol **19** was produced with consistently good ee of ca. 95–98% in FA/TEA for both catalysts. Compound **21** was formed with a lower ee (73–85%), which is consistent with the presence of two π systems that could compete as directing groups for reduction (Fig. 2). Catalyst (*R,R*)-**3** delivered products in slightly higher ee than (*S,S*)-**2** under the same conditions. Racemic standards were prepared using sodium borohydride; alcohol **21** was prepared by Luche reduction [12], while a sample of **20** was produced by a one pot reduction in the presence of palladium on carbon, acetic acid, isopropanol, and sodium borohydride [13]. The products ees were measured by

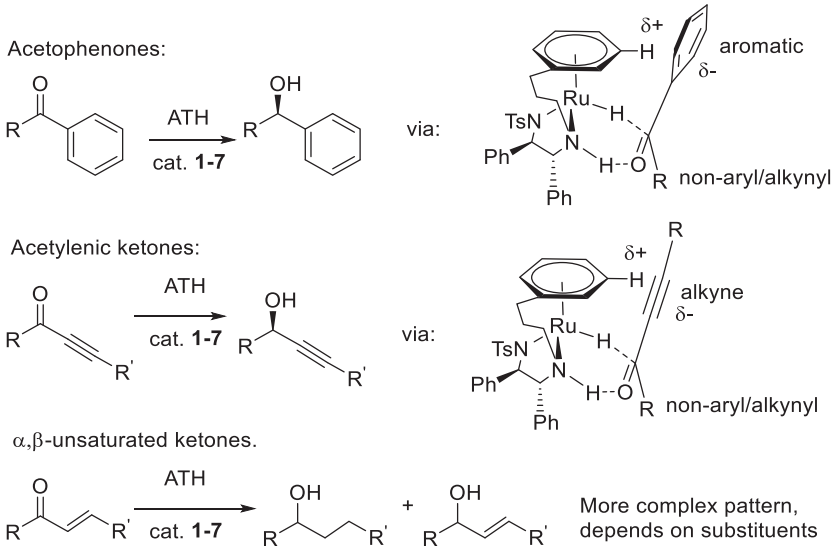


Fig. 2. Control of asymmetric reduction of various types of ketones using complex **2** (representative of **1**–**7**).

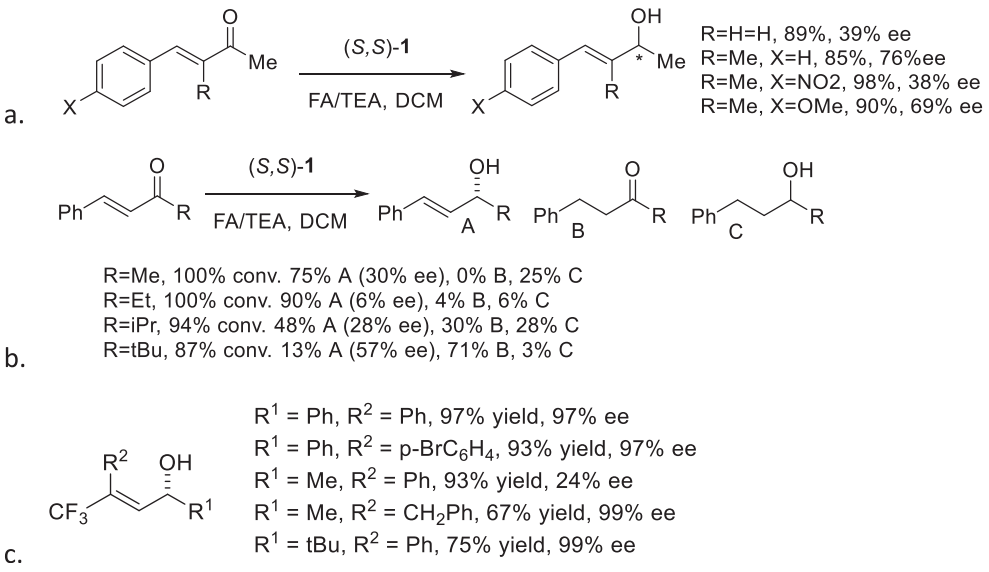


Fig. 3. a. ATH of α,β-unsaturated ketones by Deng et al. [7] b, Variation between 1,2- and 1,4-reduction of alkyl-benzylidineacetone derivatives (the ee of C was not determined) [8]. c **.** Products of selective 1,2- reduction of β-trifluoromethyl enones using catalyst **1** [9].

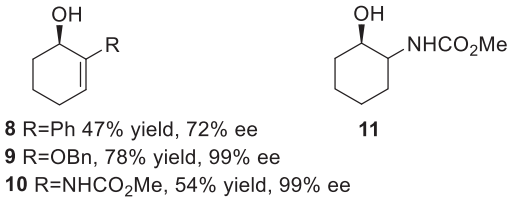


Fig. 4. Product of ATH of α−substituted cyclic enones (using catalyst **1**).

chiral HPLC, and the product ratio was determined by NMR spectroscopy to ensure that the measurement was quantitative.

Cerium trichloride [12] was tested as an additive (Table 1, entry 5), but it had only a marginal effect. However the additional methanol co-solvent was advantageous, as substrate **18** was poorly soluble in FA/TEA. Further reactions using equal quantities of FA/TEA and MeOH at lower concentration (0.5 M instead of 2 M) gave full conversion to product (Table 1, entries 3 and 4). Using H_2O/MeOH as the solvent system and sodium formate as hydrogen donor (Table 1, entry 6) [14], with (*R,R*)-**3** as the catalyst, the reduction was slower, with incomplete conversion after 45 h at 60 °C and the ee of alcohol **19** reduced to 86%. Increasing the FA/TEA/MeOH reaction temperature to 60 °C or decreasing it to 25 °C had a marginal effect on the selectivities (entries 7 and 8). Screening of alternative co-solvents in the reduction of **18** was undertaken (Supporting Information). Aprotic solvents tested performed similarly, giving similar or slightly improved 1,4-selectivity and ee compared to reactions with MeOH. Water was also tested as a co-solvent with FA/TEA, however the solubility of **18** in the aqueous FA/TEA mixture was poor, and the enantioselectivty of both products lower than for the other solvents tested.

It was expected that the configurations of both **19** and **21** were the same and this was confirmed by hydrogenating the product mixture from Table 1 entry 4 using Pt_2O as a catalyst. Given the ratio of alcohols **19** and **21**, the predicted ee of **19** after alkene hydrogenation is 97% if the configuration of both alcohols is the same, and 91% if it is different (Supporting Information). The experimental measurement of ee after hydrogenation was 97%, confirming that **19** and **21** must have the same configuration. The electronic nature of the aromatic ring adjacent to the ketone could influence the 1,4- vs 1,2-selectivity of reduction [15]. To test this, chalcone

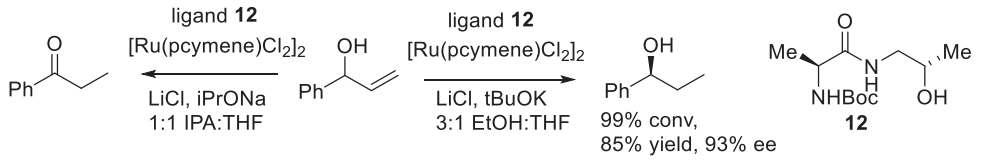


Fig. 5. Isomerisation and reduction of benzyl-vinyl alcohol [11].

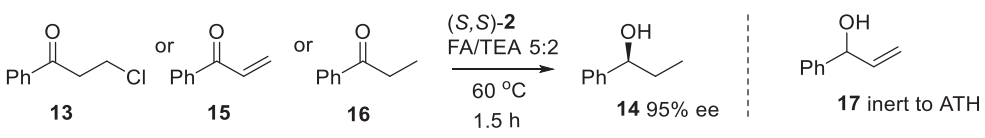
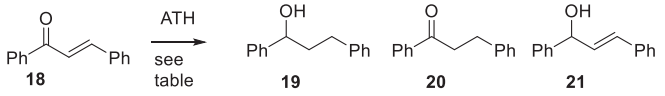


Fig. 6. Reduction of β-chloropropiophenone **13**, **14** and **15**.

Table 1
ATH of chalcone **18** and its reduction products.



Entry	Catalyst	t/h	Conv/%	20/%	**1,4**–19: **1,2**-21	19 **ee/%**	21 **ee/%**	***R/S***
1[a]	(*S,S*)-**2**	1.5	98	2	91 : 7	96	73	*S*
2[a]	(*R,R*)-**3**	4	98	2	96 : 2	98	84	*R*
3[b]	(*S,S*)-**2**	20	100	0	89 : 11	95	79	*S*
4[b]	(*R,R*)-**3**	22	100	0	96 : 4	98	85	*R*
5[c]	(*S,S*)-**2**	5.5	98	2	88 : 10	95	78	*S*
6[d]	(*R,R*)-**3**	45	94	6	94 : 0	86	–	*R*
7[b,e]	(*R,R*)-**3**	25	96	4	91 : 5	98	83	*R*
8[b,f]	(*R,R*)-**3**	18	99	1	96 : 3	96	77	*R*

Conditions.
[a] 2 M in FA/TEA, 100:1 S/C, 40 °C.
[b] 0.5 M in 5:2 FA/TEA: MeOH (1:1), 100:1 S/C, 40 °C.
[c] as b) with $CeCl_3$ additive (0.5 eq).
[d] 0.5 M in 1:1H_2O/MeOH, $NaHCO_2$, 100:1 S/C, 60 °C.
[e] at 25 °C.
[f] at 60 °C.

derivatives containing *p*-Cl, *p*-OMe and *p*-NMe_2 were reduced with catalyst (*R,R*)-**3** to products **22**–**24** (Fig. 7). Electron donating substituents slow down the rate of reduction, and increase the 1,4-selectivity. The proportion of 1,2-product was so low for the *p*-methoxy and *p*-dimethylamino products **23** and **24** respectively, that the ee of the unsaturated product could not be determined.

In order to establish the importance of each aromatic ring in the chalcone derivatives, the corresponding cyclohexyl substituted substrates were reduced by ATH (Fig. 7). The ketone with a cyclohexyl adjacent to the alkene reacted with similar selectivity to chalcone, to give **25** with a slight increase in 1,4-selectivity (97% ee). Reduction of the ketone with the cyclohexyl adjacent to the ketone, in contrast, gave different products **26** depending on which catalyst was used. In general it gave a much higher proportion of 1,2-reduction product, although 1,4-selectivity was highest under aqueous conditions using sodium formate as the hydrogen source (Fig. 7). The ee of reduction was also poor. This demonstrates the importance of the aromatic ring adjacent to the ketone for the control of enantioselectivity, but that the aromatic ring on the alkene is of secondary importance. ATH of a substrate with a β,β-disubstitution gave a product in high 1,4-selectivity, with predominant formation of the saturated alcohol **27** over the equivalent allylic alcohol although in only 55% ee.

It is known in the literature that alkynes are generally inert under ATH conditions, and are capable of acting as directing groups (Fig. 2) [3d,4,6]. It was therefore of interest to establish the outcome of the ATH of substrates containing both an alkyne and an alkene flanking the central ketone (Fig. 8).

The precursor ketones were prepared by reaction of the required lithiated acetylene with the Weinreb amide of cinnamic acid. Racemic standards were obtained for all the products and HPLC was used to directly assess the regio- and stereoselectivity of the reactions. Product ratios were also determined by ^{1}H NMR data. In the ATH of the diphenyl substrate, using (*R,R*)-**2**, the saturated and unsaturated products **28** and **29** respectively were formed in an 83:17 ratio (Fig. 8). The ee of **28** was highest, presumably because

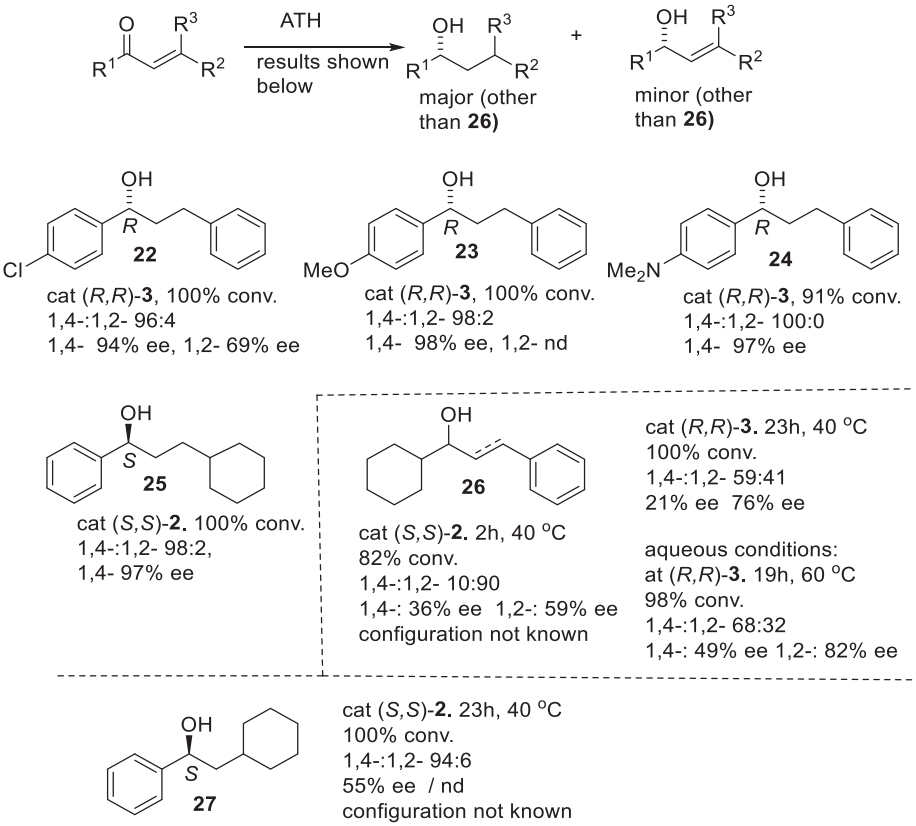


Fig. 7. Products of ATH of chalcone derivatives. Conditions: **22**–**24**: [S] = 0.5 M in 5:2 FA/TEA, MeOH (1:1), 24 h, 40 °C, 100:1 S/C, (*R,R*)-**3**. Assumed *R* product is formed by analogy with chalcone. **25**: as for **22**–**24**, catalyst (*S,S*)-**2**. **26**: run 1 and 2: as for **22**–**24**, catalyst (*S,S*)-**2**. run 3: [S] = 0.5 M in 1:1H_2O:MeOH, $NaHCO_2$, 100:1 S/C, (*R,R*)-**2**. **27**: as for **22**–**24**.

