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The attempted stereoselective synthesis of chiral 2,2′-biindoline

Mary J. Gresser, Steven M. Wales, Paul A. Keller *

Centre for Medicinal Chemistry, School of Chemistry, University of Wollongong, Northfields Avenue, Wollongong, NSW 2522, Australia

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ABSTRACT

The attempted first stereoselective synthesis of 2,2′-biindoline using a metathesis-Sharpless asymmetric dihydroxylation strategy results in the synthesis of the heterocycle in poor to modest stereoselectivity. Attempts to improve the ee by varying the heteroatom protecting groups in key intermediates did not enhance the outcome of the Sharpless AD reaction. Therefore a limitation of this AD reaction is the use of 1,4-substituted but-2-enes where these substituents are *ortho*-substituted aromatics.

1. Introduction

Chiral biamine compounds are commonly used as ligands in stereoselective metal-catalysed reactions, including Michael additions, biaryl couplings and asymmetric dihydroxylations to name just a few.[1] We are interested in chiral ligand designs based on helix sense discrimination and ligand types of appeal include biphosphines, biarsines, biamines and helical ligands that possess a mixture of heteroatoms. Our general target structures are encapsulated by **2** (Fig. 1) where the helix is defined by two stereogenic atoms, flanked by metal co-ordinating heteroatoms, thus forming an arc of helicity. The helical groove depth and degree of twist could be modulated by a range of substituents 'R', including the presence of fused rings. Importantly, an appropriate synthetic strategy towards these structures should not only be highly stereoselective, but should allow articulation to produce different ring sizes, fused-ring structures and a range of substituted ligands stereoselectively, and in an efficient manner.

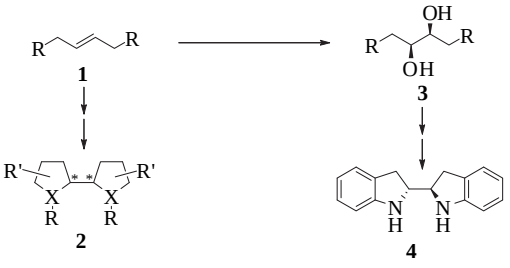

Figure 1. Metathesis—asymmetric dihydroxylation strategy towards the synthesis of bipyrrolidines and biindolines.

The importance of the indoline structure has long been recognised with reference to its place in natural product chemistry, drug design and development and in industry as a key element in catalysts. Despite this illustrious history, there has been surprisingly little investigation into the 2,2′-biindoline structure **4**[2]—even more surprising is the lack of any reporting of the stereoselective synthesis of **4** or related compounds that contain **4** as a substructure. In this paper, we report the first attempted stereoselective synthesis of the parent 2,2′-biindoline **4** starting from achiral substrates and utilising Sharpless asymmetric dihydroxylation as the key reaction for the introduction of the chiral elements.

2. Results

We, and others, have previously reported a self-metathesis—dihydroxylation strategy for the stereoselective synthesis of 2,2′-bipyrrolidine[3] and 2,2′-bistetrahydrofuran.[4] Here we utilise the same strategy (Fig. 1), starting with the protection of 2-allylaniline[20] to produce **6** in 88% yield (Scheme 1).[5] Olefin metathesis of **6** using Grubbs II catalyst in CH_2Cl_2 at reflux yielded the dimer **7** (61%) as a 92:8 mixture of the *E*/*Z* isomers—a single recrystallisation from hexanes increased the ratio to *E*/*Z* 99:1 in 37% yield. The geometric isomers were unable to be separated by column

* Corresponding author. Tel.: +61 2 4221 4692; fax: +61 2 4221 4287; e-mail address: keller@uow.edu.au (P.A. Keller).

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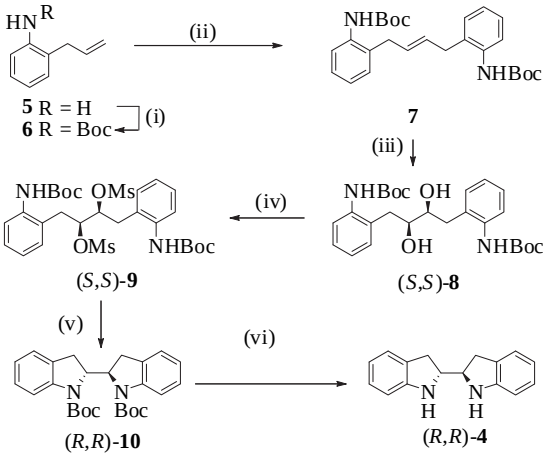
chromatography, however, the stereochemical outcome was determined by integral analysis of the ^{1}H NMR spectrum, in which the *cis* and *trans* signals from the methyl and methylene protons were baseline resolved. All attempts at this metathesis reaction using Grubbs' I resulted in significantly poorer selectivity in the *E*/*Z* ratios, at best 70:30.



Scheme 1. The attempted stereoselective synthesis of chiral 2,2′-biindoline **4**. Illustrated is the example of the synthesis of the *R*,*R*-biindoline. (i) $BocO_2$, Et_3N, Et_2O, 0 °C→rt, 4.5 h, 88%; (ii) Grubbs' II, CH_2Cl_2, Δ, 7 h, 61% (*E*/*Z* 92:8)—recrystallisation from hexanes, 37% (*E*/*Z* 99:1); (iii) ADmix α, methanesulfonamide, 1:1 ^{t}BuOH/H_2O, 30 min, (*S*,*S*)-**8** 34%, ee 50%, ADmix β: (*R*,*R*)-**8** 31%, ee 56%; (iv) MsCl, Et_3N, CH_2Cl_2, 20 min, (*S*,*S*)+*meso*-**9** 98%, (*R*,*R*)+*meso*-**9** 92%; (v) NaH, DMF, 0 °C 24 h, (*S*,*S*)-**10** 74%, (*R*,*R*)-**10** 47%; (vi) TFA, CH_2Cl_2, 12 h, (*S*,*S*)-**11** 82%, (*R*,*R*)-**11** 62%.

The Sharpless asymmetric dihydroxylation of *E*-olefin **7** was performed with ADmix α affording the (*S*,*S*)-diol **8** in 34% yield and 50% ee. Reaction with ADmix β gave the (*R*,*R*)-diol **8** in 31% yield and 56% ee.[6] The poor outcome of the dihydroxylation, in terms of both conversion and enantioselectivity, is surprising given that the substrate contains the preferred aromatic group for the binding pocket.[7] This result can, at least in part, be rationalized by the extreme hydrophobicity of the substrate, which limited its solubility in the polar reaction medium. Additionally, it is possible that the Boc substituent was too large to be accommodated by the binding pocket,[8] which encouraged stereo-indiscriminative binding at the less hindered equatorial oxygens.[9] Attempts to optimise this dihydroxylation reaction did not improve the outcome.

Although these results compromise the stereoselective synthesis and require further examination, we first needed to illustrate the overall synthetic strategy and therefore continued through with the synthesis of the 2,2′-biindoline. Therefore, the diol **8**, as a mixture of the enantiomerically enriched (*S*,*S*) and *meso* epimers,[10] was subjected to standard mesylation conditions giving **9** (*S*,*S*+*meso*, 98%; *R*,*R*+*meso*, 92%) as a mixture of diastereomers. The mixtures were then treated with excess NaH in THF yielding the biindoline **10** (*S*,*S*, 74%, ee 67%; *R*,*R*, 47%, ee 55%), and separately. the *meso*-biindoline **10**.[11] The mono cyclized indoline **11** (20%) (Fig. 2) was also isolated along with a small quantity of an unknown material. Removal of the Boc protecting group with excess TFA in CH_2Cl_2 afforded the biindoline **4** (*S*,*S*, 82%; *R*,*R*, 62%).

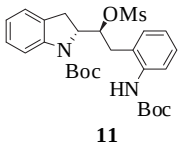
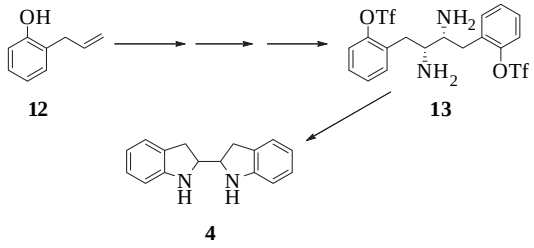


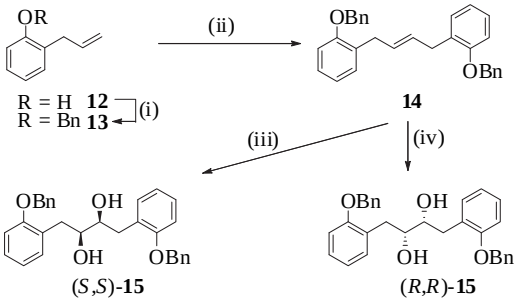
Figure 2. The structure of the minor side product assigned based ^{1}H and ^{13}C NMR, MS and HRMS analyses.

Having shown the feasibility of the strategy, we attempted the analogous reaction starting with the *o*-allylphenol **12** (Scheme 2). This would lead to the intermediate **13** where the phenolic oxygen has been converted into a triflate group, which would allow a Pd-catalysed cyclisation to yield the (2*S*,2′*S*)-biindoline.



Scheme 2. Strategy to biindolines using phenolic substituents.

The phenol **12** was protected using standard procedures (Scheme 3) and the resulting products subjected to Grubbs' I metathesis conditions to give the olefin in 81% yield with an *E*/*Z* ratio of 5.2:1. Dihydroxylation under standard conditions with ADmix α gave the (*S*,*S*)-diol **15** in 15% yield with 64% ee. The same procedure with longer reaction times (91 h) gave a 64% yield with a 33% ee. Use of ADmix β gave a 69% yield with a 91% ee.

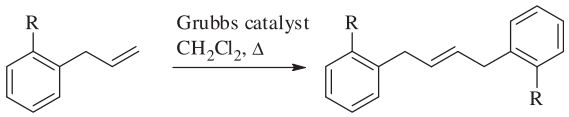


Scheme 3. Metathesis and asymmetric dihydroxylation using phenolic starting materials.

Given the unsatisfactory results of the dihydroxylation reaction, we embarked on an investigation to find the most suitable *ortho*-substituents to use in such reactions. This required the synthesis of the monomeric starting materials, which were then subjected to the metathesis reactions before treatment of the olefins to Sharpless reaction conditions. The results of these investigations are summarised in Tables 1 and 2.

The results of the metathesis reactions are surprisingly variable, with the *E*/*Z* ratios generally better using Grubbs' II catalyst. Although further optimisation of relevant reactions could proceed, the more important results were the outcome of the dihydroxylation reactions. The variations in the *O*-substituted olefins (Table 2, entries 1–6) and those containing aromatic *N*-substituents (Table 2, entries 7–9) encompassed a range of steric intrusion (both large and small) and electron donating and withdrawing character. The results were surprisingly variable both in terms of yield and in particular, enantioselectivity and would not allow the progression of a reasonable stereoselective synthesis. The most reasonable conclusion to draw was that the double *ortho* substitution was imposing excessive steric bulk and was not allowing the substrate to fit into the binding pocket of the chiral ligand. To test this steric argument, we synthesised the aromatic dimethoxy derivatives with the substituents placed *ortho*, *meta* and *para* to the butenyl chain (Table 2, entries 10–12) such that there was a decreasing steric influence on the substrate when binding to the chiral catalyst. In this series, for both ADmix α and β, there was an increase in yield

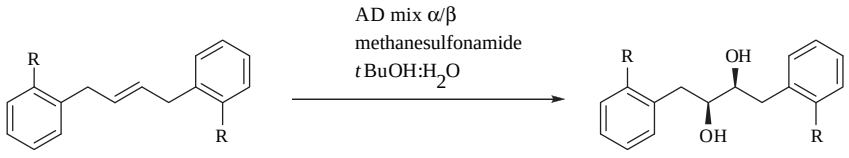
Table 1



Entry	R	Monomer	Olefin	Grubbs' I				Grubbs' II			
				Mol %	Time (h)	Yield[a] %	*E*/*Z*[b]	Mol %	Time (h)	Yield[a] %	*E*/*Z*[b]
1	OBn	**14**	**15**	6.7	4.5	81	5.2:1	5	26	93	7:1
2	OPMB	**17**	**29**	5	23	51	5:1	5	23	71	7.1:1
3	OAc	**18**	**30**	5	15	85	4:1	5	66	77	8:1
4	OTf	**19**	**31**	5	15	88	3.8:1	5	66	75	9:1
5	OTBS	**20**	**32**	5	66	85	4.3:1	5	66	95[c]	8.4:1
			—		—	—		5	7.5	95[c]	7:1
6	OH	**13**	**33**[e]	10	25	50	9:1	—	—	—	—
7	NHBoc	**6**	**7**	10	3	76	1.6:1	10	7	61	11.5:1
8	NHAc	**21**	**34**	—	—	—	—	10	17	73	*E* only
9	NO_2	**22**	**35**	—	—	—	—	5	7	26	43:1
				—	—	—	—	5	20	23	10:1
10	*o*-OMe	**23**	**36**	5	19	81	4.4:1	5	19	60[c]	5.6:1
				5	7	91	4.5:1	5	24	73[c]	5.5:1
11	*m*-OMe	**24**	**37**	2.5	15	63	4.5:1	—	—	—	—
12	*p*-OMe	**25**	**38**	2.5	4.5	97	6.2:1	—	—	—	—
13	H	**26**	**39**	5	24	69	4.8:1	3	25	0	—
				2.5	18	89	4.7:1	—	—	—	—
14	Me	**27**	**40**	2.5				—	—	—	—
15	Br	**28**	**41**[d]	—				5	23	16[c]	6.2:1

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Final yield determined by ^{1}H NMR.
[d] A mixture of olefins was produced, tentatively assigned as *E*-1,4-di(2-bromophenyl)-2-butene **41**, *Z*-1,4-di(2-bromophenyl)-2-butene, *E*-1,4-di(2-bromophenyl)-1-butene, *E*-1,5-di(2-bromophenyl)-2-pentene, *E*-3-(2-bromophenyl)-1-phenylpropene and *E*-1-(2-bromophenyl)-3-phenylpropene in a 6.3:1:1.2:1.1:1:1.2 ratio as determined by ^{1}H NMR analysis.
[e] Olefin synthesised by deprotection of **32**.

Table 2



Entry	R	Olefin	Diol	ADmix α			ADmix β		
				Time (h)	Yield % [a]	ee % [b]	Time (h)	Yield % [a]	ee % [b]
1	OBn	**15**	**16**	91	64	30	37	69	91
2	OPMB	**29**	**42**	40	Trace	—	40	Trace	—
3	OAc	**30**	**43**	24	0	—	24	0	—
4	OTf	**31**	**44**	24	25	1.4	24	58	8
5	OTBS	**32**	**45**	24	13	23	24	31	14
6	OH	**33**	**46**	24	0	—	24	0	—
7	NHBoc	**7**	**8**	90	34	31	90	31	56
8	NHAc	**34**	**47**	24	0	—	24	0	—
9	NO_2	**35**	**48**	24	18	44	24	45	58
10	*o*-OMe	**36**	**49**	24	52	34	24	37	40
11	*m*-OMe	**37**	**50**	24	77	73	24	86	76
12	*p*-OMe	**38**	**51**	24	90	85	24	96	87
13	H	**39**	**52**	24	88	93	24	84	95
14	Me	**40**	**53**	24	65	62	24	45	70

[a] Isolated yield.
[b] Determined by chiral HPLC.

and ee as the dimethoxy substituents were further away from the butenyl chain. To add support to our steric argument, we tested the aromatic unsubstituted (Table 2, entry 13) and the di-*o*-methyl substituted (Table 2, entry 14) derivatives, the latter being a relatively electronically neutral and small moiety. The former returned excellent yields, comparable to those reported[27] and ee values whereas the latter, with just a small steric intrusion, already started to induce a decrease in yield in ee. Therefore, there is strong evidence that steric hinderance is playing a significant role in the outcome of these dihydroxylation reactions.

3. Conclusion

We have shown that the metathesis—dihydroxylation strategy can be extended from the synthesis of 2,2′-bipyrrolidines to the synthesis of 2,2′-biindolines, however, it is not a valid

stereoselective synthesis with poor ee returns during the dihydroxylation reactions. We suggested that the steric intrusion of the two aromatic *ortho* substituents are responsible and that it is sufficiently general to say that the Sharpless AD reactions are not suitable conditions for any allylic bis(di-*ortho*-substituted aromatic) systems. We are currently investigating an alternative synthetic strategy towards the key intermediate diols, which avoids the Sharpless AD reaction.

4. Experimental

4.1. General procedures

Reagents and solvents were purchased reagent grade and used without further purification unless otherwise stated. THF and Et_2O were distilled from sodium/benzophenone and CH_2Cl_2 was distilled from CaH_2. All reactions were performed in standard oven-dried glassware under a nitrogen atmosphere unless otherwise stated. UV irradiation was carried out with a 500 W Iwasaki Electric Lamp at 250–400 nm. Melting points were determined using a Gallenkamp (Griffin) melting point apparatus. Temperatures are expressed in degrees Celsius (°C) and are uncorrected.

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance (NMR) spectra were recorded at 300 and 75 MHz, respectively, on a Varian Mercury 300 MHz spectrometer in $CDCl_3$. Alternatively, where stated, ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz on a Varian Inova 500 MHz spectrometer. Chemical shifts (δ) are reported in parts per million relative to TMS (δ=0 ppm) or $CDCl_3$ (δ=77.0 ppm) as internal standards. Coupling constants (J) are reported in hertz (Hz). Multiplicities are reported as singlet (s), broad singlet (br s), doublet of doublets (dd) or multiplet (m).

Chemical ionization (CI) and Electron impact (EI) mass spectra (MS) were recorded on a Shimadzu QP-5000 spectrometer and high resolution (HR) on a VG AutoSpec spectrometer. Electrospray (ES) mass spectra were recorded on a Micromass Platform LCZ spectrometer and high resolution on a Micromass QTOF2 spectrometer. Ion mass to charge (m/z) values are stated with their relative abundances as a percentage in parentheses. Peaks assigned to the molecular ion are denoted by M^+.

High Performance Liquid Chromatography (HPLC) was performed using a Waters 1515 pump and a Daicel Chiralcel OD-H column with a flow rate of 1 mL/min and a detection wavelength of 254 nm. Enantiomeric excesses (ee) were determined by analysis of analyte peak area. Thin Layer Chromatography (TLC) was performed using Merck Silica Gel F_{254} aluminium sheets. Column chromatography was performed under gravity using Merck Silica Gel 60 (0.063–0.200 mm). Eluents are in volume to volume (v/v) proportions.

For all reactions performed on mixtures of stereoisomers an overall yield is stated. Where the diastereomeric products were separated by chromatography the yields are based on the quantity of the relevant isomer in the starting mixture. The quantity of each isomer in the mixtures was in all cases determined by ^{1}H NMR analysis. Peaks in the ^{1}H and ^{13}C NMR arising due to unwanted *Z* or *meso* impurities are marked with an asterix (*).

4.2. Synthesis of biindoline—Scheme 1

4.2.1. N-tert-Butoxycarbonyl-o-allylaniline ***6***.[12] A solution of *o*-allylaniline **5** (845 mg, 6.34 mmol) in diethyl ether (10 mL) was cooled to 0 °C. To this was added triethylamine (700 mg, 6.91 mmol) followed by a solution of di-*tert*-butyldicarbonate (1.50 g, 8.61 mmol) in diethyl ether (10 mL) and the mixture was stirred at 0 °C for 10 min and then at rt for a further 4.5 h. The mixture was diluted with hexanes (15 mL) and the precipitate removed by suction filtration, washed with hexanes and dried in vacuo yielding the urea *N,N*-diBoc-1,3-bis(2-allylphenyl)urea (52 mg, 6%) as a white solid. FTIR (neat) ν_{max} 2980, 1737, 1701, 1527, 1450, 1368, 1235, 1157, 1050, 753. ^{1}H NMR: δ 3.29 (d, $^3J_{HH}$=6.0 Hz, 2H, $ArCH_2$), 4.76 (dd, $^2J_{HH}$=1.5 Hz, $^3J_{HH}$=17.0 Hz, 1H, =C*H*H), 4.92 (dd, $^2J_{HH}$=1.5 Hz, $^3J_{HH}$=10.0 Hz, 1H, =C*H*H), 5.74–5.82 (m, 1H, CH_2CH), 6.28 (br s, 1H, NH), 7.14–7.30 (m, 3H, ArH), 7.65 (d, 1H, $^3J_{HH}$=8.0 Hz, ArH); ^{13}C NMR: 36.4 ($ArCH_2$), 116.4 (=CH_2), 125.3 (ArCH), 125.9 (ArCH), 127.7 (ArCH), 130.5 (ArCH), 132.8 (ArC), 135.6 (=CH), 135.9 (ArC), 154.1 (CO); MS (ES, +ve): 293 (100%, M+H); HRMS (ES +ve) calcd for $C_{19}H_{20}N_2O$ 292.1579, found 292.1576. The filtrate was concentrated and subjected to silica gel chromatography (5% ethyl acetate/hexanes), yielding the protected *o*-allylaniline **6** (1.289 g, 88%) as a colourless oil.[12] ^{1}H NMR: δ 1.51 (s, 9H, CH_3), 3.35 (d, $^3J_{HH}$=6.0 Hz, 2H, $ArCH_2$), 5.01–5.09 (m, 1H, =C*H*H), 5.12–5.17 (m, 1H, =CH*H*), 5.88–6.01 (m, 1H, CH_2CH), 6.45 (br s, 1H, NH), 7.00–7.06 (m, 1H, ArH), 7.11–7.14 (m, 1H, ArH), 7.19–7.25 (m, 1H, ArH), 7.78 (d, $^3J_{HH}$=7.8 Hz, 1H, ArH); ^{13}C NMR: δ 28.2 (CH_3), 36.4 ($ArCH_2$), 80.2 ($C(CH_3)_3$), 116.5 (=CH_2), 121.9 (ArCH), 123.9 (ArCH), 127.3 (ArCH), 128.9 (ArC), 129.9 (ArCH), 135.8 (=CH), 136.4 (ArC), 153.1 (CO); MS (CI, +ve): 234 (20, M+H), 233 (18), 178 (100), 133 (18); HRMS (EI, +ve) calcd for $C_{14}H_{19}NO_2$ 233.1416, found 233.1415.

4.2.2. E-1,4-Di(2-N-tert-butoxycarbonylaniline)-2-butene ***7***. To a stirred solution of the protected *o*-allylaniline **6** (101 mg, 0.433 mmol) in CH_2Cl_2 (12.0 mL) was added Grubbs' II catalyst (37 mg, 0.044 mmol) and the mixture was heated at reflux for 7 h. The solvent was removed under reduced pressure and the resulting residue was subjected to silica gel chromatography (7% ethyl acetate/hexanes) affording the alkene **7** (58 mg, 61%) as a 92:8 mixture of *E*/*Z* isomers. Subsequent recrystallization from hexanes enriched the quantity of the *E* isomer to 99% (35 mg, 37%). IR (neat) ν_{max} 3360, 1693, 1516, 1453, 1301, 1242, 1158, 1055, 744. ^{1}H NMR (500 MHz): δ 1.50 (s, 18H, CH_3), 3.36 (d, $^3J_{HH}$=2.7 Hz, 4H, CH_2), 5.63–5.66 (m, 2H, =CH), 6.54 (br s, 2H, NH), 7.01–7.05 (m, 2H, ArH), 7.12 (d, $^3J_{HH}$=7.0 Hz, 2H, ArH), 7.20–7.23 (m, 2H, ArH) 7.75 (d, $^3J_{HH}$=6.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz): δ 28.3 (CH_3), 35.2 (CH_2), 80.3 ($C(CH_3)_3$), 122.1 (ArCH), 124.1 (ArCH), 127.3 (ArCH), 129.6 (ArC), 129.7 (=CH), 129.8 (ArCH), 136.3 (ArC), 153.1 (CO); MS (EI, +ve): 438 (7, M^+), 132 (100); HRMS (CI +ve) calcd for $C_{26}H_{35}N_2O_4$ 439.2597, found 439.2584.

4.2.3. Z/E Isomerization. To a stirred solution of the alkene **7** (*E*/*Z*, 46:54) (75 mg, 0.17 mmol) in benzene (5 mL) was added diphenyl disulfide (20 mg, 0.09 mmol) and the mixture was heated at reflux under UV irradiation for 7 h. The solution was concentrated under reduced pressure and the residue was subjected to gravity silica chromatography (8% ethyl acetate/hexanes) yielding the alkene **7** (*E*/*Z*, 83:17) (72 mg, 96%).

4.2.4. (2S,3S)-1,4-Di(2-N-tert-butoxycarbonylaniline)-2,3-butandiol ***8****—general procedure A.* A solution of ADmix α (200 mg, 0.57 μmol Os) and methanesulfonamide (15 mg, 0.16 mmol) in water (2.5 mL) was cooled to 0 °C. To this mixture was added a solution of the *E*-alkene **7** (99% geometrical purity) (60 mg, 0.14 mmol) in *tert*-butylalcohol (3 mL) and the resulting slurry was stirred at 0 °C in air for 90 h. Sodium sulfite (2.2 g) was added and stirring was continued for 30 min. The reaction mixture was then extracted with ethyl acetate (3×10 mL) and the combined organic layers were washed with 2 M KOH (2×10 mL) and dried ($MgSO_4$). The solution was concentrated and subjected to silica gel chromatography (13–30% ethyl acetate/hexanes) affording the (2*S*,3*S*)-diol **8** (22 mg, 34%) as a white solid, mp 140–145 °C. IR (neat) ν_{max} 3432, 3288, 2976, 1690, 1517, 1452, 1368, 1299, 1246, 1158, 1048, 1022, 756. ^{1}H NMR: δ 1.49 (s, 18H, CH_3), 2.80–2.94 (m, 4H, CH_2), 3.26 (br s, 2H, OH), 3.65–3.73 (m, 2H, C*H*OH), 7.03–7.25 (m, 6H, ArH), 7.62 (d, $^3J_{HH}$=7.8 Hz, 2H, ArH), 7.67 (s, 2H, NH); ^{13}C NMR: δ 28.4 (CH_3), 35.4 (CH_2), 74.9 (CHOH) 80.3 ($C(CH_3)_3$), 123.9 (ArCH), 124.6 (ArCH), 127.4 (ArCH), 129.9 (ArC), 130.5 (ArCH) 137.0 (ArC), 154.2 (CO); MS (EI, +ve): 472 (12, M^+), 106 (100); HRMS (EI, +ve) calcd for $C_{26}H_{36}N_2O_6$

472.2573, found 472.2568. HPLC analysis (10% 2-propanol/hexane, retention times (2*R*,3*R*)-diol **8** 8.2 min (minor), (2*S*,3*S*)-diol **8** 16.2 min (major)) showed the ee of the (2*S*,3*S*)-diol **8** was 50%.

*4.2.5. (2R,3R)-1,4-Di(2-N-tert-butoxycarbonylaniline)-2,3-butandiol **8**.* A solution of ADmix β (150 mg, 0.43 μmol Os) and methanesulfonamide (10 mg, 0.11 mmol) in water (2.5 mL) was cooled to 0 °C. To this mixture was added a solution of the *E*-alkene **7** (99% geometrical purity) (45 mg, 0.11 mmol) in *tert*-butylalcohol (3 mL) and the resulting slurry was stirred at 0 °C in air for 90 h. Sodium sulfite (2.2 g) was added and stirring was continued for 30 min. The reaction mixture was then extracted with ethyl acetate (3×10 mL) and the combined organic layers were washed with 2 M KOH (2×10 mL) and dried ($MgSO_4$). The solution was concentrated and subjected to silica gel chromatography (13–30% ethyl acetate/hexanes) yielding the (2*R*,3*R*)-diol **8** (15 mg, 31%) with physical and spectral properties identical to the (2*S*,3*S*)-diol **8**. HPLC analysis (10% 2-propanol/hexane, retention times (2*R*,3*R*)-diol **8** 8.3 min (major), (2*S*,3*S*)-diol **8** 17.8 min (minor)) showed the ee of the (2*R*,3*R*)-diol **8** was 56%.