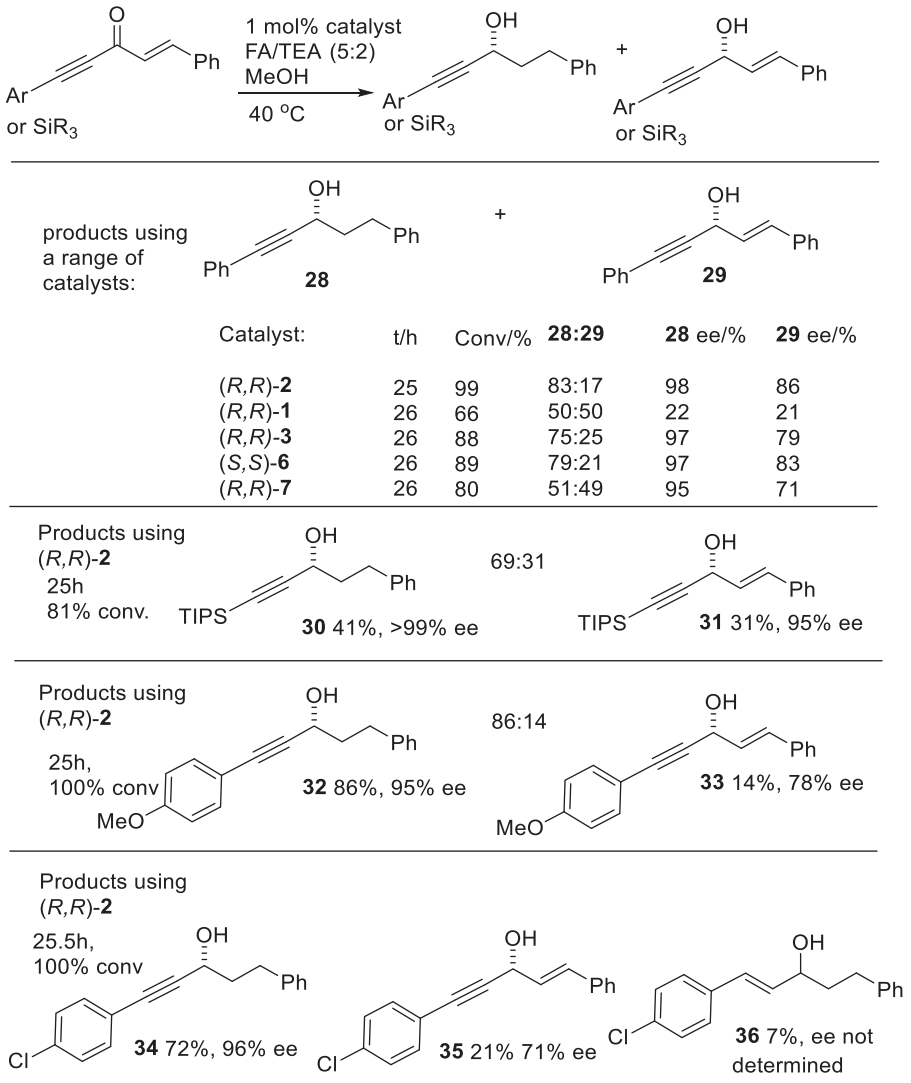


Fig. 8. Products of ATH of alkene/alkyne substrates. The illustrated configuration is that for the assumption that the alkyne dominates the selectivity as in Fig. 2. Conditions: FA:TEA 5:2 (0.5 mL), solvent (0.5 mL), 1 mol% catalyst and 40 °C unless otherwise stated.

the alkene is reduced first and the resulting propargylic ketone is selectively reduced following existing precedent [1,3d,4c]. The 1,2-reduction product **29** was formed in lower ee likely due to competing electron-rich unsaturated bonds in the CH/π of the reduction transition state (Fig. 2). The absolute configuration of the products was not unambiguously determined. However it is likely that the *R*-configuration products will be formed using the (*R,R*)-configuration catalyst, based on the precedent for this class of reductions.

A reaction/time study was completed to investigate the ATH using HPLC (Supporting Information). From an early stage in the reaction, the formation of the intermediate saturated ketone was essentially instantaneous, and a small amount of unsaturated product was also observed. As time increases, starting material and intermediate ketone disappear and the two alcohol products are formed. The effect of solvent on the reaction was also investigated and a time study for each solvent was undertaken to explore the relative rate of formation of each of the intermediate and product species over time (Supporting Information). DFT studies have indicated that using MeOH engages in hydrogen bonding interactions to the ketone during the reduction [2a,2e] and in some cases different solvents have been demonstrated to reverse the enantioselectivity [16]. However the results, whilst similar to those in Fig. 8, were inferior with respect to product selectivity, enantioselectivity and conversion. Four further ATH catalysts, **1, 3**, '4C-tethered' **6** and the 'benzyl-bridged' **7** were also used (Fig. 8). Time studies were also conducted to track the formation of products and intermediates in each case (Supporting Information). Catalyst **6** produced similar ratios of alcohols and ee values as seen with **2**, however, it gave lower conversion. Catalyst **3** gave a similar result to that of **6**. ATH with **3** at the lower temperature of 25 °C gave a more selective product ratio (79:21 **28**:**29**) with high ee's of 98% and 87% for the saturated OH and unsaturated OH respectively. However the conversion was slightly lower at 85%. Catalyst **7** gave approximately a 1:1 ratio between the saturated and unsaturated products which could be due to the hindered nature of the catalyst.

The ATH (1 mol% catalyst (*R,R*)-**2**, MeOH co-solvent at 40 °C) was tested with other substrates and in all cases, standards of the reduction products were prepared for HPLC analysis. Attempts were made at ATH of the TMS-substituted alkyne but decomposition was observed. However the ATH of the TIPS-enynone was successful. Products **30** and **31** were isolated as a mixture, in a ratio

of 69:31 and in a conversion of just 81%. The ATH was less selective for the 1,4-reduction pathway and hence, produced more of unsaturated alcohol **31**. The enantioselectivity was high for both alcoholic products however. The products of ATH of the *p*-methoxyphenyl derivative were obtained as an 86:14 mixture of **32** and **33**. Hence the electron-donating group does not appear to significantly affect the reaction mechanism or product distribution. The *p*-chlorobenzene (PCB) derivative gave a product as a mixture of **34** and **35**, with slightly lower enantioselectivity. An impurity was found in the ^{1}H NMR spectrum and it was hypothesised that this was the alkyne reduction production **36**, based on the observation of a further ABX system in the ^{1}H NMR spectrum (see the Supporting Information).

3. Conclusions

Investigation of the ATH of a range of enones showed that predominant 1,4- reactivity is favoured and the majority of aromatic-ketone substrates were reduced to their saturated alcohols with high ee. Electron-donating para substituents on the ketone favoured 1,4-reduction further. The ATH of alkene/alkyne ketones leads to a mixture of chiral alcohols *via* 1,4 and 1,2-reduction pathways, the 1,4-pathway being predominant in the reaction. A time study of the reaction confirmed that the C=C bond is rapidly reduced early in the reduction process, and the saturated products were formed in higher ee than the unsaturated ones.

4. Experimental section

4.1. General experimental

All reagents and solvents were used as purchased and without further purification, with the exception of cyclohexane carboxaldehyde which was redistilled for storage.

All reactions were carried out under a nitrogen atmosphere unless otherwise specified. Reactions at elevated temperature were maintained by thermostatically controlled oil-baths or aluminium heating blocks. A temperature of 0 °C refers to an ice slush bath, −78 °C to a dry ice acetone bath.

NMR spectra were recorded on a Bruker AV (250 MHz), Bruker DPX (300 or 400 MHz), Bruker DRX (500 MHz) or Bruker AV-II. (700 MHz). All chemical shifts are rounded to the nearest 0.01 ppm for ^{1}H spectra and the nearest 0.1 ppm for ^{13}C spectra, and are referenced to the solvent chemical shift. Coupling constants are rounded to the nearest 0.1 Hz. Mass spectra were recorded on an Esquire 2000 and high resolution mass spectra were recorded on a Bruker Micro ToF or MaXis. IR spectra were recorded on a PerkinElmer spectrum 100 and peaks are reported in wavenumbers. Optical rotations were measured on an Optical Activity Ltd. AA-1000 Polarimeter and are reported in deg dm^{-1} cm^3 g^{-1}.

The chiral GC measurements were performed using a PerkinElmer 8500 or Hewlett-Packard 1050 instrument linked to a PC running DataApex Clarity software. HPLC measurements were performed out using a Hewlett Packard 1050 Series with a quaternary pump, autosampler and variable wavelength detector linked to a PC running DataApex Clarity software.

Melting points were determined on a Stuart scientific melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel of mesh size 230–400, Thin layer chromatography was carried out on aluminium backed silica gel 60(F254) plates, visualised using 254 nm UV light, potassium permanganate, iodine stains or cerium ammonium molybdate (CAM) as appropriate. Column chromatography was performed either by gradient elution (reported as a range, eg EtOAc/Petroleum ether (2–12%), or by isocratic elution.

4.1.1. rac-1-Phenylpropan-1-ol **14**

This compound is known [17]. To a solution of propiophenone **16** (66 mg, 0.49 mmol, 1 eq) in methanol (0.9 mL) and water (0.1 mL) was added sodium borohydride (41 mg, 1.08 mmol, 2 eq) as a solid in one portion. The reaction was monitored by TLC. After stirring for 6 h, the reaction mixture was concentrated under vacuum, the residue suspended in water (1 mL) and extracted with Et_2O (3 mL total). The organic layer was dried (Na_2SO_4) and concentrated to give the product **35** as a clear oil (35 mg, 0.26 mmol, 52%). The spectroscopic data were consistent with those observed for the asymmetric product below.

4.1.2. (S)-1-Phenylpropan-1-ol **14**

This compound is known [17]. From 3-chloropropiophenone **13**: A degassed solution of 3-chloropropiophenone (170 mg, 1.01 mmol, 1.0 eq) and (*S,S*)-**2** (3.1 mg, 0.005 mmol, 0.5%) in FA/TEA (5:2, 0.5 mL) was stirred at 60 °C for 1.5 h. The mixture was diluted with ethyl acetate (5 mL) and quenched with $NaHCO_3$ (sat., 5 mL), the aqueous layer was extracted further with ethyl acetate (2 × 5 mL) and the organic extracts dried over Na_2SO_4 and concentrated to give a brown oil. The crude was dissolved in diethyl ether and passed through a silica plug to yield the product **14** as a red oil (123 mg, 0.97 mmol, 96%) in 100% conv and 95% ee as measured by GC. $[\alpha]_D^{22}$ -43.5 (*c* 0.35 in $CHCl_3$); lit [17] $[\alpha]_D^{22}$ -43.6 (*S*) (c 1.0 in $CHCl_3$); δ_H (300 MHz, $CDCl_3$) 7.29–7.15 (5H, m, Ph), 4.49 (1H, dt, J = 3.2, 6.6 Hz, C*H*OH), 1.85 (1H, brs, OH), 1.78–1.57 (2H, m, CH_2), 0.82 (3H, t, J = 7.4 Hz, CH_3); δ_C (75 MHz, $CDCl_3$) 143.9, 127.8, 126.9, 125.4, 75.4, 31.3, 9.5; Chiral GC; (CP-Chirasil-Dex-Cβ, 25 m × 0.25 mm x 0.25 μm column, oven: hold 12 min at 125 °C, then ramp 1 °C/min, final temp 145 °C, inj.: split 220 °C, det.: FID 250 °C, 18 Psi He), retention times: 11.2 (*R*) and 11.4 (*S*) minutes.

From phenyl vinyl ketone **15**: Compound **14** could also be prepared with 100% conversion and 95% ee with the same method, starting from **15** (prepared by elimination of HCl from 3-chloropropriophenone [18], 126 mg, 0.95 mmol, 1 eq), (*S,S*)-**2** catalyst (3.5 mg, 0.006 mmol, 0.5%) and FA/TEA (5:2, 0.5 mL). The product was isolated as a clear oil (103 mg, 0.76 mmol, 79%).

Attempted reduction of 1-phenylprop-2-en-1-ol **17**. Application of the same method to commercially available α-vinylbenzyl alcohol **17** (134 mg) and (*S,S*)-**2** catalyst (3.3 mg, 5 μmol, 0.5%) in FA/TEA (5:2. 0.5 mL) gave no reaction in 1.5 h at 60 °C.

4.1.3. rac-1,3-Diphenylpropan-1-ol **19**

This compound is known [19]. To a suspension of chalcone **18** (212 mg, 1.02 mmol, 1 eq) and Pd/C (5% w/w, 52 mg, 24 μmol, 2.5% Pd) in isopropanol (5 mL) was added acetic acid (124 mg, 2.06 mmol, 2 eq) followed by sodium borohydride (160 mg, 4.23 mmol, 4 eq), with vigorous effervescence. The reaction mixture was stirred at rt for 2 h and quenched slowly with HCl (0.2 M, 2.5 mL). The resulting suspension was neutralised with NaOH (2 M, ~1.5 mL) and filtered through Celite with isopropanol to remove Pd/C. The mixture was concentrated to remove excess isopropanol and then the aqueous layer was extracted with diethyl ether (3 × 20 mL), dried over Na_2SO_4 and concentrated to give the saturated alcohol **19** as a clear oil that solidifies on standing. (183 mg, 0.86 mmol, 85%). δ_H (400 MHz, $CDCl_3$) 7.34 (4H, br. s., Ph), 7.30–7.23 (3H, m, Ph), 7.22–7.14 (3H, m, Ph), 4.67 (1H, br. s., CHOH), 2.82–2.55 (2H, m, $PhCH_2$), 2.20–1.96 (2H, m, $CHCH_2$), 1.92 (1H, br. s., OH); δ_C (101 MHz, $CDCl_3$) 144.6, 141.8, 128.6, 128.5, 128.4, 127.7, 126.0, 125.9, 73.9, 40.5, 32.1; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 256 nm UV, 30 °C): retention times: 9.4 (*S*) and 10.4 (*R*) minutes.

4.1.4. rac-(E)-1,3-Diphenylprop-2-en-1-ol **21**

This compound is known [20,21]. To a suspension of chalcone **18**

(625 mg, 3.0 mmol, 1 eq) and cerium trichloride heptahydrate (1.12 g, 3.0 mmol, 1 eq) in methanol (6 mL) was added sodium borohydride (113 mg, 3.0 mmol, 1 eq) at 0 °C. The reaction was stirred for 1 h, quenched with NH_4Cl (sat., 10 mL) and extracted with diethyl ether (3 × 10 mL). The organic layers were dried over Na_2SO_4 and concentrated to give the unsaturated alcohol **21** as a clear oil that solidifies on standing (532 mg, 2.53 mmol, 84%). δ_H (400 MHz, $CDCl_3$) 7.48–7.19 (10H, m, Ph), 6.69 (1H, d, J = 15.8 Hz, =CHPh), 6.38 (1H, dd, J = 6.4, 15.8 Hz CHC*H* =), 5.39 (1H, d, J = 6.4 Hz, C*H*OH), 2.08 (1H, br. s., OH); δ_C (101 MHz, $CDCl_3$) 142.9, 136.6, 131.6, 130.6, 128.7, 128.7, 127.9, 127.2, 126.7, 126.5, 75.1; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 256 nm UV, 30 °C): retention times: 13.4 (*S*) and 16.9 (*R*) minutes.

4.1.5. (S)-1,3-Diphenylpropan-1-ol **19** and (S,E)-1,3-diphenylprop-2-en-1-ol **21**

These compounds are known [19–21]. A degassed suspension of *trans*-chalcone **18** (208 mg, 1.0 mmol, 1 eq) and (*S,S*)-**2** (6.2 mg, 0.01 mmol, 1%) in FA/TEA (5:2, 0.5 mL) was stirred at 40 °C for 1.5 h. On completion the reaction mixture was homogenous. The mixture was diluted with diethyl ether (2 mL) and quenched with $NaHCO_3$ (sat., 2 mL), the aqueous layer was extracted further with ether (2 × 2 mL) and the organic extracts dried over Na_2SO_4 and passed through a silica plug to yield the product as an off white solid (203 mg, 0.96 mmol, 96%). The product was obtained as a mixture of saturated and unsaturated alcohols in 98% conversion, ratio 91:7 by ^{1}H NMR, major product 96% ee, minor product 73% ee. The opposite enantiomer was obtained using (*R,R*)-**3** (3.3 mg, 1%), *trans*-chalcone (104 mg, 0.5 mmol), FA/TEA (0.5 mL) and methanol (0.5 mL), to give the product (102 mg, 0.48 mmol, 96%). The product was obtained as a mixture of saturated and unsaturated alcohols in 100% conversion, ratio 96:2 by ^{1}H NMR, major product 98% ee, minor product 84% ee. Spectroscopic data for asymmetric product is consistent with the prepared standards. Mp 52 °C; $[\alpha]_D^{27}$ + 29.4, *R* 98% ee (c 0.425 in $CHCl_3$); lit [19] $[\alpha]_D^{22}$ +27.3, *R* 93% ee (*c* 0.51 in $CHCl_3$); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 256 nm UV, 30 °C): retention times: 10.0 (*S*)-saturated, 11.0 (*R*)-saturated, 13.4 (*S*)-unsaturated and 16.8 (*R*)-unsaturated minutes.

4.1.6. (E)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-one

This compound is known [22]. 4′-Chloroacetophenone (1.54 g, 10.0 mmol, 1 eq) was dissolved in a solution of sodium methoxide (25 wt% in MeOH, 1.11 g, 5.1 mmol, 0.5 eq) and MeOH (20 mL) and cooled to 0 °C. Benzaldehyde (1.59 g, 15.0 mmol, 1.5 eq) in MeOH (5 mL) was added and the suspension was warmed to 40 °C. The resulting solution was stirred for 18 h, THF (10 mL) was added to dissolve solids and the reaction was then quenched by dropwise addition of HCl (0.25 M, 20 mL). The resulting yellow crystalline precipitate was isolated by filtration and purified by recrystallization from hot ethanol and water. The pure product was isolated as an off white crystalline solid (2.08 g, 8.6 mmol, 86%). Mp 93–96 °C; δ_H (400 MHz, $CDCl_3$) 7.98 (2H, d, J = 8.3 Hz, ArH), 7.83 (1H, d, J = 15.8 Hz, CH =), 7.71–7.61 (2H, m, ArH), 7.49 (2H, d, J = 8.8 Hz, o-Cl ArH), 7.50 (1H, d, J = 15.8 Hz, CH =), 7.45–7.41 (3H, m, Ph).

4.1.7. rac-1-(4-Chlorophenyl)-3-phenylpropan-1-ol **22**

This compound is known [23]. To a solution of 4-chlorobenzaldehyde (141 mg, 1.0 mmol, 1 eq) in THF (1 mL) at −78 °C was added phenethyl magnesium chloride (1 M in THF, 1 mL, 1 eq). The reaction was allowed to warm to rt over 2.5 h, quenched with sat. NH_4Cl (2 mL) and extracted with Et_2O (2 × 2.5 mL). The organic extract was dried over $MgSO_4$ and concentrated to give the product **22** as a pale yellow oil. Purification by column chromatography (5 g silica, 30% Et_2O:Petroleum ether) gave the pure product as a white solid (192 mg, 0.78 mmol, 78%). δ_H (400 MHz, $CDCl_3$) 7.35–7.24 (6H, m, Ph), 7.23–7.14 (3H, m, Ph), 4.74–4.57 (1H, m, C*H*OH), 2.81–2.54 (2H, m, $PhCH_2$), 2.15–1.93 (2H, m, $CHCH_2$), 1.91–1.84 (1H, m, OH); δ_C (101 MHz, $CDCl_3$) 143.0 (C), 141.5 (C), 133.2 (C), 128.6 (CH), 128.4 (CH), 128.4 (CH), 127.3 (CH), 125.9 (CH), 73.1 (CH), 40.5 (CH_2), 31.9 (CH_2); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 210 nm UV, 30 °C) retention times: 9.3 (*S*) and 10.6 (*R*) minutes.

4.1.8. rac-(E)-1-(4-Chlorophenyl)-3-phenylprop-2-en-1-ol

This compound is known [20,24,25]. To a suspension of (*E*)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (242 mg, 1.0 mmol, 1 eq) and cerium trichloride heptahydrate (392 mg, 1.1 mmol, 1 eq) in methanol (2 mL) was added sodium borohydride (43 mg, 1.1 mmol, 1 eq) at 0 °C. The reaction was stirred for 1 h and quenched with sat. NH_4Cl (5 mL) and extracted with diethyl ether (3 × 5 mL) and passed through a plug of activated carbon/Celite. The filtrate was concentrated to give the unsaturated alcohol as a clear oil that solidified on standing in the freezer for 3 days (239 mg). Trituation from water gave a sticky white solid that was dried under vacuum to yield pure compound as a grey solid. (174 mg, 0.71 mmol, 71%). δ_H (400 MHz, $CDCl_3$) 7.59–7.06 (9H, m, ArH), 6.68 (1H, d, J = 15.8 Hz, =CHPh), 6.32 (1H, dd, J = 15.8, 6.7 Hz, CHC*H* =), 5.36 (1H, d, J = 6.3 Hz, C*H*OH), 2.09 (1H, br. s., OH); δ_C (101 MHz, $CDCl_3$) 141.2, 136.3, 133.5, 131.1, 131.0, 128.8, 128.7, 128.0, 127.7, 126.7, 74.5; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 210 nm UV, 30 °C) retention times: 12.5 (*S*) and 17.9 (*R*) minutes.

4.1.9. (R)-1-(4-Chlorophenyl)-3-phenylpropan-1-ol **22** and (R,E)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-ol

The major compound is known in racemic form [23]. The asymmetric form has not been reported. The minor compound is known [20,24,25]. A degassed suspension of (*E*)-1-(4-chlorophenyl)-3-phenylprop-2-en-1-one (120 mg, 0.49 mmol, 1 eq) and (*R,R*)-**3** catalyst (3.3 mg, 0.005 mmol, 1%) in FA/TEA (5:2, 0.5 mL) and methanol (0.5 mL) was stirred at 40 °C for 22 h. The mixture was quenched with $NaHCO_3$ (sat., 2 mL), extracted into diethyl ether (2 mL) and dry loaded onto silica (~200 mg). Filtration with 40% Et_2O/Hexane through a silica plug (~200 mg) gave the crude product as a sticky red film (114 mg). Purification by column chromatography (15% EtOAc in petroleum ether) gave the pure mixture of alcohols as a clear oil. (98 mg, 0.40 mmol, 80%). The product was obtained as a mixture of saturated **22** and unsaturated alcohols, ratio 96:4 by ^{1}H NMR. Total conv 100%, major product 94% ee as determined by HPLC, minor product was 69% ee as determined by HPLC. $[\alpha]_D^{27}$ +12.8 *R* 94% ee (*c* 0.375 in $CHCl_3$); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 210 nm UV, 30 °C) retention times: 9.6 (*S*)-saturated, 10.8 (*R*)-saturated, 13.0 (*S*)-unsaturated and 16.1 (*R*)-unsaturated minutes.

4.1.10. (E)-1-(4-Methoxyphenyl)-3-phenylprop-2-en-1-one

This compound is known [22] 4′-Methoxyacetophenone (1.51 g, 10.1 mmol, 1 eq) was dissolved in a solution of sodium methoxide (25 wt% in MeOH, 0.43 g, 2.0 mmol, 0.2 eq) and MeOH (20 mL) and cooled to 0 °C. Benzaldehyde (1.50 g, 14.1 mmol, 1.4 eq) in MeOH (5 mL) was added and the suspension was warmed to 40 °C. The resulting solution was stirred for 48 h, then quenched by dropwise addition of HCl (0.25 M, 20 mL). The resulting white crystalline solid was isolated by filtration (2.20 g, 9.2 mmol, 92%). δ_H (500 MHz, $CDCl_3$) 8.09–8.02 (2H, m, ArH), 7.81 (1H, d, J = 15.7 Hz, =CH), 7.65

(2H, dd, J = 7.2, 2.1 Hz, ArH), 7.55 (1H, d, J = 15.7 Hz, =CH), 7.45–7.36 (3H, m, ArH), 7.02–6.96 (2H, m, ArH), 3.89 (3H, s, OCH_3); δ_C (126 MHz, $CDCl_3$) 188.7, 163.5, 144.0, 135.1, 131.1, 130.8, 130.4, 129.0, 128.4, 121.9, 113.9, 55.5.