*4.2.6. (2S,3S)-1,4-Di(2-N-tert-butoxycarbonylaniline)-2,3-dimethanesulfonylbutane **9**.* To a solution of the diol **8** ((2*S*,3*S*)/*meso*, 64:36) (80 mg, 0.17 mmol) in CH_2Cl_2 (5 mL) at 0 °C were added triethylamine (144 mg, 1.42 mmol) and methanesulfonyl chloride (102 mg, 0.89 mmol) and the mixture was stirred at rt for 20 min. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with $CuSO_4$ (15 mL), followed by satd $NaHCO_3$ (15 mL) and brine (15 mL). The organic component was dried ($MgSO_4$) and the solvent removed under reduced pressure yielding the dimesylate **9** (104 mg, 98%) as a white solid, and as a 64:36 mixture of the (2*S*,3*S*)/*meso* diastereomers. Chromatography on gravity silica gel (20% ethyl acetate/hexanes) afforded the (2*S*,3*S*)-dimesylate **9** (30 mg, 44%). FTIR ν 3431 (w), 3288 (w), 1690 (s), 1517 (m), 1452 (m), 1367 (s), 1298 (m), 1157 (s), 1047 (m), 756 (s). ^{1}H NMR: δ 1.51 (s, 18H, CH_3), 2.43 (s, 6H, SCH_3), 3.06 (dd, $^2J_{HH}$=14.7 Hz, $^3J_{HH}$=9.6 Hz, 2H, C*H*H), 3.21 (dd, $^2J_{HH}$=14.7 Hz, $^3J_{HH}$=3.6 Hz, 2H, CH*H*), 4.97–5.03 (m, 2H, OCH), 6.54 (s, 2H, NH), 7.10–7.16 (m, 2H, ArH), 7.25–7.32 (m, 4H, ArH), 7.63 (d, $^3J_{HH}$=7.8 Hz, 2H, ArH); ^{13}C NMR: δ 28.2 (CCH_3) 31.6 (CH_2), 37.2 (SCH_3), 80.8 (OCH) 80.9 (*C*(CH_3)$_3$), 125.0 (ArCH), 125.2 (ArCH), 127.9 (ArC), 128.5 (ArCH), 131.4 (ArCH) 136.6 (ArC), 153.8 (CO); MS (EI, +ve): 628 (4, M^+), 118 (100); HRMS (CI, +ve) calcd for $C_{28}H_{41}N_2O_{10}S_2$ 629.2203, found 629.2186. Further elution gave the dimesylate **9** (71 mg) as a 50:50 mixture of the diastereomers.

*4.2.7. (2R,3R)-1,4-Di(2-N-tert-butoxycarbonylaniline)-2,3-dimethanesulfonylbutane **9**.* To a solution of the diol **8** ((2*R*,3*R*)/*meso*, 72:28) (500 mg, 1.06 mmol) in CH_2Cl_2 (12 mL) at 0 °C was added triethylamine (756 mg, 7.49 mmol) and methanesulfonyl chloride (668 mg, 5.85 mmol) and the mixture was stirred at rt for 20 min. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with $CuSO_4$ (15 mL), followed by satd $NaHCO_3$ (15 mL) and brine (15 mL). The organic component was dried ($MgSO_4$) and the solvent removed under reduced pressure yielding the dimesylate **9** (612 mg, 92%) as a 74:26 mixture of the (2*S*,3*S*)/*meso* diastereomers.

*4.2.8. (2S,2′S)-N,N′-tert-Butoxycarbonylbiindoline **10** and meso-(2,2′)-N,N′-tert-butoxycarbonylbiindoline **10**.* To NaH (26 mg, 60% suspension, 0.65 mmol) at 0 °C was slowly added a solution of the dimesylate **9** (a mixture containing 45 mg, 0.072 mmol, (2*R*,3*R*)-dimesylate **9** and 11 mg, 0.018 mmol, *meso*-dimesylate **9**) in THF (8 mL) and the mixture was brought to rt and stirred for 18 h. NaH (20 mg, 60% suspension, 0.50 mmol) was again added and the mixture was stirred for a further 24 h. The mixture was cooled to 0 °C and ethanol (10 mL) was slowly added, followed by water (10 mL), and stirring was continued for 30 min. The organic component was extracted with CH_2Cl_2 (3×10 mL) and the combined extracts were washed with brine (20 mL) and dried ($MgSO_4$). The solution was concentrated and subjected to silica gel chromatography (3% ethyl acetate/hexanes) affording the (2*S*,2′*S*)-biindole **10** (23 mg, 74%) as a white solid, mp 180–185 °C. IR (neat) ν_{max} 1696, 1485, 1390, 1373, 1341, 1313, 1161, 1139, 1021, 752. ^{1}H NMR: δ 1.54 (s, 18H, CH_3), 2.72 (dd, $^2J_{HH}$=16.8 Hz, $^3J_{HH}$=2.4 Hz, 2H, C*H*H), 3.16 (dd, $^2J_{HH}$=16.8 Hz, $^3J_{HH}$=9.6 Hz, 2H, CH*H*), 4.96–5.01 (m, 2H, CHN), 6.87–6.93 (m, 2H, ArH), 7.01 (d, $^3J_{HH}$=7.2 Hz, 2H, ArH), 7.13–7.20 (m, 2H, ArH), 7.70 (br s, 2H, ArH); ^{13}C NMR: δ 28.4 (CH_3), 29.7 (CH_2), 60.0 (CHN), 81.3 (*C*(CH_3)$_3$), 115.5 (ArC), 122.5 (ArCH), 124.5 (ArCH), 127.3 (ArCH), 129.7 (ArCH), 143.3 (ArC), 152.6 (CO); MS (EI, +ve): 436 (17, M^+), 118 (100); HRMS calcd for $C_{26}H_{32}N_2O_4$ 436.2362, found 436.2345. HPLC analysis (2.5% 2-propanol/hexane, retention times (2*S*,2′*S*)-biindoline **10** 13.0 min (major), (2*R*,2′*R*)-biindoline **10** 14.8 min (minor)), showed the ee of the (2*S*,2′*S*)-biindoline **10** was 69%. Further elution gave the *meso*-biindoline **10** (5 mg, 64%) as a white solid. ^{1}H NMR: δ 1.48 (s, 18H, CH_3), 2.67 (d, $^2J_{HH}$=16.5 Hz, 2H, C*H*H), 3.23 (dd, $^2J_{HH}$=16.5 Hz, $^3J_{HH}$=10.0 Hz, 2H, CH*H*), 4.80–4.85 (m, 2H, CHN), 6.88–6.92 (m, 2H, ArH), 7.02 (d, $^3J_{HH}$=7.5 Hz, 2H, ArH), 7.09–7.13 (m, 2H, ArH), 7.46 (br s, 2H, ArH); ^{13}C NMR: δ 28.3 (CH_3), 30.4 (CH_2), 62.2 (CHN), 81.0 (*C*(CH_3)$_3$), 115.6 (ArC), 122.4 (ArCH), 124.1 (ArCH), 127.1 (ArCH), 130.7 (ArCH), 143.0 (ArC), 152.7 (CO).

*4.2.9. (2R,2′R)-N,N′-tert-Butoxycarbonylbiindoline **10**, heterocycle **11** and indoline **12**.* To NaH (60 mg, 60% suspension, 1.50 mmol) at 0 °C was slowly added a solution of the dimesylate **9** (a mixture containing 228 mg, 0.363 mmol, (2*S*,3*S*)-dimesylate **9** and 60 mg, 0.096 mmol, *meso*-dimesylate **9**) in THF (8 mL) and the mixture was brought to rt and stirred for 24 h. The mixture was cooled to 0 °C and ethanol (10 mL) was slowly added, followed by water (10 mL), and stirring was continued for 30 min. The organic component was extracted with CH_2Cl_2 (3×10 mL) and the combined extracts were washed with brine (20 mL) and dried ($MgSO_4$). The solution was concentrated and subjected to silica gel chromatography (3% ethyl acetate/hexanes) affording the (2*R*,2′*R*)-biindoline **10** (75 mg, 47%) with identical physical and spectral properties to the (2*S*,2′*S*)-biindoline **10**. HPLC analysis (2.5% 2-propanol/hexane, retention times (2*S*,2′*S*)-biindoline **10** 12.6 min (minor), (2*R*,2′*R*)-biindoline **10** 14.3 min (major)), showed the enantiomeric excess of the (2*R*,2′*R*)-biindoline **10** was 55%. Further elution gave the *meso*-biindoline **10** (14 mg, 33%) followed by a 50:50 mixture (2 mg) of the *meso*-biindoline **10** and an unknown compound (<1%). ^{1}H NMR (excluding *meso*-biindoline **10**): δ 1.51 (s, 18H, CH_3), 2.88 (dd, $^2J_{HH}$=15.9 Hz, $^3J_{HH}$=2.4 Hz, 2H, C*H*H), 3.51 (dd, $^2J_{HH}$=15.9 Hz, $^3J_{HH}$=9.9 Hz, 2H, CH*H*), 5.03–5.10 (m, 2H, CHN), 6.01 (dd, $^2J_{HH}$=16.5 Hz, $^3J_{HH}$=7.2 Hz, 2H, ArH), 6.62 (d, $^3J_{HH}$=15.6 Hz, 2H, ArH), 7.13–7.20 (m, 2H, ArH), 7.81 (d, $^3J_{HH}$=8.1 Hz, 2H, ArH). Increasing the gradient to 15% ethyl acetate/hexane lead to elution of the indoline **11** (39 mg, 20%) as a white solid. ^{1}H NMR (500 MHz): δ 1.53 (s, 18H, CH_3), 2.47 (s, 3H, SCH_3), 3.03 (dd, $^2J_{HH}$=14.0 Hz, $^3J_{HH}$=8.5 Hz, 1H, OCC*H*H), 3.14 (dd, $^2J_{HH}$=14.0 Hz, $^3J_{HH}$=6.0 Hz, 1H, OCCH*H*), 3.19–3.25 (m, 1H, NCC*H*H), 3.30–3.37 (m, 1H, NCCH*H*), 4.52 (d, $^3J_{HH}$=9.0 Hz, 1H, NCH), 5.20–5.30 (m, 1H, OCH), 6.81 (s, 1H, NH), 6.94–6.97 (m, 1H, ArH), 7.07–7.10 (m, 1H, ArH), 7.12–7.19 (m, 3H, ArH), 7.25–7.29 (m, 1H, ArH), 7.70–7.85 (m, 2H, ArH); ^{13}C NMR (125 MHz): δ 28.1 (NCCH_2), 28.3 (CH_3), 34.7 (OCCH_2), 37.4 (SCH_3), 59.9 (NCH), 80.5 (NHCOO*C*(CH_3)$_3$), 81.9 (NCOO*C*(CH_3)$_3$), 82.6 (OCH), 109.7 (ArC), 114.7 (ArCH), 122.9 (ArCH), 124.4 (ArCH), 124.5 (ArCH), 127.5 (ArCH), 128.4 (ArCH), 129.6 (ArC), 129.6 (ArCH), 130.8 (ArCH), 136.8 (ArC), 142.5 (ArC), 153.5 (CO); MS (EI, +ve): 532 (22, M^+), 118 (100); HRMS (EI, +ve) calcd for $C_{27}H_{36}N_2O_7S$ 532.2243, found 532.2249.

*4.2.10. (2S,2′S)-Biindoline **4**.* A solution of the (2*S*,2′*S*)-biindoline **10** (120 mg, 0.28 mmol) in CH_2Cl_2 (3 mL) was cooled to 0 °C. To this was slowly added TFA (310 mg, 2.73 mmol) and the mixture was

stirred at rt for 12 h. A further aliquot of TFA (103 mg, 0.91 mmol) was added and stirring continued for an additional 4 h. The mixture was diluted with CH_2Cl_2 (10 mL) and 2 M NaOH (10 mL) was added. The organic layer was extracted with CH_2Cl_2 (3×10 mL) and the combined extracts were washed with brine (20 mL) and dried ($MgSO_4$). The solution was concentrated and the crude residue subjected to silica gel chromatography (ethyl acetate/hexanes/NEt_3, 12:87:1) yielding (2*S*,2′*S*)-biindoline **4** (53 mg, 82%) as a white solid, mp 145–148 °C. FTIR ν 3360 (w), 2843 (w), 1603 (m), 1481 (m), 1460 (m), 1238 (s), 1066 (m), 745 (s). ^{1}H NMR: δ 2.75 (dd, $^2J_{HH}$=15.5 Hz, $^3J_{HH}$=7.0 Hz, 2H, C*H*H), 3.21 (dd, $^2J_{HH}$=15.5 Hz, $^3J_{HH}$=8.0 Hz, 2H, CH*H*), 3.89–3.94 (m, 2H, CHN), 4.20 (br s, 2H, NH), 6.63 (d, $^3J_{HH}$=7.5 Hz, 2H, ArH), 6.70–6.74 (m, 2H, ArH), 7.01–7.05 (m, 2H, ArH), 7.09 (d, $^3J_{HH}$=7.0 Hz, 2H, ArH); ^{13}C NMR: δ 33.4 (CH_2), 64.9 (NCH), 109.5 (ArCH), 119.0 (ArCH), 124.7 (ArCH), 127.4 (ArCH), 128.6 (ArC), 150.7 (ArC); MS (EI, +ve): 236 (5, M^+), 118 (100); HRMS (E.I +ve) calcd for $C_{16}H_{16}N_2$ 236.1313, found 236.1310.

*4.2.11. (2R,2′R)-Biindoline **4**.* A solution of the (2*R*,2′*R*)-biindoline **10** (74 mg, 0.17 mmol) in CH_2Cl_2 (3 mL) was cooled to 0 °C. To this was slowly added TFA (192 mg, 1.69 mmol) and the mixture was stirred at rt for 24 h. A further aliquot of TFA (103 mg, 0.91 mmol) was added and stirring continued for an additional 24 h. The mixture was diluted with CH_2Cl_2 (10 mL) and 2 M NaOH (10 mL) was added. The organic layer was extracted with CH_2Cl_2 (3×10 mL) and the combined extracts were washed with brine (20 mL) and dried ($MgSO_4$). The solution was concentrated and the crude residue subjected to silica gel chromatography (ethyl acetate/hexanes/NEt_3, 12:87:1) yielding (2*R*,2′*R*)-biindoline **4** (25 mg, 62%) with identical physical and spectral properties to (2*S*,2′*S*)-biindoline **4**.