4.1.11. rac-1-(4-Methoxyphenyl)-3-phenylpropan-1-ol **23**

This compound is known [26] To a suspension of (*E*)-1-(4-Methoxyphenyl)-3-phenylprop-2-en-1-one (240 mg, 1.0 mmol, 1 eq) and Pd/C (5% w/w, 54 mg, 25 μmol, 2.5% Pd) in isopropanol (5 mL) was added acetic acid (120 mg, 2.0 mmol, 2 eq) followed by sodium borohydride (152 mg, 4.0 mmol, 4 eq), with vigorous effervescence. The reaction mixture was stirred at rt for 2.5 h, then additional sodium borohydride was added (76 mg, 2.0 mmol, 2 eq). The suspension was stirred for another hour, then filtered through Celite with isopropanol (40 mL) and water (10 mL). The filtrate was partially concentrated under vacuum but continued to evolve gas, so was quenched with NH_4Cl (sat. soln, 10 mL) and concentrated at 50 °C. The concentrated residue was partitioned between diethyl ether (10 mL) and NaOH (2 M soln, 5 mL). The aqueous layer was extracted with further portions of ether (2 × 5 mL), and the combined organic layers were dried (Na_2SO_4) and concentrated under vacuum to give the crude product as a clear oil that solidifies into a sticky solid on standing (218 mg). This material was dissolved in a minimum quantity of methanol and water was added until a white emulsion formed. Concentrating the emulsion gave a the pure product as a white crystalline solid (206 mg, 0.84 mmol, 84%). Mp 52–53 °C; δ_H (400 MHz, $CDCl_3$) 7.32–7.23 (4H, m, Ph), 7.22–7.13 (3H, m, Ph), 6.88 (2H, d, J = 8.3 Hz, *o*-O Ph), 4.78–4.53 (1H, m, C*H*OH), 3.80 (3H, s, OCH_3), 2.79–2.58 (2H, m, $PhCH_2$), 2.20–1.94 (2H, m, $CHCH_2$), 1.83 (1H, br. s., OH); δ_C (101 MHz, $CDCl_3$) 159.1, 141.9, 136.7, 128.5, 128.4, 127.3, 125.9, 113.9, 73.5, 55.3, 40.4, 32.1; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 210 nm UV, 30 °C) retention times: 11.9 (*S*) and 13.1 (*R*) minutes.

4.1.12. (R)-1-(4-Methoxyphenyl)-3-phenylpropan-1-ol **23**

This compound is known [27]. A degassed suspension of (*E*)-1-(4-methoxyphenyl)-3-phenylprop-2-en-1-one (121 mg, 0.51 mmol, 1 eq) and catalyst (*R,R*)-**3** (3.3 mg, 0.005 mmol, 1%) in FA/TEA (5:2, 0.5 mL) and methanol (0.5 mL) was stirred at 40 °C for 22 h. The mixture was quenched with $NaHCO_3$ (sat., 2 mL), extracted into diethyl ether (2 mL) and dry loaded onto silica (~200 mg). Filtration with 20% Et_2O/Hexane (10 mL) through a silica plug (~0.2 g) gave the pure product **23** as a white solid (110 mg, 0.45 mmol, 89%). Total conv 100%, major product 98% ee. The ee of the unsaturated product was not determined. $[\alpha]_D^{22}$ +19.4 (*c* 0.24 in $CHCl_3$); lit [27] $[\alpha]_D^{22}$ 10.3 (*c* 0.86 in $CHCl_3$); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 7% IPA: 93% Hexane; 210 nm UV, 30 °C) retention times: 11.7 (*S*) and 13.1 (*R*) minutes.

4.1.13. (E)-1-(4-(Dimethylamino)phenyl)-3-phenylprop-2-en-1-one

This compound is known [22]. 1-(4-(Dimethylamino)phenyl) ethan-1-one [28] (1.63 g, 10 mmol, 1 eq) was dissolved in a solution of sodium methoxide (25 wt% in MeOH, 1.08 g, 5 mmol, 0.5 eq) and MeOH (20 mL) and cooled to 0 °C. Benzaldehyde (1.59 g, 15 mmol, 1.5 eq) in MeOH (5 mL) was added and the suspension was warmed to 40 °C. The resulting yellow solution was stirred for 48 h, then quenched with HCl (0.25 M, 20 mL). The resulting yellow precipitate was filtered and washed with aqueous methanol. The crude solid was purified by recrystallization from hot ethanol, to give the pure chalcone as a fluffy yellow solid, (884 mg, 3.52 mmol, 35%). Mp 168–170 °C; δ_H (500 MHz, $CDCl_3$) 8.05–7.96 (2H, m, ArH), 7.78 (1H, d, J = 15.6 Hz, ArH), 7.66–7.55 (3H, m, ArH), 7.43–7.35 (3H, m, ArH), 6.74–6.66 (2H, m, ArH), 3.07 (s, 6H)., 3.07 (6H, s, $N(CH_3)_2$); δ_C (126 MHz, $CDCl_3$) 187.8, 153.4, 142.5, 135.5, 130.8, 129.9, 128.9, 128.2, 126.0, 122.2, 110.9, 40.1.

4.1.14. rac-1-(4-(Dimethylamino)phenyl)-3-phenylpropan-1-ol **24**

This compound is known but not fully characterised [29]. To a solution of 4-(dimethylamino)benzaldehyde (152 mg, 1.02 mmol, 1 eq) in THF (1 mL) at −78 °C was added phenethyl magnesium chloride (1 M in THF, 1 mL, 1 eq). The reaction was allowed to warm to rt over 5.5 h and quenched with sat. NH_4Cl (1 mL), diluted with water (1 mL) and extracted with Et_2O (3 × 3 mL). The organic extract was dried over $MgSO_4$ and concentrated to give the product **24** as a white solid (260 mg, 1.02 mmol, 100%). Mp 67–68 °C; HRMS: found (ESI) $[M + H]^+$, 256.1692. ($C_{17}H_{22}NO$ requires 256.1696); δ_H (300 MHz, $CDCl_3$) 7.46–6.99 (8H, m, Ph), 6.73 (2H, d, J = 7.5 Hz, *o*-N Ph), 4.59 (1H, t, J = 6.5 Hz, *CH*OH), 2.95 (6H, s, NMe_2), 2.79–2.56 (2H, m, $PhCH_2$), 2.21–1.93 (2H, m, $CHCH_2$), 1.69 (1H, br. s., OH); δ_C (75 MHz, $CDCl_3$) 150.3, 142.1, 132.3, 128.5, 128.3, 127.0, 125.7, 112.6, 73.7, 40.7, 40.04, 32.3; *m/z* (ESI): 256.2 ($[M + H]^+$)); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 10% IPA: 90% Hexane; 210 nm UV, 30 °C) retention times: 10.6 (*S*) and 11.3 (*R*) minutes.

4.1.15. rac-(R)-1-(4-(Dimethylamino)phenyl)-3-phenylpropan-1-ol **24**

The asymmetric form of this compound has not been reported. A degassed suspension of (E)-1-(4-(dimethylamino)phenyl)-3-phenylprop-2-en-1-one. (129 mg, 0.51 mmol, 1 eq) and catalyst (*R,R*)-**3** (3.3 mg, 0.005 mmol, 1%) in FA/TEA (5:2, 0.5 mL) and methanol (0.5 mL) was stirred at 40 °C for 24 h. The mixture was quenched with $NaHCO_3$ (sat., 2 mL), extracted into diethyl ether (2 mL) and dry loaded onto silica (~200 mg). Filtration with 20% EtOAc/petroleum ether (10 mL) through a silica plug (~0.75 g) gave the crude product.in 91% conversion, with the remainder being the saturated ketone. (121 mg). Purification by column chromatography (20% EtOAc in petroleum ether) gave the pure product **24** as a white solid (98 mg, 0.38 mmol, 75%). in 97% ee as determined by HPLC. Spectral data matched those of the racemic compound. TLC: 30% EtOAc in petroleum ether, silica, Rf = 0.22 (SM 0.28); $[\alpha]_D^{24}$ +18.8 (c 0.295 in $CHCl_3$); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 10% IPA: 90% Hexane; 210 nm UV, 30 °C): retention times: 10.6 (*S*) and 11.2 (*R*) minutes.

4.1.16. (E)-3-Cyclohexyl-1-phenylprop-2-en-1-one

This compound is known [31]. To a suspension of sodium hydride (60 wt% dispersion in mineral oil, 0.20 g, 5.0 mmol, 1.0 eq) in THF (5 mL) at 0 °C was added dropwise a solution of the diethyl (2-oxo-2-phenylethyl)phosphonate [30] (1.25 g, 4.9 mmol, 1.0 eq) in THF (5 mL) and the resulting clear solution was stirred for 30 min at room temperature. Cyclohexanecarboxaldehyde (0.57 g, 5.1 mmol, 1.0 eq) was added neat and the reaction mixture stirred at room temperature overnight. The reaction was quenched with NH_4Cl (half saturated, 30 mL) and extracted with ethyl acetate (3 × 15 mL), the organic extracts washed with brine (25 mL), dried over Na_2SO_4 and concentrated to give the crude product as a clear oil (1.13 g). The crude was taken up in methanol (50 mL) and cooled to −72 °C. The resulting white precipitate was filtered and dried to give the pure product as a white solid (492 mg, 2.30 mmol, 45%). Mp 46–48 °C; δ_H (400 MHz, $CDCl_3$) 7.92 (2H, d, J = 7.5 Hz, *o*-Ph), 7.57–7.51 (1H, m, *p*-Ph), 7.49–7.42 (2H, m, *m*-Ph), 7.01 (1H, dd, J = 6.8, 15.6 Hz, =*CH*CH), 6.83 (1H, d, J = 15.6 Hz, CO*CH* =), 2.32–2.18 (1H, m, Cy), 1.88–1.74 (4H, m, Cy), 1.70 (1H, d, J = 12.0 Hz, Cy), 1.34–1.15 (6H, m, Cy); δ_C (101 MHz, $CDCl_3$) 191.4, 154.9, 138.2, 132.6, 128.5, 128.5, 123.4, 41.1, 31.8, 25.9, 25.8.

4.1.17. rac-3-Cyclohexyl-1-phenylpropan-1-ol ***25***

This compound is known [32]. To a suspension of (*E*)-3-cyclohexyl-1-phenylprop-2-en-1-one (215 mg, 1.0 mmol, 1 eq) and Pd/C (5% w/w, 55 mg, 26 μmol, 2.5% Pd) in isopropanol (5 mL) was added acetic acid (121 mg, 2.0 mmol, 2 eq) followed by sodium borohydride (153 mg, 4.0 mmol, 4 eq), with vigorous effervescence. The reaction mixture was stirred at rt for 2.5 h, then additional sodium borohydride was added (75 mg, 2.0 mmol, 2 eq). The reaction was stirred for an additional 2 h and then quenched slowly with HCl (0.2 M, 2.5 mL). The resulting suspension was neutralised with NaOH (2 M, ~1.5 mL) and filtered through Celite with isopropanol to remove Pd/C. The mixture was concentrated to remove excess isopropanol and then the aqueous layer was extracted with diethyl ether (3 × 10 mL), dried over Na_2SO_4 and concentrated to give the product **25** as a white solid (214 mg, 0.98 mmol, 98%). δ_H (300 MHz, $CDCl_3$) 7.39–7.31 (4H, m, ArH), 7.31–7.26 (1H, m, ArH), 4.68–4.58 (1H, m, C*H*OH), 1.88–1.57 (8H, m, alkylH), 1.39–1.06 (6H, m, alkylH), 0.93–0.79 (2H, m, AlkylH); δ_C (75 MHz, $CDCl_3$) 162.3, 128.4, 127.5, 125.9, 75.07, 37.7, 36.5, 33.5, 33.36, 26.7, 26.3; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 4% IPA: 96% Hexane; 210 nm UV, 30 °C): retention times: 7.4 (*S*) and 7.9 (*R*) minutes.

4.1.18. rac-(S)-3-Cyclohexyl-1-phenylpropan-1-ol ***25***

The asymmetric form of this compound has not been reported. A degassed suspension of (*E*)-3-cyclohexyl-1-phenylprop-2-en-1-one (107 mg, 0.5 mmol, 1 eq) and catalyst (*S,S*)-**2** (5 μmol, 100:1 S/C) in FA/TEA (5:2, 0.5 mL) and methanol (0.5 mL) was stirred at 40 °C for 3 h. On completion the reaction mixture was homogenous. The mixture was diluted with diethyl ether (2 mL) and quenched with $NaHCO_3$ (sat., 2 mL), the aqueous layer was extracted further with ether (2 × 2 mL) and the organic extracts dried over Na_2SO_4 and passed through a silica plug to yield the product. Total conversion 100%. Product obtained as a grey solid (55 mg, 0.25 mmol, 50%) containing a mixture of saturated and unsaturated alcohols, ratio 98 : 2 by ^{1}H NMR. Major product ee 97%. $[\alpha]_D^{24}$ -10.9 (c 0.245 in $CHCl_3$); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 4% IPA: 96% Hexane; 210 nm UV, 30 °C): retention times: 7.5 (*S*)-saturated and 7.9 (*R*)-saturated minutes.

4.1.19. (E)-1-Cyclohexyl-3-phenylprop-2-en-1-one

This compound is known [33]. Sodium methoxide solution (25% w/w, 5.96 g, 27.6 mmol, 1 eq) was diluted to 50 mL with methanol and added to cyclohexylmethyl ketone (3.33 g, 26.4 mmol, 1 eq). The mixture was cooled to 0 °C and a solution of benzaldehyde (2.81 g, 26,5 mmol, 1 eq) in methanol (15 mL) was added. The reaction mixture was warmed to 40 °C and stirred for 3 days. The reaction was quenched with 0.25 M HCl (100 mL) and extracted with diethyl ether (4 × 100 mL), the organic layers were dried and concentrated to give the crude product as a yellow oil that solidifies slowly on standing. The oil was dissolved in ~150 mL of methanol and cooled to −78 °C, the resulting precipitate was filtered and washed once with cold methanol and dried to give the purified product as a white solid (2.78 g, 13.0 mmol, 49%). Mp 54–58 °C; δ_H (250 MHz, $CDCl_3$) 7.60 (1H, d, J = 15.9 Hz, PhCH =), 7.60–7.52 (2H, m, *o*-Ph), 7.45–7.30 (3H, m, *m,p*-Ph), 6.82 (1H, d, J = 15.9 Hz, COCH =), 2.73–2.59 (1H, m, C*H*CO), 2.01–1.77 (4H, m, alkylH), 1.77–1.65 (1H, m, alkylH), 1.55–1.14 (5H, m, alkylH).

4.1.20. rac-1-Cyclohexyl-3-phenylpropan-1-ol ***26***

This compound is known [32]. To a solution of cyclohexane carboxaldehyde (128 mg, 1.14 mmol, 1 eq) in THF (1 mL) was added phenethyl magnesium chloride (1 M in THF, 1 mL, 1.0 mmol, 1 eq) at −78 °C. The reaction was stirred for 2.75 h while gradually warming to ~0 °C, then quenched with NH_4Cl (sat. soln, 2 mL) and water (1 mL). The suspension was extracted with Et_2O (2 × 2.5 mL), the organic layers dried over $MgSO_4$ and concentrated to give the crude product as a white solid. The crude was purified by column chromatography (10% EtOAc in petroleum ether) to give the pure product as a white powder (110 mg, 0.51 mmol, 45%). TLC: 10% EtOAc in petroleum ether, silica, Rf 0.16, $KMnO_4$; Mp 68–70 °C; δ_H (300 MHz, $CDCl_3$) 7.31–7.18 (5H, m, ArH), 3.45–3.31 (1H, m, C*H*OH), 2.91–2.78 (1H, m, CHC*H*H), 2.72–2.58 (1H, m, CHCH*H*), 1.89–1.60 (7H, m, CH_2 and Cy), 1.37–0.97 (7H, m, OH and Cy); δ_C (75 MHz, $CDCl_3$) 142.4, 128.4, 128.4, 125.8, 75.6, 43.8, 36.0, 32.4, 29.2, 27.8, 26.5, 26.3, 26.2; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 4% IPA: 96% Hexane; 210 nm UV, 30 °C): retention times: 8.3 and 13.3 min.

4.1.21. rac-(E)-1-Cyclohexyl-3-phenylprop-2-en-1-ol

This compound is known [34]. To a suspension of (*E*)-1-cyclohexyl-3-phenylprop-2-en-1-one (211 mg, 1.0 mmol, 1 eq) and cerium trichloride heptahydrate (372 mg, 1.0 mmol, 1 eq) in methanol (2 mL) was added sodium borohydride (43 mg, 1.1 mmol, 1 eq) at 0 °C. The reaction was stirred for 1.5 h, quenched with NH_4Cl (sat., 5 mL), diluted with water (3 mL), and extracted with diethyl ether (3 × 5 mL). The organic layers were dried over Na_2SO_4 and concentrated to give the unsaturated alcohol as a white solid (168 mg, 0.78 mmol, 78%). δ_H (400 MHz, $CDCl_3$) 7.40–7.22 (5H, m, ArH), 6.55 (1H, d, J = 15.9 Hz, =CHPh), 6.23 (1H, dd, J = 7.2, 15.9 Hz, =C*H*CH), 4.02 (1H, br. s., C*H*OH), 1.92 (1H, d, J = 12.0 Hz, OH), 1.83–1.61 (4H, m, Cy), 1.60–1.42 (2H, m, Cy), 1.35–0.90 (5H, m, Cy); δ_C (101 MHz, $CDCl_3$) 136.8, 131.2, 131.1, 128.6, 127., 126.5, 77.6, 44.0, 28.9, 28.7, 26.5, 26.2, 26.1); Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1 mL/min, 4% IPA: 96% Hexane; 210 nm UV, 30 °C): retention times: 9.9 and 14.4 min.

4.1.22. (E)-1-Cyclohexyl-3-phenylprop-2-en-1-ol and 1-cyclohexyl-3-phenylpropan-1-ol ***26***

The asymmetric form of these compound have not been reported. A degassed suspension of (*E*)-1-cyclohexyl-3-phenylprop-2-en-1-one (97 mg, 0.45 mmol, 1 eq) and catalyst (*S,S*)-**2** (5 μmol, 100:1 S/C) in FA/TEA (5:2, 0.5 mL) and methanol (0.5 mL) was stirred at 40 °C for 2.5 h. On completion the reaction mixture was homogenous. The mixture was diluted with diethyl ether (2 mL) and quenched with $NaHCO_3$ (sat., 2 mL), the aqueous layer was extracted further with ether (2 × 2 mL) and the organic extracts dried over Na_2SO_4 and passed through a silica plug to yield the product. Conversion 82%. Product obtained as a clear oil (78 mg, 0.36 mmol, 80%) containing a mixture of saturated and unsaturated alcohols, ratio 10 : 90 by ^{1}H NMR. Major (1,2-) product ee 59%, minor (1,4-) product ee 36%. With (*E*)-1-cyclohexyl-3-phenylprop-2-en-1-one (108 mg, 0.50 mmol) and catalyst (*R,R*)-**3**; 23 h reaction time, conversion 100%. Product obtained as a white solid (111 mg, 0.51 mmol, 100%) containing a mixture of saturated and unsaturated alcohols, ratio 59 : 41 by ^{1}H NMR. Major product ee 21%, minor product ee 76%. Aqueous reduction: Sodium formate (170 mg, 2.5 mmol, 5 eq), (*E*)-1-cyclohexyl-3-phenylprop-2-en-1-one (110 mg, 0.51 mmol, 1 eq) and (*R,R*)-**3** (3.3 mg, 5 μmol, 1%) were suspended in water (1 mL) and methanol (0.5 mL) and heated to 60 °C. The solids melt and form a brown oil on top of the aqueous phase. The mixture was stirred vigorously for 19 h before being cooled to rt and diluted with diethyl ether (2 mL). The organic layer was separated, then concentrated directly onto silica. Elution through a short silica plug with 40% diethyl ether in petroleum ether gave the product in 98% conversion as a clear oil (103 mg, 0.47 mmol, 92%) containing a mixture of saturated and unsaturated alcohols, ratio 68 : 32 by ^{1}H NMR. Major product ee 49%, minor product ee 82%.

4.1.23. 2-(1-Hydroxycyclohexyl)-1-phenylethan-1-one

This compound is known [35]. $TiCl_4$ (1 M in DCM, 12 mL, 12 mmol, 1.2 eq) was added dropwise at 0 °C to a solution of cyclohexanone (1.23 g, 12.5 mmol, 1.25 eq) in DCM (20 mL) and stirred for 25 min. To the resulting yellow suspension was added dropwise 1-phenyl-1-(trimethylsiloxy)ethylene (1.94 g, 10 mmol, 1.0 eq). The resulting orange suspension was allowed to warm to rt and stirred for 24 h before being quenched with water (35 mL). The mixture was extracted with DCM (2 × 20 mL), washed with brine (10 mL) and filtered through a plug of silica gel (~4 g) with DCM to give the crude product as a thick yellow oil that crystallises on standing (2.69 g).The crude was dissolved in hot methanol, concentrated to a thick oil and then crystallised by addition of hexane (~10 mL) to give the pure product as a white crystalline solid (0.95 g, 4.3 mmol, 43%). A second crop was isolated by concentration of the mother liquors and addition of hexane to give white plates (0.20 g, 0.91 mmol, 9%). Combined yield (1.15 g, 5.2 mmol, 52%). TLC: 20% EtOAc in petroleum ether, silica, Rf = 0.2, UV; Mp 78–79 °C; δ_H (400 MHz, $CDCl_3$) 8.00–7.91 (2H, m, *o*-Ph), 7.63–7.56 (1H, m, *p*-Ph), 7.52–7.45 (2H, m, *m*-Ph), 3.97 (1H, s, OH), 3.12 (2H, s, $COCH_2$), 1.83–1.65 (5H, m, Cy), 1.58 (1H, dd, J = 2.9, 6.2 Hz, Cy), 1.52–1.38 (4H, m, Cy), 1.36–1.23 (1H, m, Cy); δ_C (101 MHz, $CDCl_3$) 202.0, 137.5, 133.6, 128.7, 128.11, 71.0, 47.7, 37.8, 25.8, 22.0.

4.1.24. 2-Cyclohexylidene-1-phenylethan-1-one

This compound is known [36]. 2-(1-Hydroxycyclohexyl)-1-phenylethan-1-one (868 mg, 3.9 mmol, 1 eq) and *p*-toluenesulfonic acid monohydrate (613 mg, 3.2 mmol, 0.8 eq) were suspended in toluene (8 mL) and stirred at 40 °C for 4.5 h, as monitored by TLC. Na_2SO_4 (~0.5 g) and petroleum ether (5 mL) were added, and the resulting suspension filtered through a silica plug (~1 g) with 10% EtOAc in petroleum ether to give the crude product as a yellow oil. The crude product was purified by column chromatography (6% Et_2O in pentane) to give the pure product as a pale yellow oil (616 mg, 2.93 mmol, 77%). TLC: 10% EtOAc/Pet ether, silica, Rf 0.38, UV; δ_H (300 MHz, $CDCl_3$) 8.00–7.89 (2H, m, *o*-Ph), 7.57–7.48 (1H, m, *p*-Ph), 7.48–7.40 (2H, m, *m*-Ph), 6.60 (1H, s, =CH), 2.81–2.72 (2H, m, Cy), 2.35–2.28 (2H, m, Cy), 1.77–1.61 (6H, m, Cy); δ_C (75 MHz, $CDCl_3$) 192.4, 162.8, 132.3, 128.5, 128.4, 128.4, 118.8, 38.4, 30.7, 28.9, 28.0, 26.3.

4.1.25. rac-2-Cyclohexyl-1-phenylethan-1-ol ***27***

This compound is known [37]. To a suspension of 2-cyclohexylidene-1-phenylethan-1-one (215 mg, 1.08 mmol, 1 eq) and Pd/C (5% w/w, 55 mg, 26 μmol, 2.5% Pd) in isopropanol (5 mL) was added acetic acid (121 mg, 2.0 mmol, 2 eq) followed by sodium borohydride (153 mg, 4.0 mmol, 4 eq), with vigorous effervescence. The reaction mixture was stirred at rt for 2.5 h, then additional sodium borohydride was added (75 mg, 2.0 mmol, 2 eq). The reaction was stirred for an additional 2 h and then quenched slowly with HCl (0.2 M, 2.5 mL). The resulting suspension was neutralised with NaOH (2 M, ~1.5 mL) and filtered through Celite with isopropanol to remove Pd/C. The mixture was concentrated to remove excess isopropanol and then the aqueous layer was extracted with diethyl ether (3 × 10 mL), dried over Na_2SO_4 and concentrated to give the product **27** as a white solid (214 mg, 1.0 mmol, 93%). Mp 57–59 °C; HRMS: found (ESI): $[M + Na]^+$, 227.1406 ($C_{14}H_{20}NaO$ requires 227.1411); ν_{max}: 3240 (OH), 2920 (CH), 2847 (CH), 1446 (C–O), 1003, 697 (monosubsituted Ph) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.38–7.31 (4H, m, Ph), 7.31–7.24 (1H, m, Ph), 4.85 4.73 (1H, m, C*H*OH), 1.91–1.59 (6H, m, C*H*H + Cy), 1.58–1.48 (2H, m, OH + CH*H*), 1.48–1.36 (1H, m, CH), 1.31–1.08 (3H, m), 1.04–0.88 (2H, m); δ_C (126 MHz, $CDCl_3$) 145.4, 128.5, 127.5, 125.8, 72.1, 47.1, 34.3, 34.0, 32.9, 26.6, 26.3, 26.2; m/z (ESI): 227.1 ($[M + Na]^+$); Chiral HPLC; Chiralpak IA column with 97% Hexane, 3% IPA, 0.5 mL/min, 22.8 and 26.9 min.