4.3. Synthesis of allyl monomers

*4.3.1. 2-Allyl-1-benzyloxybenzene **14**.*[12] 2-Allylphenol **13** (1.74 mL, 13.41 mmol) was added dropwise to a stirred suspension of NaH (645 mg, 60% dispersion in oil, 16.11 mmol) in THF (45 mL) at 0 °C. Benzyl bromide (1.59 mL, 13.41 mmol) was added after 1 h, the reaction was allowed to warm to rt and stirring was continued for 20 h. The reaction was quenched with isopropyl alcohol and water, and extracted with EtOAc (3×50 mL). The combined organic layers were washed with NaOH (2 M) and water then dried ($MgSO_4$). The crude oil was subjected to gravity silica gel column chromatography (1% EtOAc/hexanes) to afford the protected phenol **14** (2.85 mg, 95%) as a volatile, colourless oil.[†] ^{1}H NMR (300 MHz) δ 3.45 (d, 2H, $^3J_{HH}$=6.6 Hz, CH_2CH=CH$_2$), 5.02–5.09 (m, 2H, CH=CH_2), 5.07 (s, 2H, PhCH_2), 6.02 (ddt, 1H, $^3J_{HH}$=6.7, 10.1, 16.8 Hz, C*H*=CH$_2$), 6.89–6.94 (m, 2H, ArH4 and ArH6), 7.14–7.21 (m, 2H, ArH3 and ArH5), 7.28–7.44 (m, 5H, 5×ArH′); ^{13}C NMR (75 MHz) δ 34.4 (CH_2CH=CH$_2$), 69.9 (PhCH_2), 111.7 (ArC6), 115.4 (CH=CH_2), 120.8 (ArC4), 127.1 (ArC2′), 127.3 (ArC5), 127.7 (ArC4′), 128.5 (ArC3′), 129.0 (ArC2), 129.9 (ArC3), 137.0 (C*H*=CH$_2$), 137.4 (ArC1′), 156.3 (ArC1); FTIR ν 1600 (w), 1492 (m), 1452 (m), 1240 (s), 1126 (w), 1024 (w), 913 (w), 750 (s), 735 (s); MS (CI, +ve) *m*/*z* 225 (100%, M+H), 147 (33), 131 (43); HRMS (EI, +ve) calcd for $C_{16}H_{16}O$ 224.1201, found 224.1192.

*4.3.2. 1-(4-Methoxybenzyloxy)-2-allylbenzene **17**.*[13] 4-Methoxybenzyl alcohol (0.28 mL, 2.26 mmol) was dissolved in HBr (0.6 mL, 45% solution in glacial acetic acid) and stirred for 30 min at rt. The mixture was diluted with Et_2O (20 mL) and washed with satd $NaHCO_3$ (4×20 mL), followed by satd NaCl (3×25 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo to yield the crude 4-methoxybenzyl bromide. A suspension of NaH (60% dispersion in oil, 66 mg, 1.65 mmol, washed with hexanes (×1), Et_2O (×3)) in dry THF (5 mL) was cooled to 0 °C and treated with 2-allylphenol (0.20 mL, 1.5 mmol). After stirring for 50 min at 0 °C, the crude 4-methoxybenzyl bromide was slowly added as a solution in THF (2 mL), and the mixture was allowed to warm to rt. The reaction mixture was quenched after 23 h with glacial acetic acid (2 mL), followed by water (20 mL). The aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were washed with satd $NaHCO_3$ (3×20 mL) and dried ($MgSO_4$). The crude mixture was subjected to flash silica gel column chromatography (hexanes to 1% EtOAc/hexanes) to yield the protected allylic phenol **17** (344 mg, 90%) as a colourless oil.[13] ^{1}H NMR (300 MHz) δ 3.42 (d, 2H, $^3J_{HH}$=6.7 Hz, CH_2CH=CH$_2$), 3.81 (s, 3H, OCH_3), 5.00 (s, 2H, PhCH_2), 5.01–5.08 (m, 2H, CH=CH$_2$), 6.00 (tdd, 1H, $^3J_{HH}$=16.9, $^3J_{HH}$=10.2, $^3J_{HH}$=6.7 Hz, C*H*=CH$_2$), 6.88–6.92 (m, 4H, ArH), 7.15–7.20 (m, 2H, ArH), 7.35 (d, 2H, $^3J_{HH}$=8.8 Hz, ArH3′); ^{13}C NMR (75 MHz) δ 34.4 (CH_2CH=CH$_2$), 55.3 (OCH_3), 69.7 (PhCH_2), 111.8 (ArC6), 113.9 (ArC2′), 115.4 (CH=CH_2), 120.7 (ArC4), 127.2 (ArC5), 128.8 (ArC3′), 129.0 (ArC4′), 129.4 (ArC2), 129.8 (ArC3), 137.0 (C*H*=CH$_2$), 156.4 (ArC1), 159.3 (ArC1′); MS (EI, +ve) *m*/*z* 254 (4, M^+), 121 (100); HRMS (EI, +ve) calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1307.

*4.3.3. 2-Allylphenyl acetate **18**.*[14,15] Acetic anhydride (5 mL) was added to a stirred solution of 2-allylphenol (200 mg, 0.49 mmol) in Et_3N (5 mL) at rt for 25 h. The reaction was quenched with water and extracted with CH_2Cl_2 (4×20 mL). The combined organic layers were washed with sodium hydroxide (3×20 mL) and concentrated in vacuo. The crude product was subjected to gravity silica gel column chromatography (5% EtOAc/hexanes) to afford the acetylated phenol **18** (262 mg, 99%) as a colourless, volatile liquid.[‡] ^{1}H NMR (300 MHz) δ 2.30 (s, 3H, CH_3), 3.30 (d, 2H, $^3J_{HH}$=6.6 Hz, CH_2CH=CH$_2$), 5.04–5.07 (m, 1H, CH=CH*H*), 5.09–5.10 (m, 1H, CH=C*H*H), 5.84–5.98 (m, 1H, C*H*=CH$_2$), 7.02–7.05 (m, 1H, ArH), 7.16–7.28 (m, 3H, ArH); ^{13}C NMR (75 MHz) δ 20.9 (CH_3), 34.6 (CH_2CH=CH$_2$), 116.2 (CH=CH_2), 122.3 (ArC6), 126.2 (ArC4), 127.4 (ArC5), 130.4 (ArC3), 131.9 (ArC2), 135.9 (C*H*=CH$_2$), 148.9 (ArC1), 169.3 (C=O); FTIR ν 1760 (s), 1639 (w), 1488 (w), 1453 (w), 1370 (w), 1202 (s), 1170 (s), 1118 (w), 1010 (w), 915 (w), 751 (w); MS (EI, +ve) *m*/*z* 176 (20, M^+), 147 (33), 134 (100%), 133 (67), 132 (21), 131 (79), 119 (53); HRMS (EI, +ve) calcd for $C_{11}H_{12}O_2$ 176.0837, found 176.0837.

*4.3.4. 2-Allyl-1-trifluoromethanesulfonylbenzene **19**.*[16] 2-Allylphenol (1.00 g, 7.46 mmol) was added to a stirred mixture of *N*-phenyltriflimide (3.4 g, 11.18 mmol) and K_2CO_3 (2.06 g, 14.9 mmol) in THF (50 mL). The reaction mixture was heated at reflux and after 48 h was partitioned between CH_2Cl_2 and satd NaCl. The aqueous layer was extracted with CH_2Cl_2 (3×20 mL) and the combined organic layers were washed with brine (2×20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was subjected to gravity silica gel column chromatography (1% EtOAc/hexanes) to afford the triflated phenol **19** (1.648 g, 83%) as a colourless, volatile liquid.[16] ^{1}H NMR (300 MHz) δ 3.40 (dd, 1H, $^2J_{HH}$=1.4, $^3J_{HH}$=1.4 Hz, C*H*HCH=CH$_2$), 3.42 (dd, 1H, $^2J_{HH}$=1.4, $^3J_{HH}$=1.4 Hz, CH*H*CH=CH$_2$), 5.06 (ddd, 1H, $^4J_{HH}$=1.4, $^2J_{HH}$=2.9, $^3J_{HH}$=17.0 Hz, CH=CH*H*), 5.08 (ddd, 1H, $^4J_{HH}$=1.4, $^2J_{HH}$=2.8, $^3J_{HH}$=10.2 Hz, CH=C*H*H), 5.85 (ddt, 1H, $^3J_{HH}$=6.0, 10.2, 16.8 Hz, C*H*=CH$_2$), 7.26–7.33 (m, 4H, ArH); ^{13}C NMR (75 MHz) δ 34.0 (CH_2CH=CH$_2$), 112.2, 116.5, 120.7, 125.0 (118.6, q, *J*=320 Hz, CF_3), 117.5 (CH=CH_2), 121.3 (ArC6), 128.1

[†] No physical or spectral data reported in Ref. 12.

[‡] No physical or spectral data reported in Refs. 14,15.

(ArC4), 128.4 (ArC5), 131.4 (ArC3), 132.8 (ArC2), 134.6 (*C*H=CH_2), 147.9 (ArC1); FTIR ν 1483 (w), 1420 (m), 1250 (w), 1210 (s), 1138 (s), 1073 (w), 889 (s), 766 (m); MS (EI, +ve) *m/z* 266 (9, M^+), 265 (59), 131 (99), 115 (100%), 103 (63); HRMS (EI, +ve) calcd for $C_{10}H_9F_3O_S$ 266.0225, found 266.0225.

4.3.5. 1-tert-Butyldimethylsilyloxy-2-allylbenzene ***20***.[17] 2-Allylphenol (0.20 mL, 3.0 mmol) was added to a stirred suspension of imidazole (246 mg, 3.6 mmol) in CH_2Cl_2 (10 mL). *tert*-Butyldimethylsilyl chloride (520 mg, 3.45 mmol) was added as a solid and stirring was continued at rt for 18 h. The reaction mixture was partitioned between CH_2Cl_2 and water, and the aqueous layer was extracted with CH_2Cl_2 (3×25 mL). The organic layers were combined and washed with water, dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude mixture was subjected to a flash silica gel plug (100% hexanes) to afford the TBS protected phenol **20** (740 mg, 99%) as a colourless, volatile liquid.[17] ^{1}H NMR (500 MHz) δ 0.24 (s, 6H, Si(CH_3)$_2$), 1.02 (s, 9H, C(CH_3)$_3$), 3.37 (d, 2H, *J*=6.5 Hz, CH_2CH=CH_2), 4.99–5.03 (m, 1H, CH=CH*H*), 5.05–5.06 (m, 1H, CH=C*H*H), 5.90–6.04 (m, 1H, C*H*=CH_2), 6.79 (d, 1H, *J*=8 Hz, ArH6), 6.89 (t, 1H, *J*=7.4 Hz, ArH4), 7.08 (t, 1H, *J*=7.7 Hz, ArH5), 7.14 (d, 1H, *J*=7.5 Hz, ArH3); ^{13}C NMR (75 MHz) δ −4.1 (Si(CH_3)$_2$), 18.3 (*C*(CH_3)$_3$), 25.8 (C(*C*H_3)$_3$), 34.4 (*C*H_2CH=CH_2), 115.4 (CH=*C*H_2), 118.4 (ArC6), 121.1 (ArC4), 127.0 (ArC5), 130.1 (ArC3), 130.7 (ArC2), 137.0 (*C*H=CH_2), 153.3 (ArC1); MS (EI, +ve) *m/z* 247 (39, M−H), 237 (42), 221 (47), 205 (55), 193 (63), 179 (100%), 161 (71), 131 (92), 121 (92), 115 (79); HRMS (EI, +ve) calcd for $C_{15}H_{23}OSi$ 247.1518, found 247.1516.

4.3.6. 2-Allyl-1-methoxybenzene ***23***.[18] 2-Allylphenol (507 mg, 3.73 mmol) was dissolved in acetone (40 mL) and K_2CO_3 (2.063 g, 14.9 mmol) was added, followed by a few drops of water. The reaction vessel was heated to 40 °C and methyl iodide (0.94 mL, 14.9 mmol) was added. After 20 h the solvent was removed under reduced pressure, the crude mixture dissolved in EtOAc and washed with water (3×30 mL). The organic layer was dried ($MgSO_4$) and adsorbed onto silica gel. After flash silica gel column chromatography (hexanes), the protected allylphenol **23** (482 mg, 87%) was obtained as a colourless, volatile liquid.[18] ^{1}H NMR (500 MHz) δ 3.38 (d, 2H, *J*=6.2 Hz, CH_2), 3.81 (s, 3H, OCH_3), 5.02–5.06 (m, 2H, CH=C*H*$_2$), 5.95–6.03 (m, 1H, C*H*=CH_2), 6.84 (d, 1H, *J*=8.1 Hz, ArH6), 6.89 (t, 1H, *J*=7.4 Hz, ArH4), 7.13 (d, 1H, *J*=7.3 Hz, ArH3), 7.19 (t, 1H, *J*=7.7 Hz, ArH5); ^{13}C NMR (125 MHz) δ 34.2 (CH_2), 55.3 (OCH_3), 110.3 (ArC6), 115.3 (CH=*C*H_2), 120.5 (ArC4), 127.3 (ArC5), 128.6 (ArC2), 129.7 (ArC3), 137.0 (*C*H=CH_2), 157.3 (ArC1); FTIR ν 1600 (w), 1493 (m), 1464 (w), 1243 (s), 1050 (w), 1031 (m), 912 (w), 751 (s); MS (EI, +ve) *m/z* 148 (17, M^+), 147 (90, M−H), 131 (100%), 121 (78), 105 (55); HRMS (EI, +ve) calcd for $C_{10}H_{12}O$ 148.0888, found 148.0888.

4.3.7. N-Acetyl-2-allylaniline ***21***.[21] Acetic anhydride (5 mL) was added to a stirred solution of 2-allylaniline **5** (153 mg, 1.149 mmol) in Et_3N (0.4 mL) at rt. The reaction was quenched after 3 days with water and extracted with CH_2Cl_2 (4×20 mL). The combined organic layers were washed with 2 M NaOH (3×20 mL) and concentrated in vacuo. The crude product was subjected to gravity silica gel column chromatography (20–40% EtOAc/hexanes) to afford the acetylated aniline **18** (128 mg, 65%) as a white solid, mp 90–91 °C (lit.[21] 95–96 °C) ^{1}H NMR (300 MHz) δ 1.81 (br s, 1H, NH), 2.07 (CH_3), 3.30 (dt, 2H, $^2J_{HH}$=1.4, $^3J_{HH}$=6.1 Hz, CH_2CH=CH_2), 5.02 (dd, 1H, $^2J_{HH}$=1.3 Hz, $^3J_{HH}$=17.2 Hz, CH_2CH=CH*H*), 5.10 (dd, 1H, $^2J_{HH}$=1.0 Hz, $^3J_{HH}$=10.0 Hz, CH_2CH=C*H*H), 5.90 (ddt, 1H, $^3J_{HH}$=6.1, 10.3, 16.4 Hz, C*H*=CH_2), 7.04–7.21 (m, 3H, ArH), 7.74 (d, 1H, *J*=8.0 Hz, ArC6); ^{13}C NMR (75 MHz) δ 24.2 (CH_3), 36.9 (*C*H_2CH=CH_2), 116.5 (CH=*C*H_2), 123.8 (ArC6), 125.3 (ArC4), 127.4 (ArC5), 129.9 (ArC2), 130.2 (ArC3), 136.0 (ArC1), 136.3 (*C*H=CH_2), 168.3 (C=O); FTIR ν 3273 (w), 1656 (s), 1586 (w), 1535 (m), 1450 (w), 1370 (w), 1298 (w), 917 (w), 753 (s), 716 (w); MS (ES, +ve) *m/z* 239 (5, M+K), 176 (3, M+H), 146 (80), 105 (100%); HRMS (ES, +ve) calcd for $C_{11}H_{14}NO$ 176.1075, found 176.1072.