4.1.26. rac-2-Cyclohexylidene-1-phenylethan-1-ol

This compound has been reported as part of a mixture of isomers but has not been fully characterised [38]. To a suspension of 2-cyclohexylidene-1-phenylethan-1-one (101 mg, 0.5 mmol, 1 eq) and cerium trichloride heptahydrate (185 mg, 0.5 mmol, 1 eq) in methanol (1 mL) was added sodium borohydride (29 mg, 0.8 mmol, 1.5 eq) at 0 °C. The reaction was stirred for 2 h and quenched with NH_4Cl (sat., 0.5 mL), diluted with water (0.5 mL) and extracted with diethyl ether (3 × 2 mL). The organic extracts were dried over Na_2SO_4 and concentrated to give the product as a clear oil (103 mg, 0.50 mmol, 100%). The crude product was purified by column chromatography on silica gel (2.6 g) with 10% diethyl ether in petroleum ether as eluent, to yield the pure product as a clear oil (65 mg, 0.32 mmol, 64%). The pure product decomposes at room temperature within a few days. HRMS: found (ESI): $[M + H]^+$, 225.1251. ($C_{14}H_{18}NaO$ requires 225.1250); ν_{max}: 3374 (OH), 2928 (CH), 2854 (CH), 1447 (CO), cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.42–7.29 (4H, m, Ph), 7.27–7.19 (1H, m, Ph), 5.54–5.45 (1H, m, CHOH), 5.33 (1H, d, J = 8.8 Hz, =CH), 2.41–2.21 (2H, m, Cy), 2.14–2.04 (2H, m, Cy), 1.95 (1H, br. s., OH), 1.63–1.50 (6H, m, Cy); δ_C (101 MHz, $CDCl_3$) 144.5, 143.1, 128.5, 127.2, 125.8, 124.5, 69.8, 37.1, 29.4, 28.4, 27.9, 26.7; m/z (ESI): 225.1 ($[M + Na]^+$), 185.1 (30%, $[M - OH]^+$). Chiral HPLC/GC not obtained, suitable conditions for separation were not found before the compound decomposed.

4.1.27. (S)-2-Cyclohexyl-1-phenylethan-1-ol ***27*** *and (S)-2-cyclohexylidene-1-phenylethan-1-ol*

A suspension of 2-cyclohexylidene-1-phenylethan-1-one (95 mg, 0.47 mmol, 1 eq) and catalyst (*S,S*)-**2** (3.1 mg, 0.005 mmol, 1%) in FA/TEA (5:2, 0.5 mL) and MeOH (0.5 mL) was stirred at 40 °C for 22.5 h. The mixture was diluted with diethyl ether (2 mL) and quenched with $NaHCO_3$ (sat., 2 mL), the aqueous layer was extracted further with ether (2 × 2 mL) and the organic extracts dried over Na_2SO_4 and passed through a silica plug to yield the crude product as an off white solid (86 mg, 0.42 mmol, 89%). The product was obtained in full conversion as a mixture of saturated and unsaturated alcohols, ratio 94:6 by ^1H NMR. Major product 55% ee as calculated by HPLC. Purification by chromatography on silica (8% Et_2O/Petroleum ether) separated the unsaturated alcohol and gave the purified product as a white solid (60 mg, 0.29 mmol, 62%). Spectroscopic data for asymmetric product is consistent with the prepared standards. Mp 52 °C; $[\alpha]_D^{26}$ +50.4, *R* (c 0.245 in $CHCl_3$); Chiral HPLC: Chiralpak IA column with 97% Hexane, 3% IPA, 0.5 mL/min, 22.8 and 26.9 min. 55% ee (**27**).

4.1.28. Section on ATH alkene/alkynes.The results on the reduction of the TMS-containing substrates are in the supporting information

4.1.28.1. General procedure for asymmetric transfer hydrogenation (procedure 1). To a degassed solution of substrate and catalyst was added 5:2 FA:TEA. The concentration of the reaction was set at 1.0 M. The reaction mixture was heated to 40 °C for 26 h. The reaction was monitored by TLC and/or HPLC. Once completed, the mixture was quenched with $NaHCO_3$ (sat. soln.) and extracted with EtOAc. The organic layers were combined, dried with $MgSO_4$ and concentrated in *vacuo* to give the crude product. Where appropriate further purified was undertaken.

4.1.28.2. General n-BuLi procedure for racemic alcohol synthesis (procedure 2). A degassed solution of acetylene in THF (anhyd.) was cooled to −78 °C. Once cooled, *n*-butylithium was added dropwise, the reaction mixture was left to stir at −78 °C for 30 min. Aldehyde was added dropwise and the reaction mixture was left to stir

at −78 °C. After 1 h, the reaction mixture was allowed to warm to r.t. The reaction was monitored by TLC. Once completed, the reaction was quenched with NH_4Cl (sat. soln) and extracted with EtOAc. The organic layers were combined, dried with $MgSO_4$ and concentrated in *vacuo* to give the crude product. The crude product was further purified using column chromatography to give the desired product.

4.1.28.3. General procedure for MnO_2 oxidation for ketone synthesis (procedure 3). Alcohol and activated MnO_2 were dissolved in DCM (anhyd.) and stirred at r.t. The reaction was monitored using TLC. When completed, the reaction mixture was diluted with DCM and filtered through a Celite pad and concentrated in *vacuo* to give the crude product.

4.1.29. (E)-1,5-Diphenylpent-1-en-4-yn-3-one

N-Methoxy-*N*-methylcinnamide was prepared following the published procedure [39]. This compound is known and has been fully characterised [40]. Phenylacetylene (1.34 g, 13.1 mmol, 1.20 eq.) was dissolved in THF (anhyd., 25.0 mL) and cooled to −78 °C. *n*-butyllithium (1.6 M in hexanes, 8.19 mL, 13.1 mmol, 1.20 eq.) was added dropwise and the mixture was left to stir for 30 min at −78 °C. Pre-cooled to −78 °C, *N,O*-methyoxy-*N*-methylcinnamide (2.092 g, 10.9 mmol 1.00 eq.) in THF (anhyd. 8 mL) was added to the reaction *via* cannula transfer. The reaction mixture was stirred for 1 h at −78 °C before being warmed to r.t. The reaction was monitored using TLC until starting material had disappeared. The reaction mixture was quenched with NH_4Cl (sat. soln, 10 mL) and extracted with EtOAc (3 × 10 mL). The organic layers were combined, dried with $MgSO_{4,\ filtered}$ and concentrated in *vacuo*. The crude product was purified by column chromatography (SiO_2, Rf: 0.60 (9:1) hexanes/EtOAc) to give the desired product as a yellow solid (2.125 g, 9.12 mmol, 84%). δ_H (400 MHz, $CDCl_3$) 7.92 (1H, d, J = 16.1 Hz, C*H*=CHCO), 7.70–7.57 (4H, m, ArH), 7.53–7.37 (6H, m, ArH), 6.88 (1H, d, J = 16.1 Hz, CH=C*H*CO); δ_C (101 MHz, $CDCl_3$) 178.3, 148.3, 135.0, 132.9, 131.2, 130.6, 129.1, 128.7, 128.7, 128.6, 120.2, 91.1, 86.6; LCMS (ESI) m/z: $[M+Na]^+$ 255.09; IR (ν): 3061, 3053, 2922, 2854, 2212, 1627, 1609, 1488, 1445, 1288, 1173, 971, 909, 757, 673, 579, 533, 502, 482 cm^{-1}; Mp: 67.4–69.0 °C; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm); 1.0 mL/min, IPA:Hexane (20:80); 250 nm UV, 30 °C): retention times: 5.76 (ketone) mins. Data matched that reported.

*4.1.30. rac-1,5-Diphenylpent-1-yn-3-ol **28***

This compound is known and has been fully characterised [41]. Compound **28** was prepared using General Procedure 2. Phenylacetylene (0.457 g, 4.48 mmol, 1.20 eq.) was dissolved in THF (anhyd., 5.00 mL) and *n*-butyllithium (1.6 M in hexanes, 2.91 mL, 4.66 mmol, 1.25 eq.) was added dropwise. After 30 min, 3-phenylpropanal (0.500 g, 3.73 mmol, 1.00 eq.) was added. The crude product was purified using column chromatography (SiO_2; Rf: 0.60; (4.1) hexanes/EtOAc) to give the desired product **28** as a yellow oil (0.6083 g, 2.57 mmol, 69%). δ_H (300 MHz, $CDCl_3$) 7.42–7.35 (2H, m, ArH), 7.29–7.11 (8H, m, ArH), 4.60 (1H, t, J = 6.6 Hz, C*H*OH), 2.86–2.77 (2H, m, CH_2CH_2Ph), 2.17–2.00 (2H, m, CH_2CH_2Ph), 1.89 (1H, s, OH); δ_C (75 MHz, $CDCl_3$) 141.3, 131.7, 128.6, 128.5, 128.4, 128.3, 126.0, 122.6, 89.8, 85.3, 62.3, 39.3, 31.5; LCMS (ESI) m/z: $[M+Na]^+$ 259.20; IR (ν): 3321, 3026, 2927, 2862, 1602, 1490, 1454, 1041, 1009, 755, 692 cm^{-1}; Chiral HPLC (CHIRALPAK IB column (0.46 × 25 cm); 1.0 mL/min IPA:Hexane (20:80), UV 250 nm, 25 °C). Retention times 5.52 (*R*)-unsaturated and 7.84 (*S*)-unsaturated mins. Data matched that reported.

*4.1.31. rac-(E)-1,5-Diphenylpent-1-en-4-yn-3-ol **29***

This compound is known and has been fully characterised [42]. Compound **29** was prepared using General Procedure 2. Phenylacetylene (0.2247 g, 2.63 mmol, 1.20 eq.) was dissolved in THF (anhyd., 5 mL) and *n*-butyllithium (1.6 M in hexanes, 1.71 mL, 2.75 mmol, 1.25 eq.) was added dropwise. After 30 min, *E*-cinnamaldehyde (0.290 g, 2.20 mmol, 1.00 eq.) was added. The crude was purified using column chromatography (SiO_2; Rf: 0.30; (9.1) petroleum/EtOAc) to give the desired product **29** as a yellow oil (0.426 g, 1.83 mmol, 83%). δ_H (400 MHz, $CDCl_3$) 7.43–7.34 (4H m, ArH), 7.30–7.16 (6H, m, ArH), 6.84 (1H, d, J = 15.9 Hz, C*H*=CHCHOH), 6.39 (1H, dd, J = 15.8, 6.0 Hz, CH=C*H*CHOH), 5.28 (1H, d, J = 6.0 Hz, C*H*OH), 2.15 (1H, s, OH); δ_C (101 MHz, $CDCl_3$) 136.1, 133.0, 132.1, 131.8, 129.1, 128.7, 128.4, 128.2, 128.1, 126.9, 122.4, 87.9, 86.5; LCMS (ESI) m/z: $[M+Na]^+$ 255.10, 257.10; IR (ν): 3400, 3073, 3023, 2212, 1596, 1489, 1254, 1091, 1014, 966, 753, 687 cm^{-1}; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (20:80); 250 nm UV, 30 °C): retention times: 6.31 (*R*)-unsaturated and 12.81 (*S*)-unsaturated mins. Data matched that reported.

4.1.32. 1,5-Diphenylpent-1-yn-3-one

This compound is known and has been fully characterised [43]. This compound was prepared using General Procedure 3 from compound **28** (0.200 g, 0.85 mmol, 1.00 eq.) and activated MnO_2 (1.10 g, 12.7 mmol, 15.0 eq.) to yield the desired product as a yellow solid (0.068 g, 0.30 mmol, 35%). Also contains side product impurity (25% NMR integration). δ_H (400 MHz, $CDCl_3$) 7.51–7.46 (2H, m, ArH), 7.41–7.36 (1H, m, ArH), 7.31 (2H, dd, J = 8.2, 6.7 Hz, ArH), 7.26–7.19 (2H, m, ArH), 7.19–7.11 (3H, m, ArH), 3.03–2.91 (4H, m, CH_2); δ_C (101 MHz, $CDCl_3$) 188.1, 140.3, 133.1, 130.8, 129.8, 128.7, 128.6, 128.0, 125.8, 91.1, 87.6, 47.0, 30.0; LCMS (ESI) m/z: $[M+Na]^+$ 257.20; IR (ν): 3062, 2924, 2202, 1700, 1604, 1490, 1214, 1092, 1020, 756, 689, 617 cm^{-1}; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (20:80); 250 nm UV, 30 °C): retention times: 5.00 (ketone) mins. Data matched that reported.

*4.1.33. (R)-1,5-Diphenylpent-1-yn-3-ol **28** and (R,E)-1,5-diphenylpent-1-en-4-yn-3-ol **29***

Both compounds are known and have been fully characterised [44,45]. The ATH was conducted using General Procedure 1. (*E*)-1,5-Diphenylpent-1-en-4-yn-3-one (0.1164 g, 0.50 mmol, 1.00 eq.), (*R,R*)-**2** (3.10 mg, 5.0 μmol, 0.01 eq.) and MeOH (0.5 mL) were reacted for 25 h at 40 °C. The crude product was purified using column chromatography (SiO_2; (9:1) petroleum/EtOAc) to give a mixture of both alcohol products **28** and **29** (0.114 g, 0.23 mmol, 46%). The product was obtained as a colourless oil with an NMR ratio of 83:17 of the major (Sat. OH) **28** and minor (Unsat. OH) **29**. Enantiomeric excess and conversion were determined by Chiral HPLC analysis (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: retention times: 7.66 (*R*)-saturated, 12.94 (*S*)-saturated, 9.70 (*R*)-unsaturated and 24.26 (*S*)-unsaturated mins. Conversion was determined to be 100% and the major and minor products was determined to be 98% ee (**28**) and 86% ee (**29**) respectively.

4.1.34. (E)-1-Phenyl-5-(triisopropylsilyl)pent-1-en-4-yn-3-one

This compound is known and fully characterised [46]. (*E*)-1-Phenyl-5-(triisopropylsilyl)pent-1-en-4-yn-3-one was prepared using General Procedure 3 from racemic **31** (0.501 g, 1.60 mmol, 1.00 eq.) and MnO_2 (0.970 g, 11.2 mmol, 7.00 eq.). The crude was further purified using column chromatography (SiO_2; Rf: 0.75 (95:5) petroleum/EtOAc) to yield the desired product as a yellow oil (0.4103 g, 1.31 mmol, 82%). δ_H (400 MHz, $CDCl_3$) 7.96 (1H, d, J = 16.1 Hz, C*H*=CHCO), 7.59–7.54 (2H, m, ArH), 7.50–7.41 (3H, m, ArH), 6.82 (1H, d, J = 16.1 Hz, CH=C*H*CO), 1.17 (21H, m, Si(*i*Pr)$_3$); δ_C (101 MHz, $CDCl_3$) 178.1, 149.0, 134.1, 131.2, 129.1, 128.7, 128.6, 102.6, 96.2, 18.6, 11.1; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{28}NaOSi$

335.1802, found 335.1805; IR (ν): 3060, 3012, 2891, 2154, 1628, 1449, 1228, 1196, 1120, 1070, 975, 869, 761, 676, 574 cm^{-1}; Chiral HPLC (CHIRALPAK ODH column: (0.46 × 25 cm), 0.5 mL/min, IPA:Hexane (5:95); 254 nm UV, 30 °C): retention times: 8.44 (ketone) mins. Data matched that reported.

4.1.35. rac-5-Phenyl-1-(triisopropylsilyl)pent-1-yn-3-ol **30**

This compound is known and fully characterised [47]. Compound **30** was prepared using General Procedure 2. (Triisopropylsilyl)acetylene (0.300 g, 1.64 mmol, 1.00 eq.) was dissolved in THF (anhyd. 3.00 mL) and *n*-butyllithium (2.5 M in hexanes, 0.656 mL, 1.64 mmol, 1.00 eq.) was added dropwise. After 30 min, 3-phenylpropanal (0.221 g, 1.64 mmol, 1.00 eq.) was added. The crude product was purified using column chromatography (SiO_2; Rf: 0.70 (20:1) petroleum/EtOAc) to give the desired product **30** as a colourless oil (0.4422 g, 1.41 mmol, 86%). δ_H (400 MHz, $CDCl_3$) 7.25–7.11 (5H, m, ArH), 4.38–4.30 (1H, m, C*H*(OH)), 2.75 (2H, t, J = 7.9 Hz, CH_2CH_2Ph), 2.02–1.89 (2H, m, CH_2CH_2Ph), 1.71 (1H, d, J = 5.1 Hz, OH), 1.04–0.96 (21H, m, Si(*i*Pr)$_3$); δ_C (101 MHz, $CDCl_3$) 141.4, 128.5, 128.5, 126.0, 108.5, 86.9, 62.4, 39.6, 31.5, 18.6, 11.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{32}NaOSi$ 339.2115, found 339.2110; IR (ν): 3325, 3085, 2941, 2864, 2329, 2170, 1604, 1495, 1457, 1383, 1366, 1212, 1045, 997, 882, 810, 746, 698, 665 cm^{-1}; Chiral HPLC (CHIRALPAK ODH column: (0.46 × 25 cm), 0.5 mL/min, IPA:Hexane (5:95); 254 nm UV, 30 °C): retention times: 14.2 (*S*)-saturated and 28.0 (*R*)-saturated mins. Data matched that reported.

4.1.36. rac-(E)-1-Phenyl-5-(triisopropylsilyl)pent-1-en-4-yn-3-ol **31**

This compound is known and fully characterised [48]. Compound **31** was prepared using General Procedure 2. (Triisopropylsilyl)acetylene (1.06 g, 5.30 mmol, 1.10 eq.) was dissolved in THF (anhyd. 6.0 mL) and *n*-butyllithium (2.5 M in hexanes, 2.32 mL, 5.67 mmol, 1.10 eq.) was added dropwise. After 30 min *E*-cinnamaldehyde (0.70 g, 5.30 mmol, 1.00 eq.) was added. The crude product was purified using column chromatography (SiO_2; Rf: 0.45 (9:1) petroleum/EtOAc) to give the desired product **31** as a pale-yellow oil (0.591 g, 2.04 mmol, 35%); δ_H (300 MHz, $CDCl_3$) 7.33–7.14 (5H, m, ArH), 6.77 (1H, dd, J = 15.8, 1.5 Hz, C*H*=CHCH(OH)), 6.22 (1H, dd, J = 15.8, 5.6 Hz, CH=C*H*CH(OH)), 5.04–4.91 (1H, m, C*H*CO), 1.85 (1H, d, J = 6.7 Hz, OH), 1.01–0.98 (21H, m, Si(*i*Pr)$_3$). δ_C (75 MHz, $CDCl_3$) 162.3, 132.1, 128.6, 128.1, 12.1, 126.8, 106.1, 87.9, 63.4, 18.6, 11.2. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{30}NaOSi$ 337.1958, found 337.1957. IR (ν): 3303, 3062, 3027, 2864, 2164, 2045, 1669, 1462, 1244, 965, 882, 673, 459 cm^{-1} Chiral HPLC (CHIRALPAK ODH column: (0.46 × 25 cm), 0.5 mL/min, IPA:Hexane (5:95); 254 nm UV, 30 °C): retention times: 14.7 (*S*)-unsaturated and 22.1 (*R*)-unsaturated mins. Data matched that reported.

4.1.37. 5-Phenyl-1-(triisopropylsilyl)pent-1-yn-3-one

This compound is known and fully characterised [46]. This compound was prepared using General Procedure 3 from compound **31** (0.182 g, 0.57 mmol, 1.00 eq.) and MnO_2 (0.353 g, 4.06 mmol, 7.00 eq.) to yield the desired product as a yellow oil (0.1691 g, 0.52 mmol, 92%). δ_H (300 MHz, $CDCl_3$) 7.33–7.26 (2H, m, ArH), 7.24–7.17 (3H, m, ArH), 3.05–2.87 (4H, m, CH_2CH_2Ph), 1.11–1.08 (21H, m, Si(*i*Pr)$_3$); HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{20}H_{30}NaOSi$ 337.1958, found 337.1957; IR (ν): 3028, 2943, 2865, 2171, 1675, 1632, 1496, 1461, 1281, 1104, 1071, 997, 920, 882, 804, 749, 665, 585 cm^{-1}; Chiral HPLC (CHIRALPAK ODH column: (0.46 × 25 cm), 0.5 mL/min, IPA:Hexane (5:95); 254 nm UV, 30 °C): retention times: 6.99 (ketone) mins. Data matched that reported.

4.1.38. (R)-5-Phenyl-1-(triisopropylsilyl)pent-1-yn-3-ol **30** and (R,E)-1-phenyl-5-(triisopropylsilyl)pent-1-en-4-yn-3-ol **31**

Compound **30** is known and fully characterised [49]. The ATH was conducted using General Procedure 1. Substrate (0.119 g, 0.38 mmol, 1.00 eq.), (*R,R*)-**2** (2.4 mg, 3.8 μmol, 0.01 eq.) and MeOH (0.5 mL) were reacted for 26 h at 40 °C. The crude product was purified using column chromatography (SiO_2; (9:1) petroleum/EtOAc) to give a mixture of both alcohol products **30** and **31** (0.115 g, 0.36 mmol, 95%). The product was obtained as a pale-yellow oil with an NMR ratio of 69:31 of the major (Sat. OH) **30** and minor (Unsat. OH) **31** product respectively. Enantiomeric excess and conversion determined by (CHIRALPAK ODH column: (0.46 × 25 cm), 0.5 mL/min, IPA:Hexane (5:95); 254 nm UV, 30 °C): retention times: 15.3 (*S*)-unsaturated, 23.5 (*R*)-unsaturated and 30.2 (*R*)-saturated mins. Conversion was determined to be ca. 81% (HPLC) and the ee of the major and minor product was determined to be >99% (**30**) and 95% (**31**) respectively.

4.1.39. (E)-5-(4-Methoxyphenyl)-1-phenylpent-1-en-4-yn-3-one

Synthetic route 1: This compound is novel. Ethynyl-4-methoxybenzene (0.153 g, 1.15 mmol, 1.10 eq.) was dissolved in THF (anhyd. 6.0 mL) and cooled to −78 °C. *n*-butyllithium (1.6 M in hexanes, 2.60 mL, 4.16 mmol, 1.10 eq.) was added dropwise and the mixture was left to stir for 30 min at −78 °C. Pre-cooled to −78 °C, *N,O*-methyoxy-*N*-methylcinnamide (0.200 g, 1.05 mmol 1.00 eq.) in THF (anhyd. 5 mL) was added to the reaction *via* cannula transfer. The reaction mixture was stirred for 1 h at −78 °C before being warmed to r.t. The reaction was monitored using TLC until starting material had disappeared. The reaction mixture was quenched with NH_4Cl (sat. soln, 3 mL) and extracted with EtOAc (3 × 3 mL). The organic layers were combined, dried with $MgSO_{4,\ filtered}$ and concentrated in *vacuo*. The crude product was purified by column chromatography (SiO_2; Rf: 0.60 (9:1) hexanes/EtOAc) to give the desired product as a yellow oil (0.1261 g, 0.48 mmol, 48%).

Synthetic route 2: (*E*)-5-(4-Methoxyphenyl)-1-phenylpent-1-en-4-yn-3-one was prepared using General Procedure 3 from compound **33** (0.6088 g, 2.31 mmol, 1.00 eq.) and MnO_2 (1.403 g, 16.1 mmol, 7.00 eq.). The crude product was further purified using column chromatography (SiO_2; Rf: 0.55 (9:1) petroleum/EtOAc) to yield the desired product as a yellow solid (0.6052 g, 1.80 mmol, 78%). δ_H (400 MHz, $CDCl_3$) 7.89 (1H, d, J = 16.1 Hz, CH=C*H*Ph), 7.60 (4H, dt, J = 7.4, 4.0 Hz, ArH), 7.48–7.38 (3H, m, ArH), 6.96–6.90 (2H, m, ArH), 6.86 (1H, d, J = 16.1 Hz, C*H*=CHPh), 3.85 (3H, s, OMe); δ_C (101 MHz, $CDCl_3$) 178.3, 161.6, 147.7, 135.0, 134.2, 131.1, 129.1, 128.7, 114.4, 112.0, 92.7, 86.6, 55.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{18}H_{14}NaO_2$ 285.0886, found 285.0885; IR 3073, 3024, 2847, 2176, 1645, 1591, 1507, 1447, 1253, 1163, 1095, 1018, 972, 828, 755, 690, 537 cm^{-1}; Mp 142.2 °C; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 9.83 (ketone) mins.

4.1.40. rac-1-(4-Methoxyphenyl)-5-phenylpent-1-yn-3-ol **32**

This compound is known and fully characterised [50]. Compound **32** was prepared using General Procedure 2. 1-Ethynyl-4-methoxybenzene (0.216 g, 1.64 mmol, 1.10 eq.) was dissolved in THF (anhyd. 5.0 mL) and *n*-butyllithium (1.6 M in hexanes, 1.03 mL, 1.64 mmol, 1.10 eq.) was added dropwise. After 30 min 3-phenylpropanal (0.200 g, 1.49 mmol, 1.00 eq.) was added. The crude was purified using column chromatography (SiO_2; Rf: 0.75 (4:1) petroleum/EtOAc) to give the desired product **32** as a yellow oil (0.3122 g, 1.18 mmol, 79%). δ_H (400 MHz, $CDCl_3$) 7.43–7.34 (2H, m, ArH), 7.34–7.15 (5H, m, ArH), 6.89–6.79 (2H, m, ArH), 4.58 (1H, t, J = 6.5 Hz, C*H*OH), 3.81 (3H, s, OMe), 2.86 (2H, t, J = 7.8 Hz, CH_2CH_2Ph), 2.17–2.06 (2H, m, CH_2CH_2Ph), 1.91 (1H, s, OH); δ_C (101 MHz, $CDCl_3$) 159.8, 141.4, 133.2, 128.6, 128.5, 126.0, 114.7, 114.0,

88.4, 85.3, 62.4, 55.3, 39.4, 31.5; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{18}NaO_2$ 289.1196 found 289.1199; IR (*v*): 3346, 2911, 2216, 1890, 1605, 1569, 1507, 1302, 1244, 1032, 825, 751, 697 cm^{-1}; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 10.47 (*R*)-unsaturated and 15.20 (*S*)-unsaturated mins. Data matched that reported.