4.3.8. 1-Allyl-2-nitrobenzene ***22***.[22] 1-Iodo-2-nitrobenzene (776 mg, 3.11 mmol) was dissolved in THF (5 mL) in a 25 mL flask flushed with Ar(g) and fitted with a rubber septum. The flask was placed in a slush bath of acetonitrile and N_2(l) (−40 °C). Phenylmagnesium bromide (3.44 mL, 1.0 M solution in THF) was added dropwise and stirring continued a further 10 min. A solution of copper (I) cyanide (276 mg, 3.11 mmol) and lithium chloride (264 mg, 6.22 mmol) in THF (2 mL) was added and stirring was continued for a further 10 min. Allyl bromide (0.32 mL, 3.42 mmol) was then added neat and after 2 h the reaction was quenched with satd NH_4Cl, partitioned between water and Et_2O and extracted with Et_2O (3×50 mL). The organic layers were combined and washed with satd NaCl (4×30 mL), and filtered after addition of charcoal. The filtered solution was dried ($MgSO_4$) and the crude residue was subjected to flash silica gel column chromatography (hexanes) to afford the allylated product **22** (415 mg, 82%) as a colourless oil.[22] ^{1}H NMR (300 MHz) δ 3.72 (dt, 2H, *J*=1.4, 6.3 Hz, CH_2CH=CH_2), 5.11 (ddd, 1H, $^4J_{HH}$=1.6, $^2J_{HH}$=2.8, $^3J_{HH}$=16.8 Hz, CH=CH*H*), 5.15 (ddd, 1H, $^4J_{HH}$=1.4, $^2J_{HH}$=2.9, $^3J_{HH}$=10.2 Hz, CH=C*H*H), 6.01 (ddt, 1H, $^3J_{HH}$=6.4, 10.2, 16.7 Hz, C*H*=CH_2), 7.37–7.43 (m, 2H, ArH3 and 5), 7.57 (dt, 1H, *J*=1.4, 7.6 Hz, ArH4), 7.94 (dd, 1H, *J*=1.4, 8.5 Hz, ArH6); ^{13}C NMR (75 MHz) δ 36.9 (CH_2), 117.1 (CH=*C*H_2), 124.6 (ArC6), 127.3 (ArC5), 131.9 (ArC3), 133.0 (ArC4), 134.8 (ArC2), 135.0 (*C*H=CH_2), 150.0 (ArC1); MS (ES, +ve) *m/z* 186 (5, M+Na), 146 (5), 135 (10), 121 (5), 94 (18), 83 (100%).

4.3.9. 3-Allyl-1-methoxybenzene ***24***.[28] Magnesium turnings (292 mg, 12.0 mmol) were washed sequentially with 1 M HCl, EtOH and Et_2O and placed in an oven-dried flask. The flask and magnesium were then flame-dried under a N_2(g) purge. THF (10 mL) was added and 3-bromoanisole (0.27 mL, 2.13 mmol) was slowly added. One crystal of iodine was added, and the reaction vessel was warmed in an oil bath (25 °C). The remaining 3-bromoanisole (1.0 mL, 7.87 mmol) was slowly added in four portions, over 1 h. The reaction was stirred for a further 1 h; some residual magnesium remained, and a grey precipitate was observed. Allyl bromide (1.7 mL, 20.0 mmol) was slowly added, and stirring was continued at 25 °C for 20 h. The mixture was partitioned between Et_2O and satd NH_4Cl. The aqueous layer was extracted with a Et_2O (3×25 mL), the combined organic layers dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude oil was subjected to flash silica gel column chromatography (hexanes) to afford the protected phenol **24** (855 mg, 58%) as a colourless oil.[28] ^{1}H NMR (500 MHz) δ 3.35 (d, 2H, *J*=6.6 Hz, CH_2), 3.77 (s, 3H, OCH_3), 5.05–5.10 (m, 2H, CH=C*H*$_2$), 5.95 (tdd, 1H, *J*=6.7, 9.9, 13.5 Hz, C*H*=CH_2), 6.73–6.75 (m, 2H, ArH2 and ArH6), 6.77 (d, 1H, *J*=7.5 Hz, ArH4), 7.19 (t, 1H, *J*=8.2 Hz, ArH5); ^{13}C NMR (125 MHz) δ 40.2 (CH_2), 55.0 (OCH_3), 111.4 (ArC6), 114.2 (ArC2), 115.8 (CH=*C*H_2), 120.9 (ArC4), 129.3 (ArC5), 137.2 (*C*H=CH_2), 141.6 (ArC3), 159.7 (ArC1); FTIR ν 1600 (m), 1585 (m), 1489 (m), 1455 (w), 1436 (w), 1259 (s), 1162 (w), 1149 (m), 1049 (m), 914 (m), 877 (w), 778 (m), 748 (m); MS (EI, +ve) *m/z* 148 (12, M^+), 147 (20, M−H), 131 (59), 120 (100%), 109 (83); HRMS (EI, +ve) calcd for $C_{10}H_{12}O$ 148.0888, found 148.0890.

4.4. Synthesis of olefin by metathesis

4.4.1. E-1,4-Di(2-benzyloxy)phenyl-2-butene ***15***. Grubbs' I catalyst (195 mg, 0.237 mmol, 6.7 mol %) was added to a solution of alkene **14** (820 mg, 3.68 mmol) in CH_2Cl_2 (20 mL) and the solution was heated at reflux for 4.5 h. The reaction mixture was concentrated in vacuo and subjected to gravity silica column chromatography (1% EtOAc/hexanes) yielding the dimer **15** (629 mg, 81%, *E*/*Z* 5.2:1) as

a white solid, mp 68–70 °C. ^{1}H NMR (300 MHz) δ 3.42 (d, 4H, J=4.9 Hz, CH_2), 3.54* (d, J=5.1 Hz), 5.05 (s, 4H, $PhCH_2$), 5.07*, 5.68–5.70 (m, 2H, C*H*=C*H*), 6.86–6.91 (m, 4H, ArH4 and ArH6), 7.12–7.17 (m, 4H, ArH3 and ArH5), 7.28–7.43 (m, 10H, 10×ArH′); ^{13}C NMR (75 MHz) δ 27.9*, 33.1 (CH_2), 67.9 ($PhCH_2$), 111.7 (ArC6), 120.8 (ArC4), 127.1 (ArC2′), 127.2 (ArC1′), 127.6 (ArC5), 128.5 (ArC3′), 129.6 (ArC3), 129.8 (*C*H=*C*H), 129.9 (ArC2), 137.4 (ArC1′), 156.3 (ArC1); MS (CI, +ve) m/z 421 (47, M+H), 237 (72), 147 (100%); MS (EI, +ve) 420 (10, M^+), 329 (30), 313 (10), 237 (30), 223 (40), 197 (40), 107 (100); HRMS (EI, +ve) calcd for $C_{30}H_{28}O_2$ 420.2089, found 420.2087.

4.4.2. E-1,4-Di(2-(4-methoxybenzyloxy)phenyl)-2-butene ***29***. Grubbs' II catalyst (34 mg, 0.039 mmol, 5 mol %) was added to a solution of alkene **17** (180 mg, 0.708 mmol) in CH_2Cl_2 (6 mL) and the solution was heated at reflux for 23 h. The reaction mixture was concentrated in vacuo and subjected to flash silica gel column chromatography (2% EtOAc/hexanes) to yield the dimer **29** (27 mg, E/Z 3:1) as a white solid. Further elution (2–50% EtOAc/hexanes) yielded 5 more portions of **29**, with a total mass of 121 mg (71%) and an increasing E/Z ratio (5:1 to 20:1). The fractions were combined and recrystallisation from CH_2Cl_2/hexanes gave the pure E isomer as a white solid (80 mg, 47%), mp 132–133 °C. ^{1}H NMR (300 MHz) δ 3.39 (d, 4H, J=4.8 Hz, CH_2CH=CH_2), 3.80 (s, 6H, OCH_3), 4.98 (s, 4H, $PhCH_2$), 5.66 (m, 2H, C*H*=C*H*), 6.84–6.90 (m, 8H, ArH), 7.13–7.20 (m, 4H, ArH), 7.28–7.38 (m, 4H, ArH3′); ^{13}C NMR (75 MHz) δ 33.1 (CH_2), 55.3 (OCH_3), 69.7 ($PhCH_2$), 111.7 (ArC6), 113.8 (ArC2′), 120.7 (ArC4), 127.0 (ArC5), 128.7 (ArC3′), 129.4 (ArC4′), 129.5 (*C*H=CH), 129.7 (ArC3), 129.8 (ArC2), 156.4 (ArC1), 159.2 (ArC1′); FTIR ν 1614 (w), 1587 (w), 1515 (w), 1489 (w), 1451 (w), 1378 (w), 1252 (w), 1230 (w), 1106 (w), 1032 (w), 998 (w); MS (EI, +ve) m/z 480 (5, M^+), 241 (12), 121 (100%); HRMS (EI, +ve) calcd for $C_{32}H_{32}O_4$ 480.2301, found 480.2291.

4.4.3. E-1,4-Di(2-acetyloxyphenyl)-2-butene ***30***. Grubbs' I catalyst (61 mg, 0.074 mmol, 5 mol %) was added to a solution of alkene **18** (262 mg, 1.49 mmol) in CH_2Cl_2 (12 mL) and the solution was heated at reflux for 15 h. The reaction mixture was adsorbed onto silica gel and subjected to gravity silica gel column chromatography (5–7% EtOAc/hexanes) to yield the dimer **30** (204 mg, 85%, E/Z 4:1) as a colourless oil. ^{1}H NMR (300 MHz) δ 2.24 (s, 6H, CH_3), 2.28*, 3.26 (dd, 4H, J=1.4, 3.7 Hz, CH_2), 3.38* (d, J=5.3 Hz, CH_2), 5.56–5.59 (m, 2H, C*H*=C*H*), 5.62–5.65*, 7.00–7.05 (m, 2H, ArH), 7.14–7.26 (m, 6H, ArH); ^{13}C NMR (75 MHz) δ 20.8 (CH_3), 27.9*, 33.3 (CH_2), 122.3 (ArC6), 126.1 (ArC4), 126.2*, 127.3 (ArC5), 128.2*, 129.2 (*C*H=*C*H), 129.9*, 130.3 (ArC3), 132.3 (ArC2), 132.4*, 148.8 (ArC1), 169.3 (C=O); FTIR ν 3275 (m), 1654 (s), 1533 (s), 1449 (s), 1369 (s), 1295 (s), 973 (s), 749 (s); MS (EI, +ve) m/z 324 (11, M^+), 282 (16), 264 (11), 176 (10), 147 (33), 133 (100%), 131 (68), 107 (75); HRMS (EI, +ve) calcd for $C_{20}H_{20}O_4$ 324.1362, found 324.1354.

4.4.4. E-1,4-Di(2-trifluoromethanesulfonylphenyl)-2-butene ***31***. Grubbs' I catalyst (23 mg, 0.028 mmol, 5 mol %) was added to a solution of alkene **19** (151 mg, 0.568 mmol) in CH_2Cl_2 (6 mL) and the solution was heated at reflux for 15 h. The reaction mixture was adsorbed onto silica gel and subjected to gravity silica gel column chromatography (0.5–1% EtOAc/hexanes) to afford the dimer **31** (126 mg, 88%, E/Z 3.8:1) as a colourless oil. ^{1}H NMR (300 MHz) δ 3.48 (dd, 4H, J=1.5, 3.6 Hz, CH_2), 3.59* (dd, J=0.9, 4.6 Hz, CH_2), 5.65 (ddd, 2H, J=1.5, 3.6, 5.1 Hz, C*H*=C*H*), 5.73* (ddd, J=0.9, 4.6, 5.5 Hz, C*H*=C*H*), 7.23–7.34 (m, 8H, ArH); ^{13}C NMR (75 MHz) δ 27.6*, 32.8 (CH_2), 112.2, 116.5, 120.7, 124.9 (118.6, q, J=320 Hz, CF_3), 121.3 (ArC6), 128.1 (ArC4), 128.2* (*C*H=*C*H), 128.4 (ArC5), 128.5*, 129.3 (*C*H=*C*H), 131.0*, 131.3 (ArC3), 133.0 (ArC2), 147.9 (ArC1); FTIR ν 3350 (m), 2950 (m), 1678 (s), 1525 (s), 1167 (s), 1098 (s), 740 (s); MS (EI, +ve) m/z 504 (27, M^+), 359 (13), 281 (33), 265 (100%), 239 (80), 131 (100%), 115 (93), 109 (67); HRMS (ES, +ve) calcd for $C_{18}H_{14}F_6O_6S_2$ 504.0136, found 504.0127.

4.4.5. E-1,4-Di(2- tert-butyldimethylsilyloxy)phenyl-2-butene ***32***. Grubbs' II catalyst (34 mg, 0.040 mmol, 5 mol %) was added to a solution of alkene **20** (200 mg, 0.805 mmol) in CH_2Cl_2 (8 mL) and the solution was heated at reflux for 3 days. The reaction mixture was adsorbed onto silica gel and subjected to flash silica gel column chromatography (hexanes) yielding the dimer **32** as a pale yellow semi-solid (97 mg, E/Z 12:1). Further elution yielded two more portions of **32**, with a total mass of 180 mg (95%) and a decreasing E/Z ratio (6:1 and 4:1). ^{1}H NMR (500 MHz) δ 0.20 (s, 12H, $Si(CH_3)_2$), 0.24*, 0.99 (s, 18H, $C(CH_3)_3$), 1.02*, 3.34 (d, 4H, J=3.9 Hz, CH_2), 3.47* (d, J=4.8 Hz, CH_2), 5.61–5.62 (m, 2H, C*H*=C*H*), 5.70* (t, J=4.6 Hz, C*H*=C*H*), 6.77 (d, 2H, J=8.1 Hz, ArH6), 6.87 (t, 2H, J=7.4 Hz, ArH4), 7.06 (t, 2H, J=7.6 Hz, ArH5), 7.13 (d, 2H, J=7.4 Hz, ArH3); ^{13}C NMR (125 MHz) δ −4.2 ($Si(CH_3)_2$), -4.1*, 18.25 ($C(CH_3)_3$), 18.29*, 25.81 ($C(CH_3)_3$), 25.82*, 27.8*, 33.1 (CH_2), 118.34 (ArC6), 118.39*, 121.0 (ArC4), 121.1*, 126.78*, 126.80 (ArC5), 128.7* (*C*H=*C*H), 129.6 (*C*H=*C*H), 129.7*, 130.1 (ArC3), 131.5 (ArC2), 153.3 (ArC1); FTIR ν 2952 (m), 2923 (m), 2857 (s), 1489 (s), 1448 (s), 1252 (s), 922 (s), 838 (s), 780 (s), 753 (s); MS (EI, +ve) m/z 468 (8, M^+), 411 (92), 295 (18), 281 (91), 247 (42), 221 (87), 203 (45), 179 (78), 165 (100%), 115 (92); HRMS (EI, +ve) calcd for $C_{28}H_{44}O_5i_2$ 468.2880, found 468.2866.

4.4.6. E-1,4-Di(2-hydroxyphenyl)-2-butene ***33***. Tetrabutylammonium fluoride (2.6 mL, 1 M solution in THF) was added to **32** (310 mg, 0.661 mmol, E/Z 15.6:1) under N_2(g) and the reaction mixture was stirred at rt for 21 h. The solvent was removed in vacuo, and the crude solid was dissolved in CH_2Cl_2 and washed with water. The alkene **33** (21 mg, 13%, E/Z 27:1) was recrystallised from CH_2Cl_2/hexanes as a white solid, mp 126–128 °C. Two additional crops of **33** (123 mg, 79%) were obtained by recrystallisation from the filtrate to give a total yield of 92% (144 mg). ^{1}H NMR (300 MHz, CD_3OH) δ 3.30 (dd, 4H, $^2J_{HH}$=1.4, $^3J_{HH}$=3.5 Hz, CH_2CH=CH_2), 4.89 (br s, 2H, OH), 5.61–5.65 (m, 2H, C*H*=C*H*), 6.70–6.75 (m, 4H, ArH), 6.95–7.05 (m, 4H, ArH); ^{13}C NMR (75 MHz, CD_3OH) δ 33.9 (CH_2), 115.8 (ArC6), 120.6 (ArC4), 128.0 (ArC5), 128.6 (ArC2), 130.6 (*C*H=CH), 130.8 (ArC3), 156.0 (ArC1); FTIR ν 3084 (w), 2395 (w), 1711 (w), 1369 (w), 1230 (w), 1073 (s); MS (ES, −ve) m/z 275 (23, M+Cl), 239 (100%, M−H); HRMS (ES, −ve) calcd for $C_{16}H_{15}O_2$ 239.1072, found 239.1080.

4.4.7. E-1,4-Di(2-N-acetylaniline)-2-butene ***34***. Grubbs' II catalyst (15 mg, 0.035 mmol, 10 mol %) was added to a solution of *N*-acetyl-2-allylaniline **21** (67 mg, 0.35 mmol) in CH_2Cl_2 (6 mL). The mixture was heated at reflux for 17 h then filtered to collect the metathesis product **34** (45 mg, 73%) as a white powder, decomp. 220 °C. ^{1}H NMR (300 MHz, DMSO) δ 1.99 (s, 6H, CH_3), 3.31 (d, 4H, J=4.2 Hz, CH_2), 5.50 (t, 2H, J=3.3 Hz, C*H*=C*H*), 7.04–7.17 (m, 6H, ArH), 7.37 (d, 2H, J=7.7 Hz, ArH6), 9.21 (br s, 2H, NH); ^{13}C NMR (75 MHz,) δ 23.2 (CH_3), 34.0 (CH_2), 125.2 (ArC6), 125.7 (ArC4), 126.2 (ArC5), 129.2 (ArC3), 129.3 (ArC2), 134.2 (ArC1), 135.9 (*C*H=*C*H), 169.3 (C=O); FTIR ν 3275 (w), 1655 (s), 1587 (w), 1534 (m), 1449 (w), 1369 (w), 1296 (s), 1272 (w), 973 (w), 849 (w), 750 (s), 706 (w); MS (ES, +ve) m/z 345 (5, M+Na), 323 (5, M+H), 146 (100%), 105 (40); HRMS (ES, +ve) calcd for $C_{20}H_{22}N_2O_2Na$ 345.1579, found 345.1584.

4.4.8. E-1,4-Di(2-nitrophenyl)-2-butene ***35***. Grubbs' II catalyst (48 mg, 0.057 mmol, 5 mol %) was added to a solution of 2-allylnitrobenzene **22** (185 mg, 1.14 mmol) in CH_2Cl_2 (5 mL), and the flask was flushed with Ar(g) and heated at reflux for 7 h. The reaction mixture was washed with water, and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). Charcoal was added to the combined organic layers and filtered. Hexane was added to the filtrate, and a brown solid was crystallised and collected. The brown solid was subjected to gravity silica gel column chromatography (3%

EtOAc/hexanes) to yield the homo-coupled product **35** (44 mg, 26%, *E*/*Z* 43:1) as a white solid, mp 78 °C. ^{1}H NMR (500 MHz) δ 3.65–3.66 (m, 4H, CH_2), 3.82*, 5.70 (ddd, 2H, *J*=1.5, 3.5, 5.0 Hz, C*H*=C*H*), 7.34–7.38 (m, 4H, ArH3 and 5), 7.53 (t, 2H, *J*=7.6 Hz, ArH4), 7.89 (d, 2H, *J*=8.1 Hz, ArCH6); ^{13}C NMR (125 MHz) δ 35.7 (CH_2), 124.6 (ArC6), 127.3 (ArC5), 129.5 (*C*H=*C*H), 131.8 (ArC3), 133.0 (ArC4), 135.1 (ArC2), 149.2 (ArC1); FTIR ν 2960 (w), 2351 (w), 2335 (s), 1518 (s), 1353 (s), 1086 (m), 783 (s), 723 (s); MS (ES, +ve) *m*/*z* 321 (28, M+Na), 299 (2, M+H), 297 (2), 146 (5), 105 (100%), 64 (40); HRMS (ES, +ve) calcd for $C_{16}H_{14}N_2O_4Na$ 321.0851, found 321.0854.

4.4.9. E-1,4-Di(2-methoxyphenyl)-2-butene ***36***. Grubbs' I catalyst (51 mg, 0.062 mmol, 5 mol %) was added to a solution of alkene **23** (183 mg, 1.236 mmol) in CH_2Cl_2 (10 mL) and the solution was heated at reflux for 7 h. The reaction mixture was adsorbed onto silica gel and subjected to flash silica gel column chromatography (1% EtOAc/hexanes) to afford the dimer **36** (151 mg, 91%, *E*/*Z* 4.5:1) as a colourless oil. ^{1}H NMR (300 MHz) δ 3.35 (d, 4H, *J*=4.2 Hz, CH_2), 3.50* (d, *J*=4.9 Hz), 3.81 (s, 6H, OCH_3), 5.64–5.68 (m, 2H, C*H*=C*H*), 6.83 (d, 2H, *J*=8.1 Hz, ArH6), 6.88 (dt, *J*=1.1, 7.4, 7.5 Hz, ArH4), 7.14–7.21 (m, 4H, ArH3 and ArH5); ^{13}C NMR (75 MHz) δ 32.9 (CH_2), 55.3 (OCH_3), 110.2 (ArC6), 120.4 (ArC4), 123.8 (ArC2), 127.0 (ArC5), 129.5 (*C*H=*C*H), 129.6 (ArC3), 157.2 (ArC1); FTIR ν 2956 (w), 2833 (w), 1595 (m), 1493 (s), 1460 (s), 1243 (s), 1049 (s), 1027 (s), 752 (s); MS (EI, +ve) *m*/*z* 268 (25, M^+), 147 (100%), 121 (75); HRMS (EI, +ve) calcd for $C_{18}H_{20}O_2$ 268.1463, found 268.1464.

4.4.10. E-1,4-Di(3-methoxyphenyl)-2-butene ***37***.[29] 1-Methoxy-3-allylbenzene **24** (500 mg, 3.37 mmol) was added to a solution of Grubbs' I catalyst (70 mg, 2.5 mol %) in CH_2Cl_2 (10 mL) and the flask was flushed with N_2(g). The reaction mixture was heated at reflux for 15 h and subjected to flash silica gel column chromatography (1% EtOAc/hexanes) to yield the homo-coupled product **37** (283 mg, 63%, *E*/*Z* 4.5:1) as a colourless oil.[§] ^{1}H NMR (500 MHz) δ 3.34 (d, 4H, *J*=4.3 Hz, CH_2), 3.48* (d, *J*=5.1 Hz, CH_2), 3.76*, 3.77 (s, 6H, OCH_3), 5.66–5.67 (m, 2H, *C*H=*C*H), 5.70–5.72*, 6.74 (s, 2H, ArH2), 6.72–6.81 (m, 4H, ArH4 and ArH6), 7.17–7.21 (m, 2H, ArH5); ^{13}C NMR (125 MHz) δ 33.5*, 38.9 (CH_2), 55.1 (OCH_3), 111.3 (ArC6), 113.4*, 114.0*, 114.1 (ArC2), 120.7*, 120.9 (ArC4), 129.0* (*C*H=*C*H), 129.3 (ArC5), 129.4*, 130.3 (*C*H=*C*H), 142.3 (ArC3), 159.7 (ArC1); MS (EI, +ve) *m*/*z* 268 (58, M^+), 147 (100%), 134 (47), 122 (57); HRMS (EI, +ve) calcd for $C_{18}H_{20}O_2$ 268.1463, found 268.1464.

4.4.11. E-1,4-Di(4-methoxyphenyl)-2-butene ***38***.[30] 4-Allyl-2-methoxybenzene **25** (500 mg, 3.374 mmol) was added to a solution of Grubbs' I catalyst (69 mg, 2.5 mol %) in CH_2Cl_2 (10 mL) and the flask was flushed with Ar(g). The reaction mixture was heated at reflux for 4.5 h and subjected to flash silica gel column chromatography (1% EtOAc/hexanes) to yield the homo-coupled product **38** (440 mg, 97%, *E*/*Z* 6.2:1) as a white solid, mp 61–64 °C (lit.[30] 65–66 °C) ^{1}H NMR (300 MHz) δ 3.20–3.22 (m, 4H, CH_2), 3.35–3.36*, 3.676 (s, 6H, OCH_3), 3.682*, 5.51–5.56 (m, 2H, C*H*=C*H*), 5.57–5.59*, 6.71–6.77 (m, 4H, ArH2), 6.99–7.02 (m, 4H, ArH3); ^{13}C NMR (75 MHz) δ 32.5*, 38.0 (CH_2), 55.2 (OCH_3), 113.8 (ArC2), 113.9*, 129.2* (*C*H=*C*H), 129.4 (ArC3), 130.5 (*C*H=*C*H), 132.8 (ArC4), 157.9 (ArC1); MS (EI, +ve) *m*/*z* 268 (71, M^+), 160 (62), 147 (100%), 134 (54), 121 (86); HRMS (EI, +ve) calcd for $C_{18}H_{20}O_2$ 268.1463, found 268.1469.

4.4.12. E-1,4-Diphenyl-2-butene ***39***.[25] Grubbs' I catalyst (45 mg, 2.5 mol %, 0.11 mmol) was added to a solution of allylbenzene **26** (260 mg, 2.20 mmol) in CH_2Cl_2 (10 mL) and flushed with Ar(g). The solution was heated at reflux for 18 h under an Ar(g) atmosphere. The solvent was removed in vacuo, and the crude mixture was subjected to flash silica gel column chromatography. Elution with hexanes gave the homo-coupled product **39** (204 mg, 89%, *E*/*Z* 4.7:1) as a colourless, volatile oil.[25] ^{1}H NMR (500 MHz) δ 3.36 (d, 4H, *J*=5.1 Hz, CH_2), 3.51* (d, *J*=5.5 Hz, CH_2), 5.65–5.73 (m, 2H, C*H*=C*H*), 7.17–7.31 (m, 10H, ArH); ^{13}C NMR (125 MHz) δ 33.5*, 38.9 (CH_2CH=CH_2), 125.9 (ArC4), 128.3 (ArC3), 128.4 (ArC2), 130.4 (*C*H=*C*H), 140.7 (ArC1); FTIR ν 3026 (w), 2362 (w), 1602 (w), 1494 (m), 1452 (w), 969 (w), 737 (w), 697 (s); MS (EI, +ve) *m*/*z* 208 (49, M^+), 130 (48), 117 (100%), 104 (50); HRMS (EI, +ve) calcd for $C_{16}H_{16}$ 208.1252, found 208.1257.

4.4.13. E-1,4-Di-(2-tolyl)-2-butene ***40***.[26] Grubbs' I catalyst (31 mg, 0.038 mmol, 2.5 mol %) was added to a solution of alkene **27**[24] (200 mg, 1.515 mmol) in CH_2Cl_2 (6 mL) and the solution was heated at reflux for 27 h. The solvent was evaporated and the crude mixture was subjected to flash silica gel column chromatography and eluted with hexanes to give the dimer **40** (73 mg, *E*/*Z* 6:1) as a colourless oil. Further elution yielded a second portion of **40** (64 mg, *E*/*Z* 3:1), giving a total yield of 77%.[26] ^{1}H NMR (500 MHz) δ 2.27 (s, 6H, CH_3), 2.32*, 3.33 (d, 4H, *J*=3.5 Hz, CH_2), 3.48*, 5.56 (m, 2H, C*H*=C*H*), 5.65*, 7.11–7.14 (m, 8H, ArH); ^{13}C NMR (500 MHz) δ 19.3 (CH_3), 31.3*, 36.4 (CH_2), 125.9 (ArC4 or ArC5), 126.0*, 126.1 (ArC4 or ArC5), 128.5*, 128.9 (ArC3 or ArC6), 129.4 (*C*H=*C*H), 130.0 (ArC3 or ArC6), 130.1*, 136.2 (ArC2), 138.8 (ArC1); MS (EI, +ve) *m*/*z* 236 (7, M^+), 119 (100%); HRMS (EI, +ve) calcd for $C_{18}H_{20}$ 236.1565, found 236.1565.