4.1.41. rac-(E)-5-(4-Methoxyphenyl)-1-phenylpent-1-en-4-yn-3-ol **33**

This compound is known and has been partially characterised [51]. Compound **33** was prepared using General Procedure 2. 1-Ethynyl-4-methoxybenzene (0.5497 g, 4.16 mmol, 1.10 eq.) was dissolved in THF (anhyd. 7.0 mL) and *n*-butyllithium (1.6 M in hexanes, 2.60 mL, 4.16 mmol, 1.10 eq.) was added dropwise. After 30 min *E*-cinnamaldehyde (0.500 g, 3.78 mmol, 1.00 eq.) was added. The crude was purified using column chromatography (SiO_2; Rf: 0.50 (4:1) petroleum/EtOAc) to give the desired product **33** as a yellow oil (0.7203 g, 2.72 mmol, 72%). δ_H (400 MHz, $CDCl_3$) 7.46−7.31 (4H, m, ArH), 7.31−7.26 (3H, m, ArH), 6.89−6.77 (3H, m, ArH and CH=C*H*Ph), 6.38 (1H, dd, *J* = 15.8, 6.0 Hz, C*H*=CHPh), 5.27 (1H, d, *J* = 5.2 Hz, C*H*OH), 3.74 (3H, s, OMe), 2.08 (1H, s, OH); δ_C (101 MHz, $CDCl_3$) 159.9, 138.1, 136.2, 133.3, 131.9, 128.6, 128.3, 128.1, 126.8, 114.0, 86.6, 86.5, 63.6, 55.3; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{16}NaO_2$ 287.1040, found 287.1044; IR (*v*): 3327, 2835, 2209, 1603, 1507, 1290, 1246, 1173, 1029, 967, 833, 750, 693, 534 cm^{-1}; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 11.28 (*R*)-unsaturated and 20.72 (*S*)-unsaturated mins. Data matched that reported.

4.1.42. 1-(4-Methoxyphenyl)-5-phenylpent-1-yn-3-one

This compound is novel. This compound was prepared using General Procedure 3 from compound **32** (0.3122 g, 1.17 mmol, 1.00 eq.) and MnO_2 (0.714 g, 8.22 mmol, 7.00 eq.) to yield the desired product as a yellow solid (0.1521 g, 0.57 mmol, 49%). δ_H (400 MHz, $CDCl_3$) 7.54−7.48 (2H, m, ArH), 7.33−7.17 (5H, m, ArH), 6.91−6.87 (2H, m, ArH), 3.84 (3H, s, OMe), 3.10−3.04 (2H, m, CH_2CH_2Ph), 3.08−2.95 (2H, m, CH_2CH_2Ph). δ_C (101 MHz, $CDCl_3$) 186.9, 161.7, 140.4, 135.2, 128.6, 128.4, 126.3, 114.4, 111.7, 92.4, 87.7, 55.4, 46.9, 30.1; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{18}H_{16}NaO_2$ 287.12 found 287.20; Chiral HPLC (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 6.81 (ketone) mins.

4.1.43. (R)-1-(4-Methoxyphenyl)-5-phenylpent-1-yn-3-ol **32** and (R,E)-5-(4-methoxyphenyl)-1-phenylpent-1-en-4-yn-3-ol **33**

The ATH was conducted using General Procedure 1. (*E*)-5-(4-Methoxyphenyl)-1-phenylpent-1-en-4-yn-3-one (150 mg, 0.57 mmol, 1.00 eq.), (*R,R*)-**2** (3.6 mg, 5.72 μmol, 0.01 eq.) and MeOH (0.5 mL) was reacted for 26 h at 40 °C. The crude product was purified using column chromatography (SiO_2; Rf: 0.10 (9:1) petroleum/EtOAc) to give a mixture of both alcohol products **32** and **33** (0.1375 g, 0.51 mmol, 90%). The product obtained was a pale-yellow oil with an NMR ratio of 86:14 of the major **32** and minor **33** product. Enantiomeric excess and conversion were determined by Chiral HPLC analysis (CHIRALPAK IB column: (0.46 × 25 cm), 1.0 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 9.52 (*R*)-saturated, 11.40 (*R*)-unsaturated, 12.66 (*S*)-saturated and 21.04 (*S*)-unsaturated mins. Conversion was determined to be 98% and the ee of the major and minor product was determined to be 95% (**32**) and 78% (**33**) respectively.

4.1.44. (E)-5-(4-Chlorophenyl)-1-phenylpent-1-en-4-yn-3-one

This compound is known and fully characterised [53]. 1-Chloro-4-ethynylbenzene was prepared as reported [52]. This compound was prepared using General Procedure 3 from compound **35** (0.2407 g, 0.896 mmol, 1.00 eq.) and MnO_2 (0.5390 g, 6.27 mmol, 7.00 eq.) to yield the desired product as a yellow solid (0.2146 g, 0.806 mmol, 90%).δ_H (400 MHz, $CDCl_3$) 7.88 (1H, d, *J* = 16.0 Hz, COCH=C*H*), 7.68−7.56 (4H, m, ArH), 7.49−7.30 (5H, m, ArH), 6.86 (1H, d, *J* = 16.2 Hz, COC*H*=CH); δ_C (101 MHz, $CDCl_3$) 177.9, 148.5, 137.0, 134.2, 134.0, 131.3, 129.2, 129.1, 128.8, 128.4, 118.7, 90.1, 87.4; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{11}^{35}ClNaO$ 289.0391, found 289.0392; IR (*v*): 3029, 2894, 2883, 2210, 1672, 1627, 1485, 1447, 1342, 1176, 1085, 970, 862, 815, 690, 582 cm^{-1}; Mp 145.9 °C; Chiral HPLC (CHIRALPAK ADH column: (0.46 × 25 cm), 0.7 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention time: 15.48 (ketone) mins. Data matched that reported.

4.1.45. rac-1-(4-Chlorophenyl)-5-phenylpent-1-yn-3-ol **34**

This compound is novel. Compound **34** was prepared using General Procedure 2. 1-Chloro-4-ethynylbenzene (0.407 g, 2.98 mmol, 1.00 eq.) was dissolved in THF (anhyd. 5.00 mL) and *n*-butyllithium (2.5 M in hexanes, 1.19 mL, 2.98 mmol, 1.00 eq.) was added dropwise. 3-phenylpropanal (0.400 g, 2.98 mmol, 1.00 eq.) was added after 30 min. The crude was purified using column chromatography (SiO_2; Rf:0.3 (9:1) petroleum/EtOAc) to give the desired product **34** as an orange solid (0.386 g, 1.43 mmol, 48%). δ_H (400 MHz, $CDCl_3$) 7.37−7.19 (9H, m, ArH), 4.59 (1H, q, *J* = 6.1 Hz, C*H*OH), 2.86 (2H, t, *J* = 7.8 Hz, CH_2CH_2Ph), 2.18−2.07 (2H, m, CH_2CH_2Ph), 1.87 (1H, d, *J* = 5.4 Hz, OH); δ_C (101 MHz, $CDCl_3$) 141.2, 138.2, 136.6, 134.6, 132.9, 128.7, 128.5, 128.5, 126.1, 121.0, 90.8, 84.2, 62.2, 39.2, 31.5; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{15}^{35}ClNaO$ 293.0704, found 293.0707; IR (*v*): 3209, 3060, 3025, 2952, 2919, 2858, 2229, 1902, 1801, 1719, 1648, 1487, 1453, 1395, 1087, 1012, 826, 756, 699, 522 cm^{-1}; Mp: 48.5−50.7 °C; Chiral HPLC (CHIRALPAK ADH column: (0.46 × 25 cm), 0.7 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 14.52 (*R*)-saturated and 15.54 (*S*)-saturated mins.

4.1.46. rac-(E)-5-(4-Chlorophenyl)-1-phenylpent-1-en-4-yn-3-ol **35**

This compound is novel. Compound **35** was prepared using General Procedure 2. 1-Chloro-4-ethynylbenzene (0.73 g, 5.67 mmol, 1.00 eq.) was dissolved in THF (anhyd. 8 mL) and *n*-butyllithium (2.5 M in hexanes, 2.27 mL, 5.67 mmol, 1.00 eq.) was added dropwise. After 30 min, *E*-cinnamaldehyde (0.75 g, 5.67 mmol, 1 eq.) was added. The crude product was purified using column chromatography (SiO_2; Rf: 15:1 (9:1) petroleum/EtOAc) to give the desired product **35** as a yellow oil (0.2327 g, 0.85 mmol, 15%). δ_H (400 MHz, $CDCl_3$) 7.40−7.19 (9H, m, ArH), 6.75 (1H, dd, *J* = 15.8, 1.4 Hz, CH=C*H*Ph), 6.30 (1H, dd, *J* = 15.8, 6.1 Hz, C*H*=CHPh), 5.20 (1H, d, *J* = 5.9 Hz, CHOH), 2.07 (1H, s, OH); δ_C (101 MHz, $CDCl_3$) 136.0, 134.7, 133.0, 132.2, 128.7, 128.7, 128.3, 127.8, 126.9, 120.9, 88.9, 85.3, 63.5; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{13}^{35}ClNaO$ 291.0546, found 293.0547; IR (*v*): 3298, 3028, 2852, 2661, 2228, 1648, 1475, 1447, 1398, 1248, 1202, 1090, 1060, 1020, 967, 828, 760 cm^{-1}; Chiral HPLC (CHIRALPAK ADH column: (0.46 × 25 cm), 0.7 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 23.68 (*R*)-unsaturated and 27.11 (*S*)-unsaturated mins.

4.1.47. 1-(4-Chlorophenyl)-5-phenylpent-1-yn-3-one

This compound is novel. This compound was prepared using General Procedure 3 from compound **34** (0.285 g, 1.42 mmol, 1 eq.) and MnO_2 (0.855 g, 9.95 mmol, 7 eq.) to yield the desired product as a yellow solid (0.246 g, 0.91 mmol, 64%). δ_H (300 MHz, $CDCl_3$) 7.52−7.44 (2H, m, ArH), 7.38−7.21 (7H, m, ArH), 3.09−2.96 (4H, m, CH_2CH_2Ph); δ_C (75 MHz, $CDCl_3$) 162.3, 161.6, 140.5, 134.6, 129.1, 128.6, 128.4, 126.4, 116.9, 89.6, 88.5, 46.9, 29.9; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd for $C_{17}H_{13}^{35}ClNaO$ 291.0547, found 291.0552; IR (*v*):

3085, 3059, 2954, 2898, 2201, 1806, 1667, 1588, 1485, 1399, 1296, 1173, 1083, 1012, 823, 744, 697, 529 cm^{-1}; Mp 62.6 °C; Chiral HPLC (CHIRALPAK ADH column: (0.46 × 25 cm), 0.7 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 9.90 (ketone) mins.

*4.1.48. (R)-1-(4-Chlorophenyl)-5-phenylpent-1-yn-3-ol **34** and (R,E)-5-(4-chlorophenyl)-1-phenylpent-1-en-4-yn-3-ol **35***

Both compounds 34 and 35 are novel. The ATH was conducted using General Procedure 1. (*E*)-5-(4-Chlorophenyl)-1-phenylpent-1-en-4-yn-3-one (60.4 mg, 0.27 mmol, 1 eq.), (*R,R*)-2 (approximately 1.4 mg, 2.27 μmol, 0.01 eq.) and DCM (0.5 mL) were reacted for 26 h at 40 °C. The crude product was purified using column chromatography (SiO_2; Rf: 0.20 (9:1) petroleum/EtOAc) to give a mixture of both Sat OH and Unsat OH product (0.043 g, 0.16 mmol, 70%) The product was obtained as a yellow oil with an NMR ratio of 72:21 of the major (Sat. OH) and minor (Unsat. OH) product. There was also a small side product with 0.1 integration (NMR ratio approx. 7%) in relation to the major and minor products. Enantiomeric excess and conversion determined by Chiral HPLC analysis (CHIRALPAK ADH column: (0.46 × 25 cm), 0.7 mL/min, IPA:Hexane (10:90); 250 nm UV, 30 °C): retention times: 14.65 (*R*)-saturated, 23.90 (*R*)-unsaturated, 15.66 (*S*)-saturated and 27.38 (*S*)-unsaturated mins. Conversion was determined to be 100% and the major and minor product was determined to be 96% ee (34) and 71% ee (35) respectively. The 1H NMR of the crude mixture contain an additional alkene peak which was tentatively assigned to 36; δ_H (400 MHz, $CDCl_3$) 6.81 (d, J = 15.8 Hz, 0.29H; 35), 6.55 (d, J = 16.0 Hz, 0.10H; 36), 6.36 (dd, J = 15.8, 6.1 Hz, 0.29H; 35), 6.26–6.16 (m, 0.10H; 36), 5.26 (d, J = 5.8 Hz, 0.28H; 35), 4.58 (t, J = 6.5 Hz, 1H, 34), 4.27 (q, J = 6.5 Hz, 0.1H; 36), 2.84 (t, J = 7.8 Hz, 2.1H; 34 and 35), 2.15–2.08 (m, 2.1H; 34 and 35) (see the Supporting Information).

Data sharing statement

The research data (and/or materials) supporting this publication can be accessed at http://wrap.warwick.ac.uk/.

Declaration of competing interest

The authors declare no conflicting interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131771.

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