4.4.14. E-1,4-Di(2-bromophenyl)-2-butene ***41***. To a solution of **28**[23] (140 mg, 0.71 mmol) in DCM (5 mL) was added Grubbs' II catalyst (30 mg, 0.036 mmol, 5 mol %) and the reaction was heated at reflux for 23 h. The solvent was removed in vacuo and the crude mixture was subjected to flash silica gel column chromatography (hexanes) to give a mixture of alkenes *E*-**41**/*Z*-**41**/*E*-1,4-di(2-bromophenyl)-1-butene:*E*-1,5-di(2-bromophenyl)-2-pentene:*E*-3-(2-bromophenyl)-1-phenylpropene:*E*-1-(2-bromophenyl)-3-phenylpropene (6.3:1:1.2:1.1:1:1.2, determined by ^{1}H NMR analysis), with a total mass of 34 mg. *E*-**41** (18 mg, 14%): ^{1}H NMR (500 MHz) δ 3.49 (dd, 4H, *J*=1.6, 3.4 Hz, CH_2), 5.65–5.67 (m, 2H, CH=CH), 7.04–7.57 (m, 8H, ArH). Compound *Z*-**41** (3 mg, 2%): ^{1}H NMR (500 MHz) δ 3.63 (d, 4H, *J*=5.3 Hz, CH_2), 5.61–5.63 (m, 2H, CH=CH), 7.04–7.57 (m, 8H, ArH). *E*-1,4-di(2-bromophenyl)-1-butene (3.5 mg, 3%): ^{1}H NMR (500 MHz) δ 2.55–2.60 (m, 2H, CH=CHCH_2), 2.92–2.95 (m, 2H, CH_2Ar), 6.20 (dt, 1H, *J*=6.9, 6.9, 15.6 Hz, ArCH=C*H*), 6.74 (d, 1H, *J*=15.7 Hz, ArC*H*=CH), 7.04–7.57 (m, 8H, ArH). *E*-1,5-di(2-bromophenyl)-2-pentene (3.2 mg, 2%): ^{1}H NMR (500 MHz) δ 2.31–2.37 (m, 2H, C$H_2$$CH_2$Ar), 2.79–2.82 (m, 2H, CH_2CH_2Ar), 3.43–3.45 (m, 2H, ArCH_2CH=CH), 5.55–5.58 (m, 2H, C*H*=C*H*), 7.04–7.57 (m, 8H, ArH). *E*-3-(2-bromophenyl)-1-phenylpropene (3 mg, 2%): ^{1}H NMR (500 MHz) δ 3.71 (dd, 2H, *J*=1.3, 7.0 Hz, CH_2), 6.34 (dt, 1H, *J*=6.7, 6.7, 15.8 Hz, CH_2C*H*=CH), 6.45 (d, 1H, *J*=15.9 Hz, CH_2CH=C*H*), 7.04–7.57 (m, 9H, ArH). *E*-1-(2-bromophenyl)-3-phenylpropene (3.5 mg, 3%): ^{1}H NMR (500 MHz) δ 3.66 (dd, 2H, *J*=0.9, 6.7 Hz, CH_2), 6.27 (dt, 1H, *J*=6.9, 6.9, 15.6 Hz, CH=C*H*CH_2), 6.82 (d, 1H, *J*=15.7 Hz, C*H*=CHCH_2), 7.04–7.57 (m, 9H, ArH).

4.5. Synthesis of diols

4.5.1. (2R,3R)-Di(2-benzyloxyphenyl)-2,3-butanediol ***16***. The diol (*R*,*R*)-**16b** was synthesised by General procedure A using alkene **15** (80 mg, 0.19 mmol, *E*/*Z* 8.5:1), ADmix β (267 mg), methanesulfonamide (18 mg, 0.19 mmol), sodium sulfite (238 mg) in ^{t}BuOH (1.5 mL), water (1 mL) and THF (0.45 mL), for 37 h. The crude residue was subjected to gravity silica column chromatography (10–20% EtOAc/hexanes) to yield the chiral diol (*R*,*R*)-**16** (60 mg, 69%) as a white solid, mp 57–59 °C, as a mixture of chiral/*meso* diastereomers (7.2:1). HPLC analysis (20–70% 2-propanol/hexane, retention times (*R*,*R*)-diol **16** 24.0 min (major), (*S*,*S*)-diol **16**

[§] No physical or spectral data reported in Ref. 29.

33.7 min (minor)) showed the ee of the (*R*,*R*)-diol **16** was 91%. ^{1}H NMR (300 MHz) δ 2.24 (br s, 2H, OH), 2.75 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=7.7 Hz, C*H*H), 2.87 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=5.2 Hz, CH*H*), 2.99* (dd, $^2J_{HH}$=13.7 Hz, $^3J_{HH}$=2.4 Hz), 3.66 (dd, 2H, *J*=5.7, 5.7 Hz, C*H*OH), 3.76* (d, *J*=8.1 Hz), 4.90 (s, 4H, $PhCH_2$), 5.98*, 6.78–6.85 (m, 4H, ArH4 and ArH6), 7.05–7.10 (m, 4H, ArH3 and ArH5), 7.23–7.29 (m, 10H, 10×ArH′); ^{13}C NMR (75 MHz) δ 33.3*, 35.1 (CH_2), 70.1 ($PhCH_2$), 70.2*, 73.1 (CHOH), 74.4*, 111.8 (ArC6), 111.9*, 121.0 (ArC4), 121.1*, 127.2 (ArC2′), 127.6 (ArC4′), 127.9 (ArC5), 128.6 (ArC3′), 131.5 (ArC3), 131.7*, 136.8 (ArC1′), 156.6 (ArC1); MS (CI, +ve) *m*/*z* 455 (100%, M+H), 419 (84); FTIR ν 3396 (m), 2931 (m), 2360 (m), 2331 (m), 1491 (s), 1444 (s), 1225 (s). 1045 (s), 752 (s), 728 (s); MS (ES, +ve) *m*/*z* 477 (100%, M+Na); HRMS (ES, +ve) calcd for $C_{30}H_{30}O_4Na$ 477.2042, found 477.2044.

*4.5.2. (2S,3S)-Di(2-benzyloxyphenyl)-2,3-butanediol **16**.*

4.5.2.1. Procedure 1. The diol (*S*,*S*)-**16** was synthesised by General procedure A using alkene **15** (376 mg, 0.90 mmol, *E*/*Z* 3.1:1), ADmix α (1.253 g), methanesulfonamide (85 mg, 0.90 mmol), sodium sulfite (1.120 g) in ^{t}BuOH (4.5 mL), water (4.5 mL) and THF (1.2 mL), for 91 h. Purification via gravity silica column chromatography (2–50% EtOAc/hexanes) isolated the diol (*S*,*S*)-**16** as a white solid (280 mg, 64%) as a mixture of chiral/*meso* diastereomers (15:1), mp 58–59 °C, which exhibited identical spectral properties to the (*R*,*R*)-diol. HPLC analysis (20–70% 2-propanol/hexane, retention times (*R*,*R*)-diol **16** 23.4 min (minor), (*S*,*S*)-diol **16** 32.4 min (major)) showed the ee of the (*S*,*S*)-diol **16** was 33%.

4.5.2.2. Procedure 2. The diol (*S*,*S*)-**16** was synthesised by General procedure A using alkene **15** (171 mg, 0.41 mmol, *E*/*Z* 3.9:1), ADmix α (0.54 g), methanesulfonamide (39 mg, 0.41 mmol), sodium sulfite (0.552 g) in ^{t}BuOH (2 mL), water (2 mL), for 24 h. Purification via gravity silica column chromatography (10–20% EtOAc/hexanes) isolated the diol (*S*,*S*)-**15** as a white solid (27 mg, 15%) as a mixture of chiral/*meso* diastereomers (4.8:1). HPLC analysis (20–70% 2-propanol/hexane, retention times (*R*,*R*)-diol **15** 24.3 min (minor), (*S*,*S*)-diol **15** 33.0 min (major)) showed the ee of the (*S*,*S*)-diol **15** was 64%.

*4.5.3. (2R,3R)-1,4-Di(2-trifluorosulfonylphenyl)-2,3-butandiol **44**.* The diol (*R*,*R*)-**44** was synthesised by General procedure A using alkene **31** (120 mg, 0.238 mmol, *E*/*Z* 9.1:1), ADmix β (333 mg), methanesulfonamide (23 mg, 0.238 mmol), sodium sulfite (211 mg) in ^{t}BuOH (1.2 mL) and water (1.2 mL). The crude residue was subjected to gravity silica gel column chromatography (10–50% EtOAc/hexanes) to yield the diol **44** (74 mg, 58%) as a white solid as a mixture of chiral/*meso* diastereomers (27:1). Recrystallisation of the mixture from CH_2Cl_2/hexanes removed the *meso* isomer. The filtrate was concentrated in vacuo to give the chiral diol (*R*,*R*)-**44** (60 mg, 47%), mp 114–115 °C. HPLC analysis (20% 2-propanol/hexane, retention times (*R*,*R*)-diol **44** 8.73 min (major), (*S*,*S*)-diol **44** 9.39 min (minor)) showed the ee of the (*R*,*R*)-diol **44** was 8%. ^{1}H NMR (300 MHz) δ 2.21 (d, 2H, *J*=6.4 Hz, OH), 2.96 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=7.5 Hz, C*H*H), 3.03 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=4.2 Hz, CH*H*), 3.73–3.90 (m, 2H, C*H*OH), 7.23–7.45 (m, 8H, ArH); ^{13}C NMR (300 MHz) δ 34.8 ($CH_2CH{=}CH_2$), 72.8 (CHOH), 112.1, 116.4, 120.6, 124.8 (118.5, q, *J*=320 Hz, CF_3), 121.5 (ArC6), 128.5 (ArC4), 128.6 (ArC5), 131.1 (ArC2), 132.5 (ArC3), 148.3 (ArC1); FTIR ν 3268 (w), 1483 (w), 1416 (w), 1228 (w), 1207 (w), 1134 (w), 1096 (w), 903 (w), 809 (w), 772 (w), 635 (w); MS (ES, +ve) *m*/*z* 561 (100%, M+Na), 556 (15, M+NH_4); HRMS (ES, +ve) calcd for $C_{18}H_{20}F_6O_8S_2N$ 556.0535, found 556.0535.

*4.5.4. (2S,3S)-1,4-Di(2-trifluorosulfonylphenyl)-2,3-butandiol **44**.* The diol (*S*,*S*)-**44** was synthesised by General procedure A using alkene **31** (110 mg, 0.523 mmol, *E*/*Z* 3.6:1), ADmix α (333 mg), methanesulfonamide (23 mg, 0.238 mmol) and sodium sulfite (211 mg) in ^{t}BuOH (1.2 mL) and water (1.2 mL). The crude residue was subjected to gravity silica gel column chromatography (10–50% EtOAc/hexanes) to yield the diol **44** (32 mg, 25%) as a white solid, mp 110–112 °C, as a mixture of chiral/*meso* diastereomers (24:1), which had identical spectral properties to the (*R*,*R*)-**44** enantiomer. HPLC analysis (20% 2-propanol/hexane, retention times (*R*,*R*)-diol **44** 8.76 min (minor), (*S*,*S*)-diol **44** 9.42 min (major)) showed the ee of the (*S*,*S*)-diol **44** was 1.4%.

*4.5.5. (2S,2R)-1,4-Di(2-tert-butyldimethylsilyloxyphenyl)-2,3-butandiol **45** and (2R,3R)-1,4-di(2-tert-butyldimethylsilyloxyphenyl)-2,3-butandiol **45**.* The diol (*R*,*R*)-**45** was synthesised by General procedure A using alkene **32** (88 mg, 0.188 mmol, *E*/*Z* 6:1), ADmix β (263 mg), methanesulfonamide (18 mg, 0.188 mmol), sodium sulfite (166 mg) in ^{t}BuOH (1 mL) and water (1 mL). The crude residue was subjected to gravity silica gel column chromatography (1–100% EtOAc/hexanes) to yield the *meso* diol **45** (4 mg, 4%) as a white solid. ^{1}H NMR (300 MHz) δ 0.25 (d, 12H, *J*=3.8 Hz, $Si(CH_3)_2$), 1.01 (s, 18H, $C(CH_3)_3$), 2.56 (d, 2H, *J*=3.0 Hz, OH), 2.84 (dd, 2H, $^2J_{HH}$=13.7 Hz, $^3J_{HH}$=8.6 Hz, C*H*H), 3.04 (dd, 2H, $^2J_{HH}$=13.7 Hz, $^3J_{HH}$=2.6 Hz, CH*H*), 3.76–3.83 (m, 2H, C*H*OH), 6.83 (dd, 2H, *J*=0.9, 8.0 Hz, ArH6), 6.92 (dt, 2H, *J*=1.0, 7.4 Hz, ArH4), 7.11 (dt, 2H, *J*=1.7, 7.8 Hz, ArH5), 7.21 (dd, 2H, *J*=1.7, 7.5 Hz, ArH3); ^{13}C NMR (75 MHz) δ −4.1 and −4.0 ($Si(CH_3)_2$), 18.2 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 33.4 (CH_2), 74.7 (CHOH), 118.7 (ArC6), 121.5 (ArC4), 127.5 (ArC5), 129.1 (ArC2), 131.8 (ArC3), 153.8 (ArC1); MS (ES, +ve) *m*/*z* 1027 (100%, 2M+Na), 525 (25, M+Na), 503 (5%, M+H); HRMS (ES, +ve) calcd for $C_{28}H_{47}OSi_2$ 503.3013, found 503.3020.

Further elution gave the chiral diol (*R*,*R*)-**45** (25 mg, 27%) as a viscous oil. HPLC analysis (2.5% 2-propanol/hexane, retention times (*R*,*R*)-diol **45** 13.3 min (major), (*S*,*S*)-diol **45** 12.1 min (minor)) showed the ee of the (*R*,*R*)-diol **45** was 14%. ^{1}H NMR (300 MHz) δ 0.20 (s, 12H, $Si(CH_3)_2$), 0.97 (s, 18H, $C(CH_3)_3$), 2.47 (d, 2H, *J*=5.7 Hz, OH), 2.82 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=5.6 Hz, C*H*H), 2.93 (dd, 2H, $^2J_{HH}$=13.3 Hz, $^3J_{HH}$=7.9 Hz, CH*H*), 3.67–3.73 (m, 2H, C*H*OH), 6.78 (dd, 2H, *J*=1.1, 8.0 Hz, ArH6), 6.88 (dt, 2H, *J*=1.2, 7.4 Hz, ArH4), 7.09 (dt, 2H, *J*=1.8, 8.6 Hz, ArH5), 7.14 (d, 2H, *J*=1.7, 7.4 Hz, ArH3); ^{13}C NMR (75 MHz) δ −4.2 and −4.1 ($Si(CH_3)_2$), 18.2 ($C(CH_3)_3$), 25.8 ($C(CH_3)_3$), 35.2 (CH_2), 73.2 (CHOH), 118.6 (ArC6), 121.4 (ArC4), 127.5 (ArC5), 128.9 (ArC2), 131.6 (ArC3), 153.7 (ArC1); MS (ES, +ve) *m*/*z* 1027 (100%, 2M+Na), 525 (45, M+Na), 503 (6%, M+H); HRMS (ES, +ve) calcd for $C_{28}H_{47}OSi_2$ 503.3013, found 503.3008.

*4.5.6. (2S,3S)-1,4-Di(2-tert-butyldimethylsilyloxyphenyl)-2,3-butandiol **45**.* The diol (*S*,*S*)-**454** was synthesised by General procedure A using alkene **32** (97 mg, 0.207 mmol, *E*/*Z* 12:1), ADmix α (290 mg), methanesulfonamide (18 mg, 0.188 mmol) and sodium sulfite (166 mg) in ^{t}BuOH (1 mL) and water (1 mL). Flash silica gel column chromatography (1–100% EtOAc/hexanes) isolated the diol **45** (15 mg, 13%) as an oil as a mixture of chiral/*meso* diastereomers (12:1), which exhibited identical spectral properties to the (*R*,*R*)-diol. HPLC analysis (2.5% 2-propanol/hexane, retention times (*R*,*R*)-diol **45** 13.4 min (minor), (*S*,*S*)-diol **45** 12.3 min (major)) showed the ee of the (*S*,*S*)-diol **45** was 23%.

*4.5.7. (2R,3R)-1,4-Di(2-nitrophenyl)-2,3-butandiol **48**.* Compound (*R*,*R*)-**48** was synthesised using General procedure A, alkene **35** (20 mg, 0.067 mmol, *E*/*Z* 18:1), ADmix β (94 mg), methanesulfonamide (6 mg, 0.067 mmol), sodium sulfite (100 mg) and a 1:1 mixture of ^{t}BuOH and water (0.7 mL), The crude solid was subjected to flash silica gel column chromatography (20–30% EtOAc/hexanes) to afford the diol **48** (10 mg, 45%) as a white solid, mp 132–134 °C, as a mixture of chiral/*meso* diastereomers (16:1). HPLC analysis (35% 2-propanol/hexane, retention times (*R*,*R*)-diol **48** 19.4 min (major), (*S*,*S*)-diol **48** 31.0 min (minor))

showed the ee of the (*R*,*R*)-diol **48** was 58%. ^{1}H NMR (300 MHz) δ 2.48 (br s, 2H, OH), 3.13 (dd, 2H, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$=8.5 Hz, CH*H*), 3.27 (dd, 2H, $^2J_{HH}$=13.3 Hz, $^3J_{HH}$=3.3 Hz, CH*H*), 3.90 (dd, 2H, $^3J_{HH}$=3.0, 7.0 Hz, C*H*OH), 7.41 (t, 2H, $^3J_{HH}$=7.0 Hz, ArH5), 7.46 (d, 2H, $^3J_{HH}$=7.7 Hz, ArH3), 7.57 (t, 2H, $^3J_{HH}$=7.5 Hz, ArH4), 7.94 (d, 2H, $^3J_{HH}$=8.2 Hz, ArH6); ^{13}C NMR (75 MHz) δ 37.3 (CH_2), 74.1 (CHOH), 124.9 (ArC6), 127.8 (ArC5), 133.1 (ArC4), 133.3 (ArC3), 133.4 (ArC2), 149.9 (ArC1); FTIR ν 1513 (w), 1344 (w), 1255 (m), 1077 (w), 1023 (m, br), 797 (m), 660 (s), 673 (s), 626 (s); MS (ES, +ve) *m*/*z* 355 (28, M+Na), 350 (8, M+NH_4), 233 (10), 211 (12), 146 (70), 105 (100%); HRMS (ES, +ve) calcd for $C_{16}H_{16}N_2O_6Na$ 355.0906, found 355.0904.

*4.5.8. (2S,3S)-1,4-Di(2-nitrophenyl)-2,3-butandiol **48**.* The diol (*S*,*S*)-**47** was synthesised by General procedure A using alkene **35** (20 mg, 0.067 mmol, *E*/*Z* 18:1), ADmix α (94 mg), methanesulfonamide (6 mg, 0.067 mmol), sodium sulfite (100 mg) and a 1:1 mixture of ^{t}BuOH and water (0.68 mL). The crude mixture was subjected to flash silica gel column chromatography (20–30% EtOAc: hexanes) to yield the diol (*S*,*S*)-**48** (4 mg, 18%) as a mixture of chiral/*meso* diastereomers (4:1), which was spectroscopically identical to the (*R*,*R*)-**48** enantiomer. HPLC analysis (35% 2-propanol/hexane, retention times (*R*,*R*)-diol **48** 19.4 min (minor), (*S*,*S*)-diol **48** 30.6 min (major)) showed the ee of the (*S*,*S*)-diol **48** was 44%.

*4.5.9. (2S,3S)-1,4-Di(2-methoxyphenyl)-2,3-butandiol **49**.*[19] The diol (*S*,*S*)-**49** was synthesised by General procedure A using alkene **36** (75 mg, 0.28 mmol), ADmix α (392 mg), methanesulfonamide (27 mg, 0.28 mmol), sodium sulfite (420 mg) in a 1:1 mixture of ^{t}BuOH and water (2.8 mL). The crude solid was subjected to flash silica gel column chromatography (10% EtOAc/hexanes to 100% EtOAc) to yield the diol **49** (44 mg, 52%) as a viscous, colourless oil, as a mixture of chiral/*meso* diastereomers (6:1).[19] HPLC analysis (20–40% 2-propanol/hexane, retention times (*R*,*R*)-diol **49** 22.8 min (minor), (*S*,*S*)-diol **49** 26.7 min (major)) showed the ee of the (*S*,*S*)-diol **49** was 34%. ^{1}H NMR (500 MHz) δ 2.66 (br s, 2H, OH), 2.89 (dd, 2H, $^2J_{HH}$=13.2 Hz, $^3J_{HH}$=7.4 Hz, CH*H*), 2.92 (dd, 2H, $^2J_{HH}$=13.2 Hz, $^3J_{HH}$=4.6 Hz, C*H*H), 3.05* (dd, $^2J_{HH}$=13.8 Hz, $^3J_{HH}$=2.1 Hz, CH*H*), 3.72–3.73 (m, 2H, C*H*OH), 3.78 (s, 6H, OCH_3), 3.83*, 6.85 (d, 2H, *J*=8.2 Hz, ArH6), 6.89 (t, 2H, *J*=7.3 Hz, ArH4), 7.16 (d, 2H, *J*=7.3 Hz, ArH3), 7.20 (t, 2H, *J*=8.5 Hz, ArH5); ^{13}C NMR (125 MHz) δ 33.1*, 34.9 (CH_2), 55.3 (OCH_3), 73.4 (CHOH), 74.3*, 110.4 (ArC6), 120.8 (ArC4), 126.9 (ArC2), 127.7 (ArC5), 131.3 (ArC3), 157.4 (ArC1); FTIR ν 1496 (w), 1265 (w), 1245 (w), 1055 (w), 853 (w), 828 (w), 815 (w), 753 (s), 745 (s); MS (ES, +ve) *m*/*z* 325 (50, M+Na), 320 (28, M+NH_4), 303 (100%, M+H), 285 (45, M−H_2O); HRMS (ES, +ve) calcd for $C_{18}H_{23}O_4$ 303.1596, found 303.1595.

*4.5.10. (2R,3R)-1,4-Di(2-methoxyphenyl)-2,3-butandiol **49**.*[19] The diol (*R*,*R*)-**49** was synthesised by General procedure A using alkene **36** (75 mg, 0.28 mmol), ADmix β (392 mg), methanesulfonamide (27 mg, 0.28 mmol), sodium sulfite (420 mg) in a 1:1 mixture of ^{t}BuOH and water (2.8 mL). Flash silica gel column chromatography (10–20% EtOAc/hexanes) yielded the diol (*R*,*R*)-**49** (31 mg, 37%) as a viscous, colourless oil, which had identical spectral properties to the diol (*S*,*S*)-**49**. HPLC analysis (20–40% 2-propanol/hexane, retention times (*R*,*R*)-diol **49** 22.4 min (major), (*S*,*S*)-diol **49** 26.6 min (minor)) showed the ee of the (*R*,*R*)-diol **49** was 40%.

*4.5.11. (2S,3S)-1,4-Di(3-methoxyphenyl)-2,3-butandiol **50**.* The diol (*S*,*S*)-**50** was synthesised by General procedure A using alkene **37** (98 mg, 0.366 mmol, *E*/*Z* 4.3:1), ADmix α (512 mg), methanesulfonamide (35 mg, 0.366 mmol) and sodium sulfite (549 mg) in a 1:1 mixture of ^{t}BuOH and water (3.7 mL). The crude diol was subjected to flash silica gel column chromatography to give (*S*,*S*)-**50** (85 mg, 77%) a white solid, mp 52–54 °C. HPLC analysis (40% 2-propanol/hexane, retention times (*R*,*R*)-diol **50** 13.1 min (minor), (*S*,*S*)-diol **50** 16.1 min (major)) showed the ee of the (*S*,*S*)-diol **50** was 73%. ^{1}H NMR (500 MHz) δ 2.05 (br s, 2H, OH), 2.83 (dd, 2H, $^2J_{HH}$=13.6 Hz, $^3J_{HH}$=8.3 Hz, C*H*H), 2.89 (dd, 2H, $^2J_{HH}$=13.6 Hz, $^3J_{HH}$=4.3 Hz, CH*H*), 3.75–3.82 (m, 2H, C*H*OH), 3.79 (s, 6H, OCH_3), 6.77 (s, 2H, ArH2), 6.79–6.82 (m, 4H, ArH4 and ArH6), 7.23 (t, 2H, *J*=7.8 Hz, ArH5); ^{13}C NMR (125 MHz) δ 40.4 (CH_2), 55.2 (OCH_3), 74.0 (CHOH), 111.9 (ArC6), 115.1 (ArC2), 121.7 (ArC4), 129.6 (ArC5), 139.6 (ArC3), 159.8 (ArC1); FTIR ν 3329 (br), 1611 (w), 1583 (m), 1487 (m), 1454 (w), 1264 (m), 1104 (w), 1043 (s), 930 (w), 763 (w); MS (ES, +ve) *m*/*z* 325 (100%, M+Na), 320 (90, M+NH_4); HRMS (ES, +ve) calcd for $C_{18}H_{22}O_4Na$ 325.1416, found 325.1403.

*4.5.12. (2R,3R)-1,4-Di(3-methoxyphenyl)-2,3-butandiol **50**.* The diol (*R*,*R*)-**50** was synthesised by General procedure A using alkene **37** (98 mg, 0.366 mmol, *E*/*Z* 4.3:1), ADmix α (512 mg), methanesulfonamide (35 mg, 0.366 mmol) and sodium sulfite (549 mg) in a 1:1 mixture of ^{t}BuOH and water (3.7 mL). The diol (*R*,*R*)-**50** (94 mg, 85%) was purified via flash silica gel column chromatography as a white solid, mp 52–56 °C, which had identical spectral properties to the diol (*S*,*S*)-**50**. HPLC analysis (40% 2-propanol/hexane, retention times (*R*,*R*)-diol **50** 12.8 min (major), (*S*,*S*)-diol **50** 16.2 min (minor)) showed the ee of the (*R*,*R*)-diol **50** was 76%.

*4.5.13. (2S,3S)-1,4-Di(4-methoxyphenyl)-2,3-butandiol **51**.*[30] The diol (*S*,*S*)-**51** was synthesised by General procedure A using alkene **38** (200 mg, 0.745 mmol, *E*/*Z* 6.2:1), ADmix α (1.043 g), methanesulfonamide (71 mg, 0.745 mmol) and sodium sulfite (1.113 g) in a 1:1 mixture of ^{t}BuOH and water (7.4 mL). The diol (*S*,*S*)-**50** was recrystallised from CH_2Cl_2/hexanes as a white powder (202 mg, 90%) as a mixture of chiral/*meso* diastereomers (8.8:1), mp 100–102 °C.[30] HPLC analysis (40% isopropanol/hexane, retention times (*R*,*R*)-diol **51** 12.3 min (minor), (*S*,*S*)-diol **51** 13.8 min (major)) showed the ee of the (*S*,*S*)-diol **51** was 85%. ^{1}H NMR (500 MHz) δ 2.01 (br s, 2H, OH), 2.77 (dd, 2H, $^2J_{HH}$=13.8 Hz, $^3J_{HH}$=8.1 Hz, C*H*H), 2.84 (dd, 2H, $^2J_{HH}$=13.8 Hz, $^3J_{HH}$=4.2 Hz, CH*H*), 2.92* (dd, $^2J_{HH}$=13.9 Hz, $^3J_{HH}$=2.6 Hz, C*H*H), 3.67–3.69 (m, 2H, C*H*OH), 3.79 (s, 6H, OCH_3), 6.84 (d, 4H, *J*=8.5 Hz, ArH2), 7.13 (d, 4H, *J*=8.4 Hz, ArH3); ^{13}C NMR (125 MHz) δ 37.4*, 39.4 (CH_2), 55.2 (OCH_3), 74.0 (CHOH), 74.7* (CHOH), 114.0 (ArC2), 114.1*, 130.0 (ArC4), 130.3 (ArC3), 158.3 (ArC1); FTIR ν 3352 (br), 1614 (w), 1512 (s), 1468 (w), 1248 (s), 1178 (m), 1032 (s), 1021 (s), 804 (s); MS (ES, +ve) *m*/*z* 325 (100%, M+Na), 320 (90, M+H); HRMS (ES, +ve) calcd for $C_{18}H_{22}O_4Na$ 325.1416, found 325.1407.

*4.5.14. (2R,3R)-1,4-Di(4-methoxyphenyl)-2,3-butandiol **51**.*[30] The diol (*R*,*R*)-**51** was synthesised by General procedure A using alkene **38** (200 mg, 0.745 mmol, *E*/*Z* 6.2:1), ADmix β (1.043 g), methanesulfonamide (71 mg, 0.745 mmol) and sodium sulfite (1.113 g) in a 1:1 mixture of ^{t}BuOH and water (7.4 mL). The diol (*R*,*R*)-**51** (217 mg, 96%) was recrystallised from CH_2Cl_2/hexanes as a white powder as a mixture of chiral/*meso* diastereomers (9.1:1), mp 104–105 °C, which had identical spectral properties to the (*S*,*S*)-**51** diol. HPLC analysis (40% isopropanol/hexane, retention times (*R*,*R*)-diol **51** 12.0 min (major), (*S*,*S*)-diol **51** 14.1 min (minor)) showed the ee of the (*R*,*R*)-diol **51** was 87%.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.06.035.

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